

# Influence of Supercritical CO<sub>2</sub> on the Polymerization of D,L-Lactide and Glycolide

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Homopolymerizations of D,L-lactide and glycolide have been carried out in bulk and in supercritical conditions in similar experimental conditions taking as base a previously optimized protocol. Polymers have been characterized using gel permeation chromatography (GPC), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA) and infrared spectroscopy (FTIR).

Polyglycolide (PGA) obtained with both methods was crystalline, but the grade of crystallinity was slightly lower in supercritical media than in bulk due to the polymer swelling which facilitates the transesterification reactions that produce a decrease the crystallinity. Both kinds of polymerization showed a high conversion in low reaction time.

Regarding polylactide (PLA), the most important difference found was the lower molecular weight in supercritical carbon dioxide than in bulk polymerization. This is probably due to precipitation polymerization is taking place instead of pseudo-suspension.

## Introduction

The polymerization of D,L-lactide and glycolide in supercritical carbon dioxide shows certain advantages with respect to traditional polymerizations, like kinetic advantages due to the good diffusivity of CO<sub>2</sub>, possibility of in situ purification of residual monomer or catalyst traces or easy polymer processing due to the possibility of swelling and plasticizing of the polymer [1].

Despite that, the kinetic data are scant and the majority of them use tin octoate (SnOct<sub>2</sub>) as catalyst due to its high effectiveness although it presents a certain level of cytotoxicity [2,3]. For this reason, other authors have proposed new compounds [4], like the less toxic zinc octoate (ZnOct<sub>2</sub>) which has been the one used for this work.

In this study, bulk and supercritical homopolymerizations of D,L-lactide and glycolide have been performed, using zinc octoate as catalyst and methanol as initiator to compare the experimental results and consequently propose a possible explanation on the different mechanism followed by the polymerization in each reaction media.

## Materials and methods

The materials used were glycolide (1,4-dioxane-2,5-dione; Purac Biochem bv, The Netherlands) and D,L-lactide (3,6-dimethyl-1,4-dioxane-2,5-dione; Purac Biochem bv,

The Netherlands) both with purity higher than 99.5%. Zinc octoate (zinc (II) 2-ethylhexanoate; Nusa, Spain) with a metal content of 12%. Methanol anhydrous (MeOH) (SDS S.A., Spain) with purity higher than 99.85%. Tetrahydrofuran (THF) (HPLC grade, SDS S.A., Spain). And carbon dioxide (Carbueros Metálicos, S.A., Spain) with a purity of 99.8%.

Experiments in supercritical media were carried out in the lab-scale unit described in a previous paper [5]. The procedure followed was: the amounts of monomers, catalyst and initiator were directly charged in the reactor at room temperature. The recipe followed was: 5 g of monomer; the molar ratio of monomer to catalyst (M/C) was 100; the molar ratio of initiator to catalyst (I/C) was 0.5; and the temperature set point was fixed at 160 °C. Reactor was sealed and filled with 100 g of CO<sub>2</sub>. Stirring (1000 rpm) and heating started. Zero time was considered when temperature was 80 °C. Then, the reaction was run for reaction time fixed to each experiment. To quench the reaction, reactor was cooled near to room temperature and later reactor was depressurized, opening it and taking samples for characterization. Bulk reactions were carried out in a stirred-tank reactor with nitrogen atmosphere, constant stirring rate of 100 rpm and controlled temperature. Firstly, 100 g of monomer was added and heated until 160°C. After complete thermal equilibration, the same molar ratios M/C and I/C as in supercritical conditions were injected into the reactor. The duration of the reaction experiments was 180 minutes.

The molecular weight distribution of polymers and mass conversion for the polymerization of D,L-lactide were determined by gel permeation chromatography (GPC) using THF as mobile phase [5]. Infrared analysis using Fourier transform infrared spectrometer (FTIR 16 PC, Perkin Elmer, Spain) was used to characterize the samples mainly for polymerization of glycolide (like the described in a previous paper) [5]. In order to determine the conversion, the thermogravimetric analysis was used. A TGA (TA Instruments, Q600) with a refrigerated cooling system and purged with nitrogen gas. A DSC (TA Instruments Q1000) equipped with a refrigerated cooling system and autosampler was used for the measurement of the enthalpy of fusion, glass transition temperature and percent of crystallinity. The sample (4-10 mg) was heated until 250 °C followed by a cooling until -50 °C and, finally, was heated until 250 °C again. Heating and cooling were carried out with a heating rate of 10 °C min<sup>-1</sup>.

## Results

Homopolymerizations of D,L-lactide and glycolide have been carried out in bulk and in supercritical carbon dioxide to contrast the same process in different media. FTIR of both bulk and supercritical polymers were identical. A summary of the results of glycolide polymerization in bulk and supercritical CO<sub>2</sub> are shown in Table 1. The values of T<sub>g</sub> at lowest times in bulk are anomalous and are not given. Probably the presence of non-reacted monomers in the samples at low reaction times is the reason of these values without tendency. It was not possible to measure molecular weight for PGA due to its insolubility in THF (mobile phase of GPC apparatus).

**Table 1.** Results for homopolymerizations of glycolide in supercritical CO<sub>2</sub> and in bulk. Common reaction conditions: Catalyst: ZnOct<sub>2</sub>, Initiator: MeOH, M/C: 100, I/C: 0.5, T: 160°C. Particular conditions in supercritical media: CO<sub>2</sub>/M: 20, N: 1000 rpm, m<sub>CO<sub>2</sub></sub>: 100 g. Particular conditions in bulk media: N: 100 rpm.

scCO <sub>2</sub>					
t (min)	X <sub>TGA</sub> (%)	T <sub>g</sub> (°C)	ΔH <sub>f</sub> (J/g)	Melting range (°C)	X <sub>c</sub> (%)
10	84.3	40.47	57.2	174.39-178.61	27.7
15	85.7	36.58	50.91	166.15-172.33	24.6
20	87	10.05	41.41	182.99-188.34	20
30	85.9	1.5	57.16	161.24-170.61	27.7
40	85.1	-17.9	44.99	133.15-151.39	21.8
Bulk					
t (min)	X <sub>TGA</sub> (%)	T <sub>g</sub> (°C)	ΔH <sub>f</sub> (J/g)	Melting range (°C)	X <sub>c</sub> (%)
1.5	89.36	-	-	-	-
3	88.13	-	-	-	-
4.5	90.5	21.73	118.3	186.39 - 206.41	57.3
6	96.6	39.36	108.9	204.38 - 218.60	52.7

As can be seen in Table 1 very high conversions were achieved in relatively low reaction times due to the elevated reactivity of glycolide [6]. Comparing the obtained results at 10 minutes in supercritical polymerization and the ones at 6 minutes, it seems that the reaction was much faster in bulk. In fact, in the sixth minute the polymer was so viscous that the stirring became impossible and the reaction had to be stopped.

In supercritical media, T<sub>g</sub> decreases with the reaction time. Since T<sub>g</sub> depends directly on the molecular weight, it seems that molecular weight increased for the bulk polymerization as it was expected, but it decreased for the polymerization in scCO<sub>2</sub>. Such decrease could be imputed to some degradation reaction because of the long reaction times. Such decrease could be imputed to some degradation reaction between CO<sub>2</sub> and the polymer chains.

The enthalpy of fusion is directly related with crystallinity. The percentage of crystallinity was calculated using the equation (1):

$$X_c = \frac{\Delta H_f}{\Delta H_{c_{PGA}}} \quad (1)$$

where ΔH<sub>c<sub>PGA</sub></sub> is the melting enthalpy of a pure crystal of polyglycolide with 206,6 J/g [7].

The values of crystallinity in bulk are almost the same that others previously reported in literature [8], but in the case of supercritical reactions they are considerably lower. This fact can be due to transesterification reactions in supercritical CO<sub>2</sub> which decrease the packing, since crystallinity is a measure of the packing grade of the polymer chains. The production of cyclic chains and the presence of supercritical CO<sub>2</sub> that favours a constant movement of chains readjusting continuously the molecular weight prevent the packing and reduce the crystallinity [9].

For supercritical and bulk D,L-lactide polymerizations the main results: mass conversion by TGA and GPC, number average molecular weight (M<sub>n</sub>), polydispersity index (PD) and glass transition temperature, are summarized in Table 2.

**Table 2.** Results for both homopolymerizations of D,L-lactide. Common conditions: Catalyst: ZnOct<sub>2</sub>, Initiator: MeOH, M/C: 100, I/C: 0.5, T: 160°C. Conditions only for supercritical media: CO<sub>2</sub>/M: 20, N: 1000 rpm, m<sub>CO<sub>2</sub></sub>: 100 g. Conditions only for bulk media: N: 100 rpm.

scCO <sub>2</sub>								
t (min)	X <sub>TGA</sub> (%)	Mn <sup>a</sup> (g/mol)	PD	Mn <sup>b</sup> (g/mol)	Mn <sup>c</sup> <sub>theoretical</sub> (g/mol)	Tg <sub>DSC</sub> (°C)	Tg <sup>d</sup> <sub>theoretical</sub> (°C)	
30	85.6	580	1.123	427	12391	5.99	-113.89	
60	87.9	682	1.238	496	12725	-6.61	-90.25	
90	88.3	753	1.29	549	12783	4.08	-76.05	
120	87	671	1.22	487	12594	-14.93	-92.74	
Bulk								
t (min)	X <sub>TGA</sub> (%)	X <sub>GPC</sub> (%)	Mn <sup>a</sup> (g/mol)	PD	Mn <sup>b</sup> (g/mol)	Mn <sup>c</sup> <sub>theoretical</sub> (g/mol)	Tg <sub>DSC</sub> (°C)	Tg <sup>d</sup> <sub>theoretical</sub> (°C)
5	50.9	0.01	1868	9.07	1364	-	1.95	3.5
15	58	30.7	2022	1.62	1511	4428	19.06	8.7
30	64.2	38.5	2984	2.13	2281	5540	25	25
60	74	68.2	5066	2.58	3997	9815	37.83	38.73
120	94.8	90.9	5231	3.99	4220	13088	29.28	39.7
180	95.6	97.9	5129	4.24	4233	14100	38.31	39.75

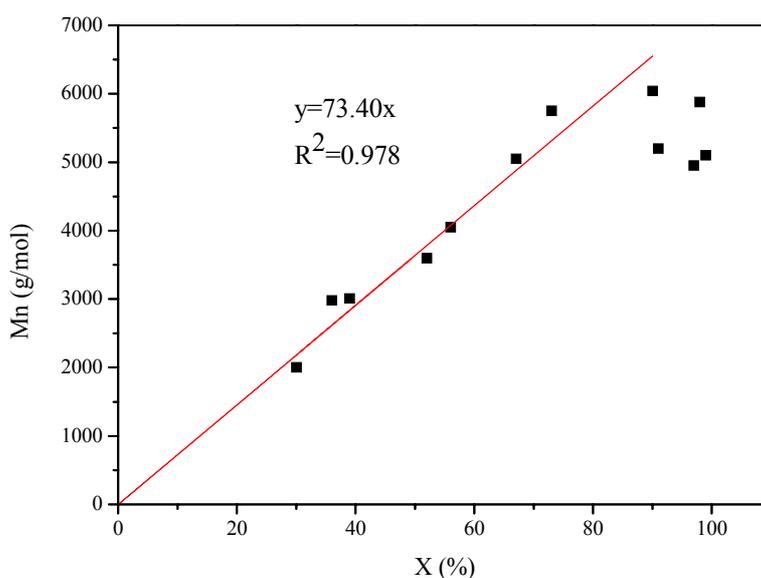
<sup>a</sup>: Number average molecular weight obtained directly from the calibration with polystyrene by GPC.

<sup>b</sup>: Absolute number average molecular weight obtained using Mark-Houwink equation and its constants for both polymers [10].

<sup>c</sup>: Theoretical Mn calculated by  $Mn = (M/C) \times M_{MW} \times \text{Conversion} (\%) / 100$ , where M is the monomer molar quantity; C, the catalyst molar quantity times two; and M<sub>MW</sub>, the molecular weight of monomer.

<sup>d</sup>: Theoretical Tg calculated by equation (2).

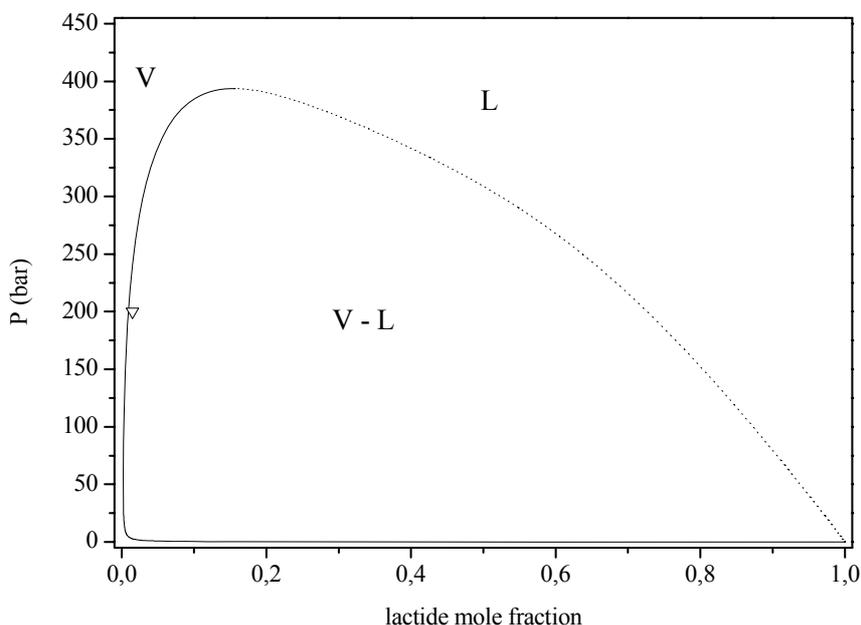
The conversion of D,L-lactide in both cases is lower than the glycolide, due to the lower reactivity of the D,L-lactide with respect to that monomer. In bulk conversion values were lower than in supercritical media so the reaction was faster in supercritical CO<sub>2</sub>.



**Figure 1.** Mn vs X graph. Bulk homopolymerization of D,L-lactide. Catalyst: ZnOct<sub>2</sub>, Initiator: MeOH, M/C: 100, I/C: 0.5, CO<sub>2</sub>/M: 20, N: 1000 rpm, T: 160°C.

Also in the case of D,L-lactide polymerization, the presence of non-reacted monomers in the samples at low reaction times is the reason of the anomalous values of thermogravimetric conversion, so that conversion was also calculated using GPC chromatograms. Although there are differences at short reaction times it has been checked that TGA is an appropriate technique for higher conversions.

About molecular weight, the most outstanding result is that the absolute number average molecular weight and the theoretical one have not correspondence, overall in the supercritical polymerization. According to the Figure 1, there is a linear relationship between number molecular weight and conversion until values of 90% where the growth of the polymer chain ends and even it is possible that some degradation happens.



**Figure 2.** Isothermal liquid-vapour (L-V) prediction of the equilibria for the system lactide + carbon dioxide with the Peng-Robinson EOS by GPEC [11]. Point represents experimental conditions for supercritical homopolymerization of D,L-lactide.

Up to now it has been generally accepted that homopolymerization of D,L-lactide in carbon dioxide follows an emulsion or suspension polymerization pathway [12,13]. Recently some data on the solubility of lactide in scCO<sub>2</sub> have appeared [14]. These experimental data have been correlated using the software GPEC [11] to obtain the equilibrium chart of lactide in scCO<sub>2</sub> shown in Figure 2. As it can be seen in our experimental conditions (represented by an inverted triangle) all the monomer is initially dissolved and a precipitation polymerization is taking place. In this case the molecular weight achieved may be the maximum Mw of PLA soluble in CO<sub>2</sub>. On the other hand, for the bulk polymerization, the absolute molecular weight increases proportionally with conversion as it is expected for a pseudo-living polymerization like the ring opening of lactide. However, the absolute Mn is lower than theoretical one, probably because there are some additional interchange reactions which can regenerate the alkoxide or the catalyst starting new growing chains [15].

This is also observed for samples with lower molecular weight obtained in the bulk polymerization. However, the agreement between T<sub>g</sub> theoretical and experimental is quite good for samples with high molecular weight.

## Conclusions

The rate of glycolide polymerization is slower in bulk than in supercritical media due to the lower percent of crystallinity of PGA obtained by supercritical polymerization. So the crystallinity depends on the polymerization media. The production of cyclic chains and the presence of scCO<sub>2</sub> that favours a constant movement of chains readjusting continuously the molecular weight prevent the packing and reduce the crystallinity. However, conversions achieved are not so different between the both methods.

In the homopolymerization of D,L-lactide exists more discrepancy than in glycolide due to the lower values of conversion in bulk as a consequence of the low reactivity of the D,L-lactide. In supercritical media, precipitation polymerization can be happening and the molecular weight obtained is the maximum molecular weight of PLA soluble in scCO<sub>2</sub>.

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