Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

Molecular weight-based fractionation of poly-l- and poly-d,l-lactic acid polymers via a simple inclusion compound based process

Douglas G. Hayes[a]; Anne-Lee Asplund[b]; James M. Van Alstine[c]; Xun Zhang[d]
[a] Department of Chemical and Materials Engineering, University of Alabama in Huntsville, Huntsville, AL, U.S.A. [b] Department of Chemical Engineering and Technology, Royal Institute for Technology, Stockholm, Sweden [c] Amersham Pharmacia Biotech, Uppsala, Sweden [d] DuPont Photomasks, Inc., Danbury, CT, U.S.A.

To cite this Article Hayes, Douglas G. , Asplund, Anne-Lee , Van Alstine, James M. and Zhang, Xun(2002) 'Molecular weight-based fractionation of poly-l- and poly-d,l-lactic acid polymers via a simple inclusion compound based process', Separation Science and Technology, 37: 4, 769 — 782

To link to this Article: DOI: 10.1081/SS-120002216

URL: http://dx.doi.org/10.1081/SS-120002216

SEPARATION SCIENCE AND TECHNOLOGY, 37(4), 769–782 (2002)

MOLECULAR WEIGHT-BASED FRACTIONATION OF POLY-L- AND POLY-D,L-LACTIC ACID POLYMERS VIA A SIMPLE INCLUSION COMPOUND BASED PROCESS

Douglas G. Hayes,[1,*] Anne-Lee Asplund,[2]
James M. Van Alstine,[2,†] and Xun Zhang[1,#]

[1]Department of Chemical and Materials Engineering,
University of Alabama in Huntsville, 130 Engineering
Building, Huntsville, AL 35899
[2]Department of Chemical Engineering and Technology,
Royal Institute for Technology, Teknikringen 28,
SE-100 44 Stockholm, Sweden

ABSTRACT

Urea inclusion compound (UIC) formation was used to fractionate carbohydrate polymers, poly-L- and poly-DL-lactic acid, by molecular weight. The UIC fractionation process employed was rapid, simple, scalable, and may have potential for use in preparative- and large-scale purification of polymers. Differential scanning calorimetry measurements reflect the formation of UICs for both polymer types. Under the conditions employed, the resultant UIC-rich solid phase contained polylactic acids of

---

[*] Corresponding author. Fax: (256) 824-6839; E-mail: dhayes@che.uah.edu
[†] Current address: Amersham Pharmacia Biotech, Björkgatan 30, 75184 Uppsala, Sweden.
[#] Current address: DuPont Photomasks, Inc., 4 Finance Drive, Danbury, CT 06810.

molecular weight distribution similar to the process feed sample, whereas the solvent-rich phase contained polymer of significantly lower molecular weight. The difference in molecular weight increased with the average molecular weight of the polymer and the degree of incorporation of polymer in the solid phase, and was greater for poly-D,L- than poly-L-lactic acid. The distribution of urea between the solid and the solvent-rich phases was independent of the molecular weight of the polymer or stereochemistry for a given polymer–urea–solvent ratio in the mixture.

Key Words: Extraction; Polymer fractionation; Poly(lactic acid) fractionation; Urea inclusion compounds

INTRODUCTION

Few methods are available to separate or fractionate polymers on a large scale. Most separations are performed using chromatography, which can be technically challenging and costly to scale up. Novel technologies must be developed, particularly technically simple methods that involve recyclable reagents. Inclusion compound formation is potentially useful to fractionate polymers on the basis of molecular weight, degree of branching, stereochemistry, and other structural differences. The basis for this is the ability or inability of molecules to be retained within the narrow channels, formed by inclusion compound forming substances. Polymers have been demonstrated to form inclusion compounds with urea and its homologues (1), as well as with cyclodextrins (2,3), coordination compounds (4), and cyclotriphosphazene derivatives (5,6).

Urea inclusion compounds or UICs consist of spiral hydrogen-bonded networks of urea that form in the presence of narrow, linear "guest" molecules such as hydrocarbons. Such guests become incorporated into the narrow (0.55–0.58 nm diameter) channels in the urea helices [reviewed in Ref. (1)]. Molecules that are branched, polyunsaturated, and bulky (particularly in the middle of a molecular chain) are much less likely to serve as UIC guests. The UICs have been applied extensively to fractionate alkanes and fatty acids (1,7). The study of inclusion compound formation with polymer guests is relatively new. Only a few of the recent studies have focused on polymer fractionation. These involved the UIC-based fractionation of linear polymers such as poly(tetrahydrofuran) and poly(ethylene adipate) (8–10), as well as poly(ethylene glycol), or PEG (3) by molecular weight. In addition, molecular weight-based fractionation of PEG using cyclodextrins (3), and separation of polymer mixtures by molecular weight, degree of branching, and end group structure using cyclotriphosphazene derivatives (5,6) has been observed.

Most investigators have formed UICs by the slow cooling of a homogeneous mixture of urea, UIC guest molecules, and nonUIC-forming solvent. The authors reported recently that the formation of UICs by rapid cooling was quite effective for fatty acid fractionation (11–13). One of the products, the UIC guests, was released from UICs by the addition of warm water, which removed urea from the solid phase. A similar process was used to remove urea and solvent from the remaining solvent-rich phase, leaving behind the second product, the nonUIC-forming feed material. Combining the UIC formation and dissolution steps yielded a rapid, efficient, and scalable separation process, readily modeled on the basis of mass balances and phase equilibria (13).

The goal of the present study is to demonstrate that a similar process could be applied to fractionate polymers on the basis of molecular weight and stereochemical structure. Polylactic acids (PLAs) were used as they represent a commercially and biomedically important class of carbohydrate polymers of varying molecular weight and stereochemistry. Poly-L-lactic acid (PLLA) is known to form UICs (14,15), whereas poly-D,L-lactic acid (PDLLA), which consists of randomly distributed L- and D-lactic acid monomeric units, has a larger extended chain conformational cross-section and was speculated to be less satisfactory as a UIC guest (16). Results shared here demonstrate that the UIC formation fractionated both PLLA and PDLLA samples by molecular weight successfully. This finding may be significant in regard to the preparation of PLAs of defined molecular weight for various applications.

EXPERIMENTAL

PLA samples of varying molecular weight values (Table 1) were obtained from Birmingham Polymers, Inc. (Birmingham, AL) and PURAC (Gorinchem, Netherlands). All other reagents and solvents were of high purity and were used without further purification. Deionized water was employed throughout the process.

Prior to UIC formation, a homogeneous solution was created by adding a PLA/methylene chloride mixture at 35°C drop-wise to urea/methanol at 40°C. Then, the mixture was cooled rapidly to 22°C by applying cold running water to the outside of the vessel. This resulted in the formation of two phases, a solvent-rich liquid phase and a solid phase containing UICs. The two phases were separated via filtration. In order to facilitate separation of polymer and urea, the solid phase was broken into a fine powder mechanically, then treated with warm (60°C) water and methylene chloride. Urea partitioned to the aqueous phase,

Table 1. Summary of Results: Urea Inclusion Compound (UIC)-Based Fractionation of Polylactic Acid (PLA)

Polymer Type	M_n	M_w/M_n	R^s_{PLA}	SEP[a]
PLLA[b]	24,000	1.3	75.8[d]	55.0 ± 36.8
PLLA[b]	104,000	1.7	97.5 ± 4.9[e]	<5
PLLA[b]	303,000	1.9	95.2 ± 5.7[e]	32.4 ± 22.3
PLLA[c]	599,000	2.1	98.0 ± 4.6[e]	<5
PLLA[c]	1,400,000	2.2	98.9 ± 3.3[e]	54.0 ± 54.4
PDLLA[b]	36,100	1.3	3.7 ± 4.6	<5
PDLLA[b]	81,500	1.7	60.7[d]	41.0 ± 19.8
PDLLA[b]	159,000	1.9	81.4[d]	61.0 ± 31.1
PDLLA[c]	620,000	2.2	67.1 ± 29.7[e]	62.0 ± 31.1
PDLLA[c]	936,000	2.1	90.4 ± 10.2[e]	62.9 ± 20.6

Row and column headings: PLLA = poly(L-lactic acid), PDLLA = poly(D,L-lactic acid); M_n = number-averaged molecular weight of original PLA sample, M_w/M_n = ratio of weight-averaged to number-averaged molecular weight, or polydispersity index, for original PLA sample, R^s_{PLA} = percent recovery of PLA in the solid phase, SEP = polymer separation factor, defined in Eq. (1).

All runs employed the PLA/urea/solvent system, with methylene chloride/methanol 1:1 serving as solvent system, with a constant urea/PLA ratio of 3:1 g/g, and urea mass fraction values for the entire mixture of either 0.044 or 0.065.

[a] All data based only on run(s) yielding highest values, and multiple analyses using both the low- and high-molecular weight GPC columns.

[b] From Birmingham Polymers, Inc. (Birmingham, AL).

[c] From PURAC (Gorinchem, Netherlands).

[d] Based on a single run.

[e] Based on average of all runs that yielded above 50% incorporation of polymer.

while PLA resided in the organic layer. The PLA was then recovered from the isolated methylene chloride solution by evaporating away the solvent. After removing the solvent (methanol and methylene chloride), PLA was isolated from urea in the liquid-phase extraction product by the same procedure employed to isolate PLA from the solid phase. The distribution of PLA between the solid and solvent-rich (filtrate) phase was determined gravimetrically. In all cases, the total mass recovery of PLA was over 85% and in most cases over 90%. The distribution of urea was determined through mass balances that employed the measured weights of the solid phase, the solvent-rich phase after evaporation of solvent, and the mass of polymer recovered from each phase.

The formation of UICs was verified by monitoring thermal transitions via differential scanning calorimetry (DSC) on a Model DSC 30 instrument from

Mettler-Toledo (Columbus, OH). The apparatus included a purge stream of dessicated N_2. Prior to analysis, samples were air-dried for several days until the sample's mass reached a constant value. The samples were placed in 40 μL crucibles, then subjected to two successive heating cycles (from 30 to 250°C at 10°C/min, followed by -200°C/min until 30°C was achieved). Thermograms were referenced with respect to an empty crucible undergoing the same temperature program. Fourier transform infrared spectroscopy (FTIR) analysis was also employed to verify UIC formation, using a model FTS 60A instrument from Bio-Rad (Hercules, CA) between the frequencies of 1000 and 4000 cm^{-1} with a resolution of 1 cm^{-1}. Samples consisted of compact thin films of UICs mixed with KBr.

Gel permeation chromatography (GPC) was employed with an high pressure liquid chromatography (HPLC) system containing an evaporative light scattering detector to determine the number-averaged molecular weight (M_n), the weight-averaged molecular weight (M_w), hence, the polydispersity index (M_w/M_n) for PLA samples. A "PL gel Mixed C" 300 mm × 7.5 mm column from Polymer Laboratories (Amherst, MA) was employed for most analyses, with a "Styragel HR-4E" 300 mm × 7.8 mm column from Waters (Milford, MA) employed to verify separations for low-molecular weight ($< 500,000$) samples. Both columns employed methylene chloride as mobile phase at a flow rate of 1.0 mL/min and were calibrated using polystyrene molecular weight standards.

RESULTS AND DISCUSSION

Differential Scanning Calorimetry and Fourier Transform Infrared Spectroscopic Analysis

Differential scanning calorimetry analysis provided strong evidence for the formation of UICs. According to previous reports (2,3,5,6,8–10,15,17–21), the occurrence of UICs is reflected by two changes in the thermogram generated by DSC: the thermogram peak for urea (~ 134°C) is shifted to higher temperatures; and, the peak attributed to free guest molecules disappears upon inclusion in the urea channel. Solid-phase products generated from the rapid cooling process described above produced thermogram peaks at 137.0 and 136.7°C for PLLA and PDLLA, respectively, indicating the formation of UICs for both cases (Fig. 1). For PLLA-UICs, the position of the main urea peak at 137°C, with a shoulder at 131.6°C is in strong agreement with a previous report for the same inclusion compound (15). The shoulder is reported to represent the occurrence of free (noncomplexed) urea (15). A physical mixture of urea and PLLA resulted in a thermogram peak centered at 133.9°C (Fig. 1), in strong agreement with the peak position of a PDLLA/urea physical mixture (not shown) and the position

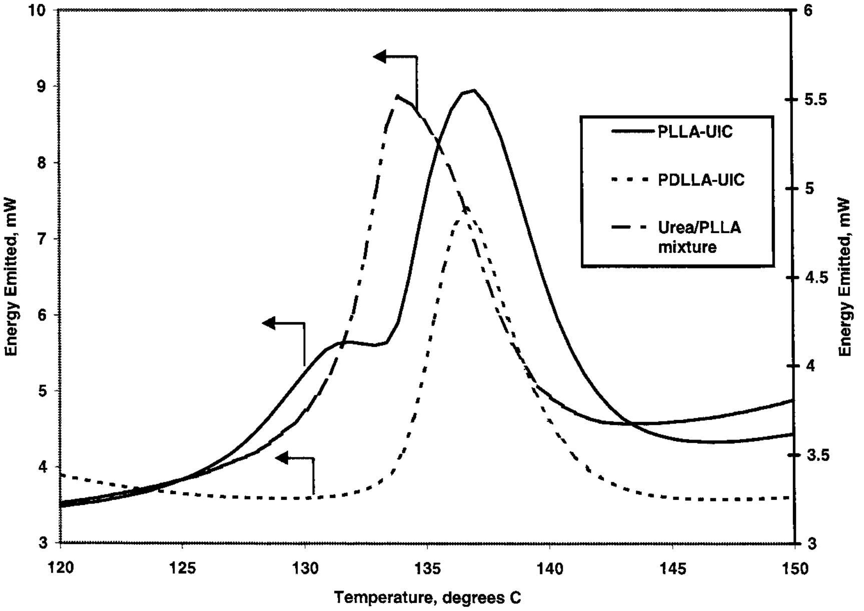

Figure 1. Thermograms of PLLA-UICs, PDLLA-UICs, and a physical mixture of urea and PLLA, obtained from DSC.

reported for free urea (15). The occurrence of an irreversible degradation process for urea at ~165°C prevented the evaluation of the polymer thermogram peaks (or absence thereof) to determine the latter's inclusion into urea channels, since PLLA produced a peak at 180°C, and PDLLA melted at a temperature above 250°C (15). The absence of a shoulder for the PDLLA-UIC thermogram suggests the absence of free urea.

The occurrence of UICs was further supported by FTIR spectroscopy. Tonelli and co-workers demonstrated that the UICs containing polymer hosts yield spectra with shifted positions for urea's bands in the 1400–1700 cm^{-1} region relative to pure urea (2,3,13,15,17,19–22). The direction of the shifting is frequently to lower wavenumbers, indicative of an increase in hydrogen bonding activity. Pure urea possesses bands at 1468 cm^{-1} (N–C–N stretch), 1614 and 1638 cm^{-1} (N–H bending), and 1686 cm^{-1} (carbonyl stretching) (Fig. 2). The solid-phase materials resulting from fractionation of PLLA and PDLLA possessed shifted values relative to pure urea, with N–C–N and carbonyl stretching band positions residing at 1461 and 1669 cm^{-1} for PLLA-derived fractionation and 1465 and 1670 cm^{-1} for PDLLA-derived fractionation (Fig. 2). Although the shift of these two peaks supports the formation of UICs, the peak positions and widths

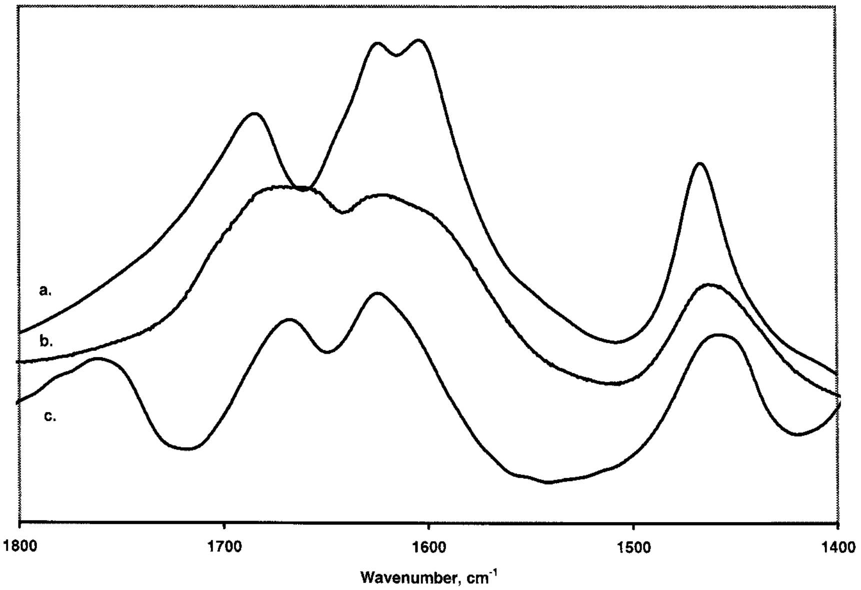

Figure 2. Fourier transform infrared spectra between 1400 and 1800 cm^{-1} of urea (a) and solid-phase materials resulting from fractionation of PDLLA (b), and PLLA (c). Spectra a and c were smoothed in order to enhance appearance. Data smoothing did not alter band position or shape appreciably. The ordinate represents arbitrary absorbance units.

differ slightly from that reported for PLLA-UICs and for other hexagonal crystalline UICs (15). For instance, the occurrence of two distinct bands is reported for the carbonyl stretch of free urea and urea within UICs (20), whereas a broad band occurred for us (Fig. 2). In addition, two distinct N–C–N stretching bands are reported for free urea and urea within UICs at 1467 and 1491 cm^{-1} (20). In contrast, a broad band, centered at a position of lower wavenumbers (1461–1465 cm^{-1}), was obtained by us (Fig. 2). This may suggest that the UICs formed during our experiments possess a UIC structure that is nonhexagonal. [Most UICs, e.g., containing hydrocarbons, fatty acids, and linear polymers such as PLLA as guests, form needle-like hexagonal crystalline structures, with the channels oriented lengthwise, in contrast with the tetragonal crystalline structure of free urea (1,15).] The broad band at 1763 cm^{-1} for PLLA-UICs in Fig. 2 represents the carbonyl stretching of the polymer. The absence of a carbonyl stretching peak for PDLLA-UICs is an interesting result that cannot yet be explained.

To support further, the presence of broad bands and of N–C–N stretching band shifted to lower wavenumbers is consistent with UICs of low molecular weight PEG and of polypropylene, both reported to have nonhexagonal, "expanded tetragonal" UIC structure (20,22). Both these guests have too large an extended chain conformational cross-section to serve as UIC guests. While PLLA-UICs have been reported (14,15) this is, to the authors' knowledge, the first report of PDLLA-containing UICs. On the basis of molecular modeling studies, Tonelli (16) estimated that the channel inner diameter for a hexagonal UIC would have to be about 0.75 nm to accommodate PDLLA, which is well above the 0.55–0.58 nm range reported. Perhaps the formation of "expanded tetragonal" UICs will allow accommodation of PLLA within the channels. A more detailed analysis of the structure of PDDLA- and PLLA-UICs is ongoing.

Evaluation of UIC Fractionation Process

The process employed was simple, rapid, inexpensive, and effective for fractionating different PLLA and PDLLA samples by molecular weight (Table 1). However, for some fractionations employing the lowest molecular weight PLLA samples, and for several separations of PDLLA (particularly those of low molecular weight) (Table 1) the recovery of PLA in the solid phase, R^{s}_{PLA}, was low; and, the degree of separation by molecular weight was insignificant. It is not clear whether UICs formed during these runs, or if the solid phase consisted of a co-precipitant of polymer and tetragonal urea crystals. Such runs were therefore not analyzed further.

For many experiments, the variance for the R^{s}_{PLA}, values were quite high, in contrast to UIC-based fractionation of free fatty acids (11). This might be expected due to the larger molecular weight of the guest molecules. Thus, in addition to sample heterogeneity, one source of variance may be the lack of careful temperature control during UIC formation by cooling. In keeping with this, Schmidt et al. (8) reported that formation of polymer-containing UICs can occur slowly over a 10-hr period at a constant temperature.

Distribution of Urea

For a given urea–polymer–solvent ratio, the distribution of urea between the solid and liquid phase was independent of the PLA molecular weight and stereochemistry (Table 2). The chemical potential of urea in the solvent-rich phase is not expected to change significantly with PLA molecular weight or stereochemistry, since PLA consists of only a very small fraction of this phase ($< 0.015\,\mathrm{g/g}$). Assuming the two phases resulting from UIC-based fractionation are at equilibrium, the chemical potential of urea in the solid phase must also be independent of the PLA inclusion guest properties. This is in keeping with UIC

Table 2. Distribution of Urea During Urea Complex-Based Fractionation of Polylactic Acid (PLA)

	R^{s}_{U}	
Polymer Type	$X^{m}_{U} = 0.044$	$X^{m}_{U} = 0.065$
PLLA	40.5 ± 8.8	57.7 ± 10.6
PDLLA	35.3 ± 6.1	57.1 ± 12.8

Listed are the averages for all runs that employed the PLA/urea/solvent system, with methylene chloride/methanol 1:1 serving as solvent system, with a constant urea/PLA ratio of 3:1 g/g, either $X^{m}_{U} = 0.044$ or 0.065, and employing PLAs of several different molecular weight values, and averaging results from runs that yielded a wide range of R^{s}_{PLA}.
Row and column headings: PLLA = poly(L-lactic acid), PDLLA = poly(D,L-lactic acid), R^{s}_{U} is the percent recovery of urea in the solid phase, and X^{m}_{U} is the mass fraction of urea in the mixture.

structure to be relatively independent of the inclusion guest. In agreement with other UIC fractionations (11), the percent recovery of urea in the solid phase, R^{s}_{urea}, decreased with an increase in solvent (at constant urea/polymer ratio) (Table 2).

In UIC-based fatty acid fractionation (11–13), the distribution of urea between the phases was strongly interrelated to the distribution of guest fatty acid types, the latter determined by the degree of unsaturation. In contrast, in the present PLA fractionation studies, the phase distribution of urea was independent of PLA distribution (Table 2). This contradiction may be related to the composition of the solid phase. Most alkyl chain-containing molecules such as free fatty acids yield a solid phase consisting of almost entirely UICs (1). In contrast, other researchers have suggested that 20–35% of solid phase urea molecules exist as “free” urea when PLLA- and other polymer-containing UICs are formed (15,17,20,21). The DSC results support the occurrence of free urea, particularly for PLLA-UICs (discussed above).

On the basis of x-ray diffraction and FTIR spectroscopic analysis, solid phase urea/polymer monomer unit mole ratios between 1 and 4 have been reported for polymer-containing UICs (8,10,18,19,22). In the present study, runs achieving a PLA recovery (R^{s}_{PLA}) over 50% yielded mole ratio values of 1.59 ± 0.40 for PLLA and 1.70 ± 0.51 for PDLLA. (Solid-phase mole ratios of 20 or higher resulted from experiments yielding R^{s}_{PLA} values of 15% or less.) For hexagonal UICs, each urea molecule comprises approximately 0.183 nm of the channel length, based on x-ray crystallography (18,23). When one divides the molecular length of a PLA monomeric unit (0.349 nm) by 0.183 nm, an estimate of the urea–monomeric unit ratio is obtained: 1.91. Since the calculated ratios for both PLLA and PDLLA are smaller than 1.91 (and since a significant portion of the solid-phase urea molecules do not participate in UIC formation for PLLA, according to the DSC results), the solid phase must also contain free (uncomplex) polymer. In designing a process for UIC-based polymer fractionation, one must choose between rapid cooling, which probably yields less UICs hence a lower separation efficiency, and a slower cooling process, which would be more efficient, but will reduce the overall process' productivity.

Molecular Weight-Based Fractionation of Polylactic Acid

The present UIC-based method was very successful in fractionating PLA by molecular weight. Under the conditions employed, the greatest difference in molecular weight, relative to the PLA feed, occurred for PLA recovered from the solvent-rich phase. For most fractionations, M_n of PLA recovered from the solid phase nearly equaled the feed M_n while the solvent phase M_n decreased as R^{s}_{PLA} increased (Fig. 3). In general, the polydispersity of the fractionated PLA samples recovered from either phase was nearly identical with that of the original feed polymer sample (data not shown).

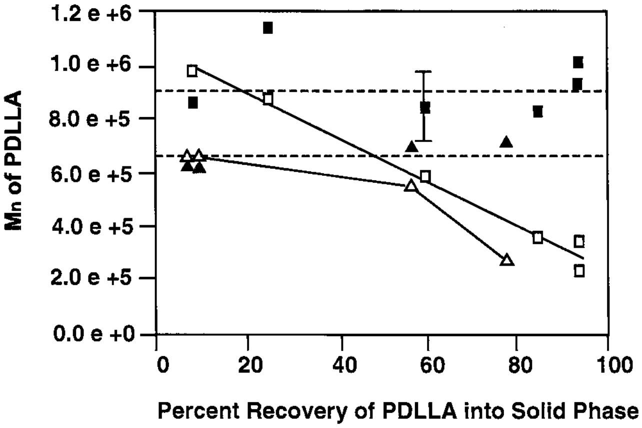

Figure 3. Effect of M_n values for PDLLA in the solvent-rich (open symbols) and solid (filled symbols) phase as a function of the percent incorporation of PDLLA into the solid phase. M_n of original PLLA = (square) 936,000 and (triangle) 620,000, as indicated by horizontal dashed lines drawn in figure. All runs employed the same initial media: $X^{m}_{U} = 0.044$, $X^{m}_{PLA} = 0.015$, $X^{m}_{S} = 0.941$, where the solvent consisted of methylene chloride/methanol, 1:1 v/v.

The degree of separation by polymer molecular weight and stereochemistry was evaluated by calculation of a separation factor, "SEP", defined as:

$$\text{SEP} = 100 \times [M_n \text{ of Solid Phase} - M_n \text{ of Liquid Phase}]/M_n \text{ of Feed} \quad (1)$$

The greatest degrees of separation (i.e., the largest SEP values) were obtained generally with higher molecular weight polymer samples and for PDLLA relative to PLLA. This trend is consistent with the increase of $R^{\mathrm{s}}_{\mathrm{PLA}}$ with PLA molecular weight (Table 1), which would yield a lower M_n value for PLA recovered from the liquid phase relative to the feed (Fig. 1), i.e., a greater value of SEP. In addition, the original polymer samples were more polydisperse as molecular weight increased (Table 1), which would permit higher values of SEP to occur. The fact that such results could be obtained with commercial PLA samples suggests that the process studied may be used to improve existing large-scale PLA fractionation technology. The original PLLA sample of mean molecular weight 599,000 was an exception, achieving a high value of $R^{\mathrm{s}}_{\mathrm{PLA}}$, but a low degree of molecular weight-based fractionation (Table 1). Reasons for this discrepancy are not known.

CONCLUSIONS

Unlike typical UIC-based fractionation processes, the simple process studied allowed for simple rapid cooling of a urea and polymer containing solution, and should be scalable readily, as well as adaptable for reagent recycling. It appears to fractionate both PLLA and PDLLA by molecular weight; the degree of fractionation increasing with sample molecular weight. The UIC-based polymer fractionation mimics but is not completely analogous to UIC-based fractionation of lower molecular weight substances. It may be a viable means of (primary) polymer purification in preparative- and large-scale processes, and its application to the fractionation of other polymers or mixtures of interest is suggested. Perhaps urea analogues that form wider inclusion channels such as thiourea or other inclusion compounds may be useful for fractionation of polymers with larger extended chain conformational cross-section, to expand the utility of the separation method.

NOMENCLATURE

M_{n}	number-averaged molecular weight
M_{w}	weight-averaged molecular weight
R^i_j	recovery of species i in phase j
SEP	a measure of the degree of molecular weight-based fractionation by UIC formation of polymers (Eq. 1)

X_j^i mass fraction of species *i* in phase *j*

Superscripts

s solid phase

m original mixture, prior to UIC formation

Subscripts

PLA polylactic acid

S solvent

U urea

ACKNOWLEDGMENTS

Ms. Britni Newton and Ms. Opey Moyegun are acknowledged gratefully for assisting in the collection of GPC data. We also thank Mr. Mart Eenink (Purac) and Dr. John Middleton (Birmingham Polymers) for their technical assistance and their kind donation of samples. Financial support for this work came from the Swedish NUTEK and NFR organizations, as well as the American NSF-EPSCOR program. We thank Dr. Jimmy W. Mays (Department of Chemistry, University of Alabama–Birmingham) for kindly making his DSC facilities available for this work, Mr. Jinchuan Yang and Mr. Jason Jimmerson for conducting the DSC analyses, Dr. K. K. Chittur (Department of Chemical and Materials Engineering, University at Alabama–Huntsville) for kindly permitting use of his FTIR facilities, and Mr. Ashish Bezawada for obtaining the FTIR spectra and preparing the KBr films used as FTIR samples.

REFERENCES

1. Hollingsworth, M.D.; Harris, K.D. Urea, Thiourea, and Selenourea. In *Comprehensive Supramolecular Chemistry*; MacNicol, D.D., Toda, F., Bishop, R., Eds.; Pergamon Press: Oxford, 1996; Vol. 6, 177–237.
2. Huang, L.; Allen, E.; Tonelli, A.E. Inclusion Compounds Formed Between Cyclodextrins and Nylon 6. Polymer **1999**, *40*, 3211–3221.
3. Rusa, C.C.; Tonelli, A.E. Separation of Polymers by Molecular Weight through Inclusion Compound Formation with Urea and α-Cyclodextrin. Macromolecules **2000**, *33*, 1813–1818.
4. Takamaizawa, S.; Furihata, M.; Takeda, S.; Yamaguchi, K.; Mori, W. Synthesis and Characterization of Novel Inclusion Complexes Between Micorporous Molybdenum(II) Dicarboxylates and Organic Polymers. Macromolecules **2000**, *33*, 6222–6227.

5. Allcock, H.R.; Primrose, A.P.; Sunderland, N.J.; Rheingold, A.L.; Guzei, I.A.; Parvez, M. Inclusion of Polymers Within the Crystal Sturcture of Tris(*o*-phenylenedioxy)cyclotriphosphazene. Chem. Mater. **1999**, *11*, 1243–1252.
6. Allcock, H.R.; Sunderland, N.J. Separation of Polymers and Small Molecules by Crystalline Host Systems. Macromolecules **2001**, *34*, 3069–3076.
7. Swern, D. Urea and Thiourea Complexes in Separating Organic Compounds. Ind. Eng. Chem. **1955**, *47*, 216–221.
8. Schmidt, G.; Enkelmann, V.; Westphal, U.; Droscher, M.; Wegner, G. Preparation of Urea–Poly(tetrahydrofuran) Complexes and Their Application of Oligomers. Colloid Polym. Sci. **1985**, *263*, 120–127.
9. Chenite, A.; Brisse, F. Poly(tetrahydrofuran)–Urea Adduct: A Structural Investigation. Macromolecules **1992**, *25*, 776–782.
10. Chenite, A.; Brisse, F. Structural Investigations of Urea–Aliphatic Polyester Adducts. Macromolecules **1993**, *26*, 3055–3061.
11. Hayes, D.G.; Bengtsson, Y.; Van Alstine, J.M.; Setterwall, F.N. Urea Complexation for the Rapid, Cost Effective, Ecologically Friendly Fractionation of Fatty Acid from Seed Oil. J. Am. Oil Chem. Soc. **1998**, *75*, 1403–1408.
12. Hayes, D.G.; Van Alstine, J.M.; Setterwall, F.N. Urea Based Fractionation of Fatty Acids and Glycerides of Polyunsaturated and Hydroxy Fatty Acid Seed Oils. J. Am. Oil Chem. Soc. **2000**, *77*, 207–213.
13. Hayes, D.G.; Van Alstine, J.M.; Asplund, A.L. Use of Triangular Phase Diagrams and Partition Coefficients to Predict the Results of Urea-Based Fractionation of Fatty Acids. Sep. Sci. Technol. **2001**, *36*, 45–58.
14. Howe, C.; Sankar, S.; Tonelli, A.E. ^{13}C-NMR Observations of Poly(L-lactide) in the Narrow Channels of its Inclusion Compound with Urea. Polymer **1993**, *34*, 2674–2676.
15. Howe, C.; Vasanthan, N.; MacClamrock, C.; Sankar, S.; Shin, I.D.; Simonsen, I.K.; Tonelli, A.E. Inclusion Compound Formed Between Poly(L-lactic acid) and Urea. Macromolecules **1994**, *27*, 7433–7436.
16. Tonelli, A.E. Polylactides in Channels. Macromolecules **1992**, *25*, 3581–3584.
17. Vasanthan, N.; Tonelli, A.E.; Nojima, S. Inclusion Compounds Formed Between a Poly(ε-caprolactone)–Polybutadiene Diblock Copolymer and Urea. Macromolecules **1994**, *27*, 7220–7221.
18. Choi, C.; Davis, D.D.; Tonelli, A.E. Inclusion Compound Formed Between Poly(ε-caprolactone) and Urea. Macromolecules **1993**, *26*, 1468–1470.
19. Vasanthan, N.; Shin, I.D.; Tonelli, A.E. Structure, Conformation, and Motions of Polytetrahydrofuran (PTHF) in the Hexagonal Form of the

PTHF-Urea Inclusion Compound. J. Polym. Sci. B. Polym. Phys. **1995**, *33*, 1385–1393.
20. Eaton, P.; Vasanthan, N.; Shin, I.D.; Tonelli, A.E. Formation and Characterization of Polypropylene-Urea Inclusion Compounds. Macromolecules **1996**, *29*, 2531–2536.
21. Vasanthan, N.; Shin, I.D.; Huang, L.; Nojima, S.; Tonelli, A.E. Formation, Characterization, and Segmental Mobilities of Block Copolymers in Their Urea Inclusion Compound Crystals. Macromolecules **1997**, *30*, 3014–3025.
22. Vasanthan, N.; Shin, I.D.; Tonelli, A.E. Structure, Conformation, and Motions of Poly(ethylene oxide) and Poly(ethylene glycol) in Their Urea Inclusion Compounds. Macromolecules **1996**, *29*, 263–267.
23. Smith, A.E. The Crystal Structure of the Urea–Hydrocarbon Complexes. Acta Crystallogr. **1952**, *5*, 224–235.

Received March 2001
Revised July 2001

Downloaded At: 10:36 25 January 2011

Request Permission or Order Reprints Instantly!

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the U.S. Copyright Office for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on Fair Use in the Classroom.

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our Website User Agreement for more details.

Order now!

Reprints of this article can also be ordered at
http://www.dekker.com/servlet/product/DOI/101081SS120002216