

초임계 유체를 포함한 생분해성 고분자와의 고압상거동

박 철 · 변헌수 · 이하연 · 강하성
여수대학교 화학공학과

High Pressure Phase Behavior of Biodegradable Polymer in Supercritical Fluids

Chol Park · Hun-Soo Byun⁺ · Ha-Yeun Lee · Ha-Sung Kang

Department of Chemical Engineering, Yosu National University, Chonnam 550-749, Korea

INTRODUCTION

Supercritical fluids are an attractive alternative to incompressible liquid solvents, since they can have liquid-like dissolving power while exhibiting the transport properties of a gas. They have been used in a variety of polymer processes such as chemical process, extraction, separation, and industrial application.[1,2]

Copolymers of glycolide, a dimer of glycolic acid, and lactide, a dimer of lactic acid, (PLGA_x) have been utilized in the medical industry, beginning with biodegradable sutures that were first approved in the 1960s.[3] Since that time PLGA has been tested for numerous biological applications including polymeric drug delivery devices, synthetic bone scaffolding, and even dental prosthetic devices. Since PLGA is used in biological applications, the solvents used to process these copolymers should be pharmacologically acceptable. Recently supercritical CO₂ has been investigated as a viable solvent for processing PLGA copolymers. Although, to the best of our knowledge, the phase behavior of PLGA copolymers in CO₂ has not been reported, this fact is not surprising since CO₂ at pressures well below 700 bar does not dissolve PLGA copolymers, but it does lower the glass transition of the copolymer sufficiently to make it processible near ambient temperatures.[4]

The solvents used this study are CO₂, CHF₃, and CHClF₂. Notice that the polarizability of CO₂ and CHF₃ are identical, which implies that the impact of the quadrupole moment of CO₂ can be contrasted to the impact of the dipole moment of CHF₃ on the phase behavior. Since the dipole moments of CHF₃ and CHClF₂ are very close, the phase behavior of the PLGA copolymers in CHF₃ and CHClF₂ can be compared to determine the impact of polarizability on the phase behavior. However, the hydrogen bonding between the hydrogen on CHF₃ and CHClF₂ and ester linkage in PLGA make this comparison more tenuous since hydrogen-bonding interactions are close to ten times stronger than nonpolar dispersion interactions.[5,6] Several other studies have also shown that CHClF₂ is an excellent solvent for polar polymers that can cross-associate with the acidic hydrogen in this solvent.[7]

EXPERIMENTAL

A high-pressure view cell is used in this study to obtain cloud point data.[6,7] The body of the cell is a high nickel content steel (Nitronic 50) with a 5.7 cm OD by 1.59 cm ID, and with approximately 30 cm³ working volume. A 1.9 cm OD × 1.9 cm thick sapphire window is fitted to one end of the cell so that the phase behavior can be determined visually. The cell contents are compressed to the desired operating pressure by displacing a movable piston fitted within the cell using water pressurized with a high pressure generator (HIP, Inc., Model 37-5.75-60). The temperature of the cell, measured to

within $\pm 0.2^\circ\text{C}$ with a type-E thermocouple (Omega) connected to a digital multimeter, is also maintained to within $\pm 0.2^\circ\text{C}$.

Cloud points are measured for solutions with a fixed copolymer or polymer concentration of $\sim 5\text{wt } \%$ that we expected to be close to the maximum in the pressure-composition isotherm. Cloud point are measured and reproduced at least twice to within ± 2.8 bar and $\pm 0.4^\circ\text{C}$. The cloud point pressure is defined as the point at which the solution becomes so opaque that it is no longer possible to see the stir bar in solution. Cloud point obtained in this manner are identical within reproducibility limits to those defined as the point at which there is a 90% drop in transmitted light through the solution.

Materials

The polymers used in this study were obtained from Polysciences Inc. (Warrington, PA). CHF_3 (98 % minimum purity) was obtained from Aldrich Chemical Company, Inc., CO_2 (99.8 % minimum purity) was obtained from Daesung Co., and CHClF_2 (99.8 % minimum purity) was obtained from Dongil Gas Co. All of the solvents were used as received.

RESULTS AND DISCUSSION

Figure 1 shows the effect of glycolide content in the backbone of the copolymer on the pressure needed to obtain a single phase in pure CO_2 . It is apparent that the pressures needed to obtain a single phase are fixed more by the glycolide content in the backbone of the copolymer rather than the copolymer weight average molecular weight (M_w). In fact, if M_w governed the location of the cloud point curve, the PLGA_{15} and PLGA_{25} curves would be at pressures below that needed to dissolve PLA_H rather than at higher pressures as shown in Figure 1. It is not possible to dissolve PLGA_{50} in CO_2 to pressures of 2,600 bar.

Figure 2 shows the impact of CHClF_2 cosolvent on the phase behavior of the PLA-CO_2 system. These cloud point curves exhibit a slight positive slope relative to the curves in Figure 1; however, the pressure axis is very impacted in Figure 2. The cloud point curves in Figure 2 decrease the increasing CHClF_2 content as compared to a pressure difference of 1100 bar between the PLA-CO_2 and PLA-CHClF_2 curves.

The phase behavior curve shows clearly that adding 25 mol % glycolide to the backbone of PLA shifts the CHF_3 cloud point pressures by as much as 800 bar at 40°C . This shift is not quite as large as that observed with CO_2 as shown in Figure 1. Both CO_2 and CHF_3 have approximately the same polarizability and both have some polarity since CHF_3 has a dipole moment of 1.6D and CO_2 has a quadrupole moment of $-4.3 \times 10^{-26} \text{ erg}^{1/2} \text{ cm}^{5/2}$. However, CHF_3 has an acidic proton that is capable of hydrogen bonding with the ester groups in PLGA whereas CO_2 is not expected to form any type of complex with PLGA. More than likely, the ability of CHF_3 to form a complex with PLGA makes it a better solvent than CO_2 especially since any change in favorable energetic interactions is magnified in these dense SCF solvents.

Figure 3 shows a different type of phase behavior for PLGA in CHClF_2 . In this instance lower critical solution temperature (LCST) behavior is exhibited that is sensitive to the glycolide content in PLGA. As the glycolide content in PLGA increases, the two-phase region expands. Although it is not possible to dissolve PLGA_{50} in pure CO_2 , this copolymer readily dissolves in CHClF_2 even at temperatures as low as 20°C .

CONCLUSION

Supercritical CO₂ is a poor quality solvent for PLGA copolymers. As the glycolide content in the backbone increases, the pressures needed to obtain a single phase also increase substantially and it is not possible to dissolve PLGA₅₀ to pressures of 2,600 bar.

The CHClF₂ data strongly suggest that a polar cosolvent capable of hydrogen bonding to the ester linkage in PLGA is needed if low pressure, single-phase processing of this copolymer is desired. However, PLGA copolymers can be intimately mixed with a variety of insoluble materials at low pressures in pure CO₂ since the glass transition temperature of the PLGA is significantly lowered by the plasticization effect of supercritical CO₂.

Acknowledgement

This work was supported by grant No. R05-2001-000-01177-0 from the Basic Research Program of Korea Science & Engineering Foundation.

REFERENCES

1. McHugh, M. A.; Krkonis, V. J., Supercritical Fluid Extraction, Principles and practice, 2nd ed.; Butterworth-Heinemann: Boston, MA (1994).
2. McHugh, M. A.; Kirby, C. F., Chem., Rev., 99, 565 (1999).
1. Middleton, J. C.; Tipton, A. J. Med Plastics Biomat Mag, March/April (1998).
2. Mandel, F. S.; Wang, J. D, Inorg. Chim. Acta, 294, 214 (1999).
3. Christensen, J. J.; Post, M. E.; McFall, T. A.; Izatt, R. M., Thermochem Acta, 50,73 (1981).
4. Christensen, J. J.; Christensen, S. P.; Schofield, R. S.; Faux, P. W.; Harding, P. R.; Izatt, R. M., Thermochem Acta, 68, 223 (1983).
5. Meilchen, M. A.; Hasch, B. M.; McHugh, M. A., Macromolecules, 24, 4874 (1991).
6. Byun, H. S.; DiNoia, T. P. McHugh, M. A., J. Chem. Eng. Data, 45, 810 (2000) .
7. Byun, H. S.; Park, C., J. Korean Chem. Eng., 19, 126 (2002).

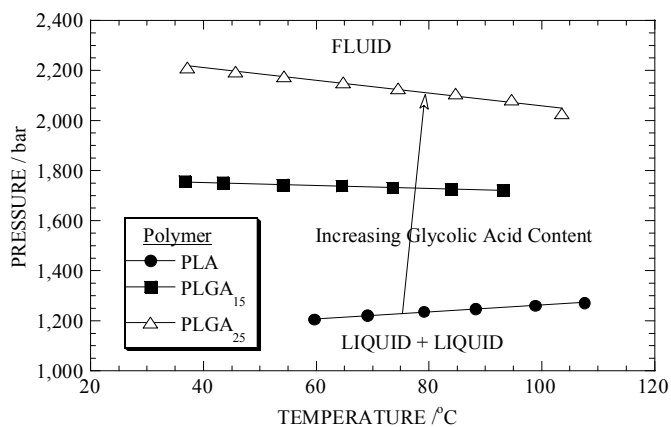


Figure 1. Impact of glycolic acid (glycolide) content on the phase behavior of PLA, PLGA₁₅, and PLGA₂₅ in pure supercritical CO₂.

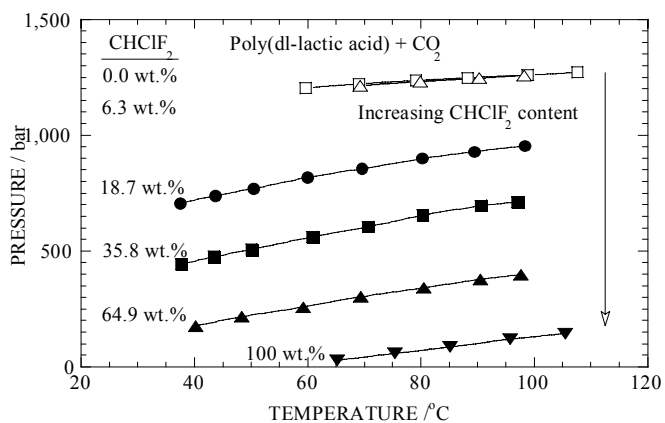


Figure 2. Effect of CHClF₂ as a cosolvent for 5 wt% poly(dl-lactic acid) in CO₂.

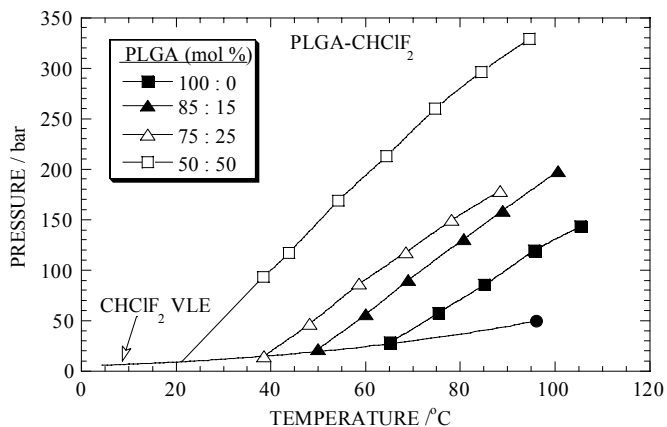


Figure 3. Impact of glycolide content on the phase behavior of PLA, PLGA₁₅, PLGA₂₅ and PLGA₅₀ in CHClF₂. The solid circle is the critical point of CHClF₂. The cloud point curves of open squares terminate on the vapor pressure curve of CHClF₂.