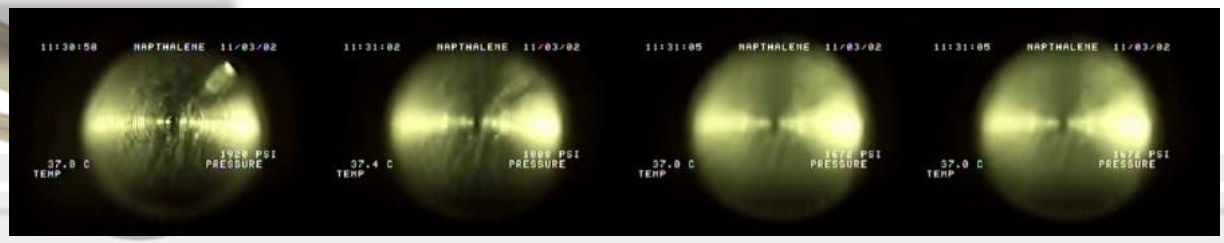
The Solubility of PCL (polycaprolactone) in various solvents with and without CO_2



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Supercritical Fluids/
Green Process Lab.

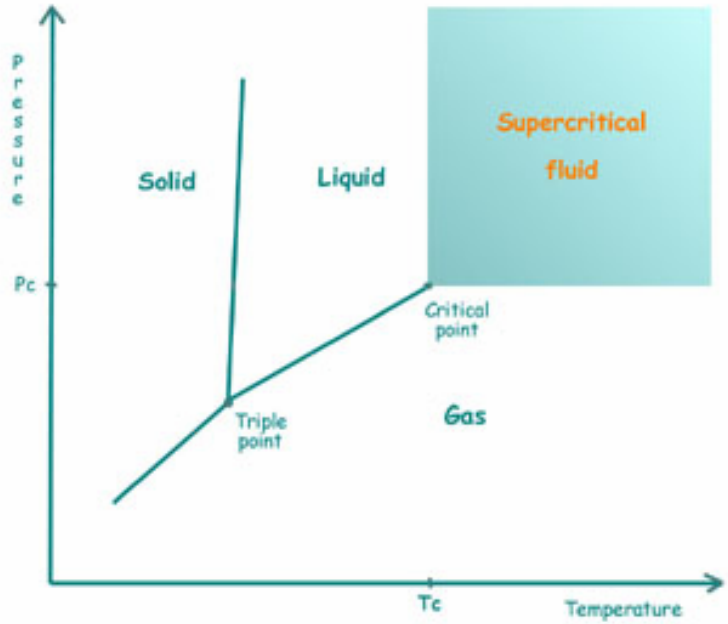
Introduction
What's is the supercritical fluid?

Supercritical fluid

- above its critical temperature & critical pressure.
- only one state-of-the-fluid

- **gas-like properties**
  low surface tension → excellent penetration
  high diffusivity → fast transfer rate
  low viscosity → good hydrodynamic features

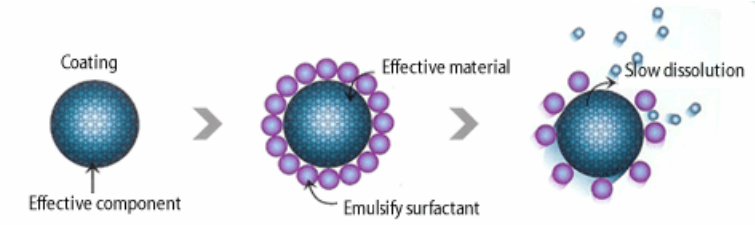
- **liquid-like properties**
  high density → high solvent power



Approach to DDS (Drug Delivery System)
- Supercritical Fluid Technology -

Applications to DDS

pulmonary drug



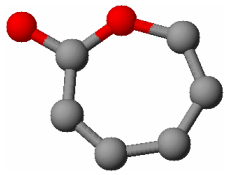
slow dissolution drug

Why should we make particles with Supercritical Fluid Technology?

- Several stable processes invented to make small particles (micro ~ nano)
- Narrow diameter dispersion, high degree of purity
- No solvent existence
- can use the very low solubility materials
- reduce several separating and refining processes
- stable and safety from the thermal threat

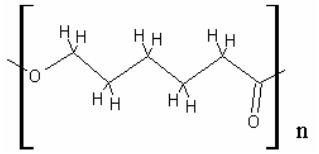
Solute
Polycaprolactone (PCL)

Polycaprolactone – biodegradable polymer



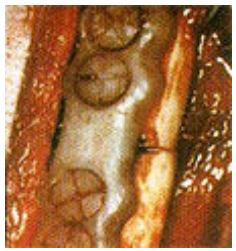
Caprolactone

Ring Opening Polymerization



Polycaprolactone

- **usage** : Contraceptive pill, Artificial skin, Surgical thread, Film & coating material for DDS



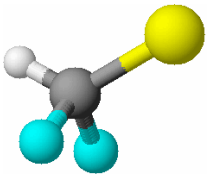
- **Essential conditions of PCL for DDS**

No rejection symptoms in the body
Non-toxic residual product
Dissolved materials is eliminated by metabolism

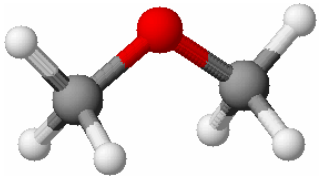
Solvents

Dimethyl Ether (DME), HCFC-22, CO_2

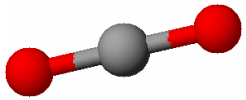
Solvents



HCFC-22



Dimethyl Ether (DME)



CO_2

- Physical properties of solvents used in this study

Solvent	Chemical formula	M.W.	Tc/K	Pc/MPa	Dipole moments
Dimethylether (DME)	CH_3OCH_3	46.06	400.00	5.24	1.3
Chlorodifluoromethane (HCFC-22)	$CHClF_2$	84.46	369.30	4.97	1.4
Carbon dioxide	CO_2	44.01	304.18	7.38	0

Apparatus
schematic diagram

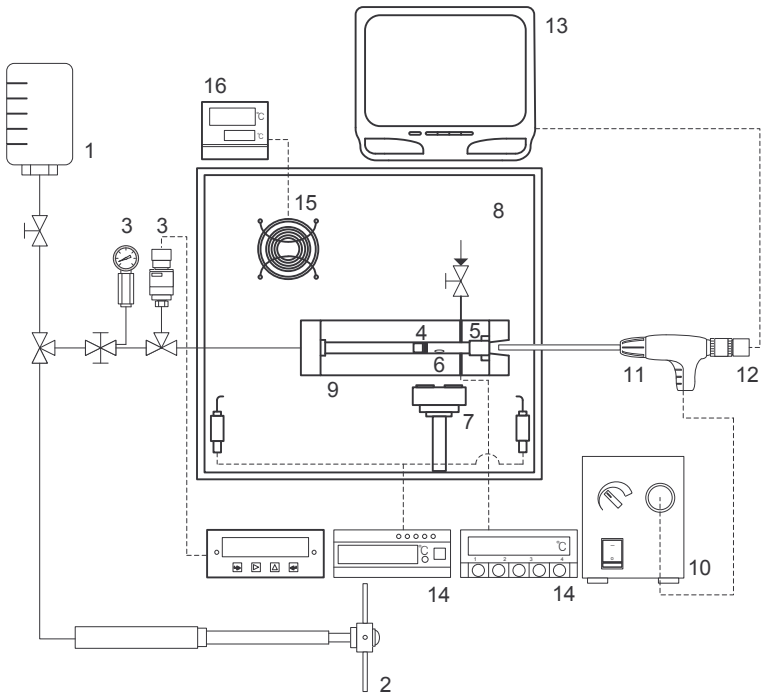
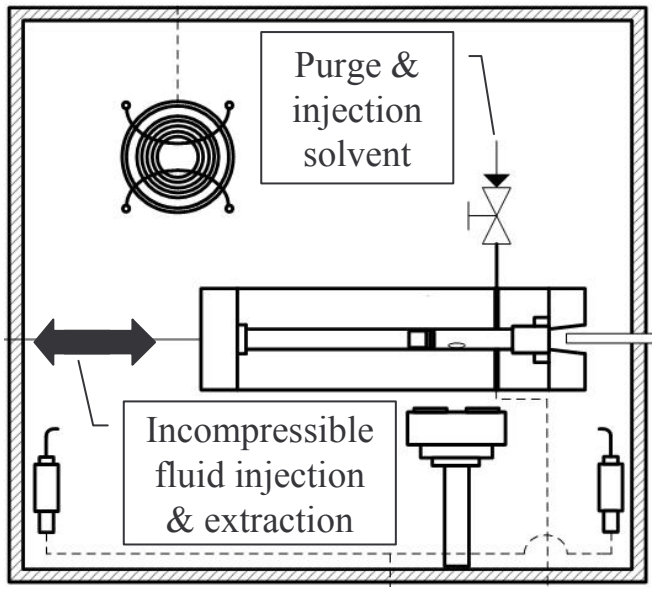


Figure 1. Schematic diagram of experimental apparatus

1. Water for pressuring 2. Pressure generator 3. Pressure gauge 4. Piston 5. Sapphire window 6. Magnetic bar 7. Stirrer 8. Air bath 9. Variable-volume cell 10. Light source 11. Borescope 12. Camera 13. Monitor 14. Temperature gauge 15. Heater 16. Heating Controller

Solubility Measurement

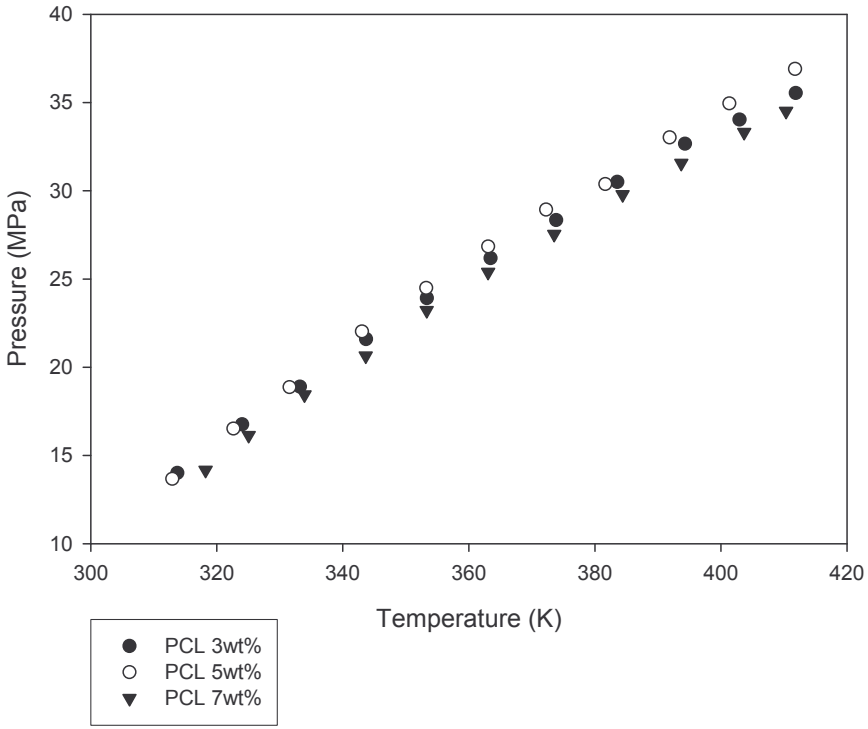


- The cell charged with a certain weight-percent PCL
- Purge 3 times with solvent in order to remove air
- Inject the solvent into the cell
- Control the temperature in the air bath
- Using the pressure generator, put incompressible fluid into the other side of cell to make one-state-of-fluid
- Extract the incompressible fluid from the cell slowly, the magnetic bar spinning in the cell would be disappeared ← That's the cloud point !!!

Results & discussion

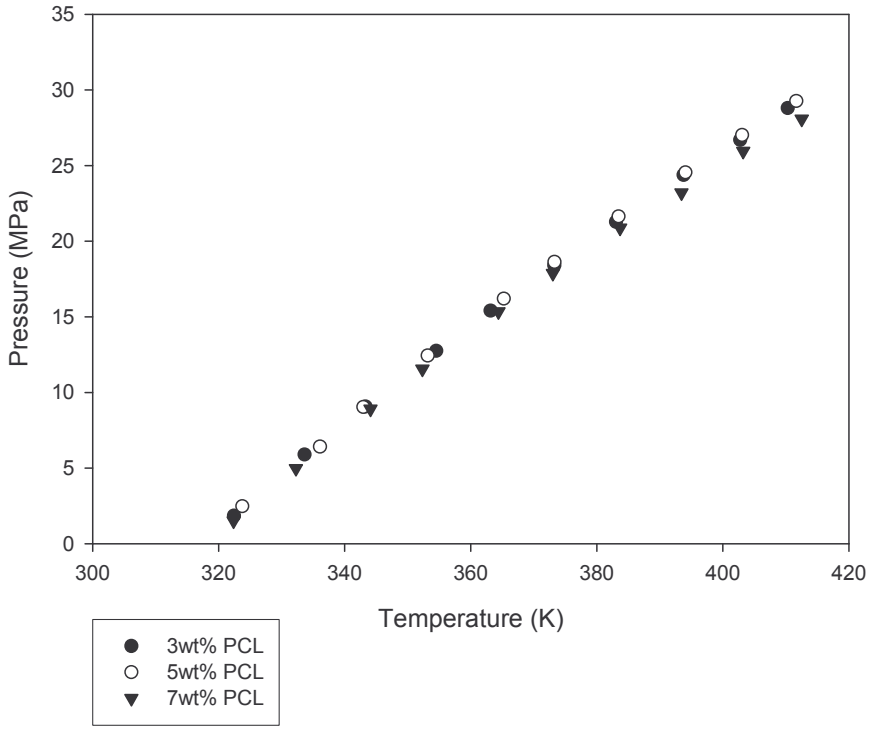
PCL (M_w=103,750) + DME

P-T isopleths of cloud points of polycaprolactone
in a DME at various polymer molecular weight



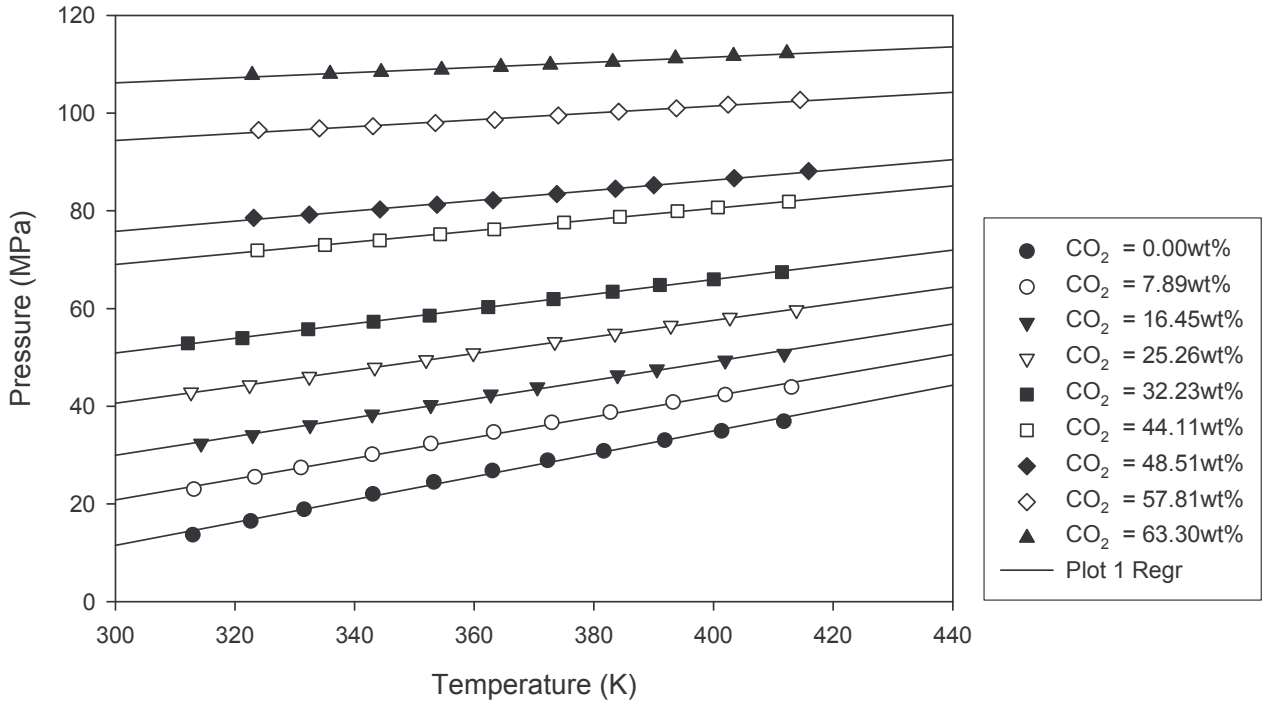
PCL (M_w=103,750) + HCFC-22

P-T isopleths of cloud points of polycaprolactone in a HCFC-22 at various polymer molecular weight



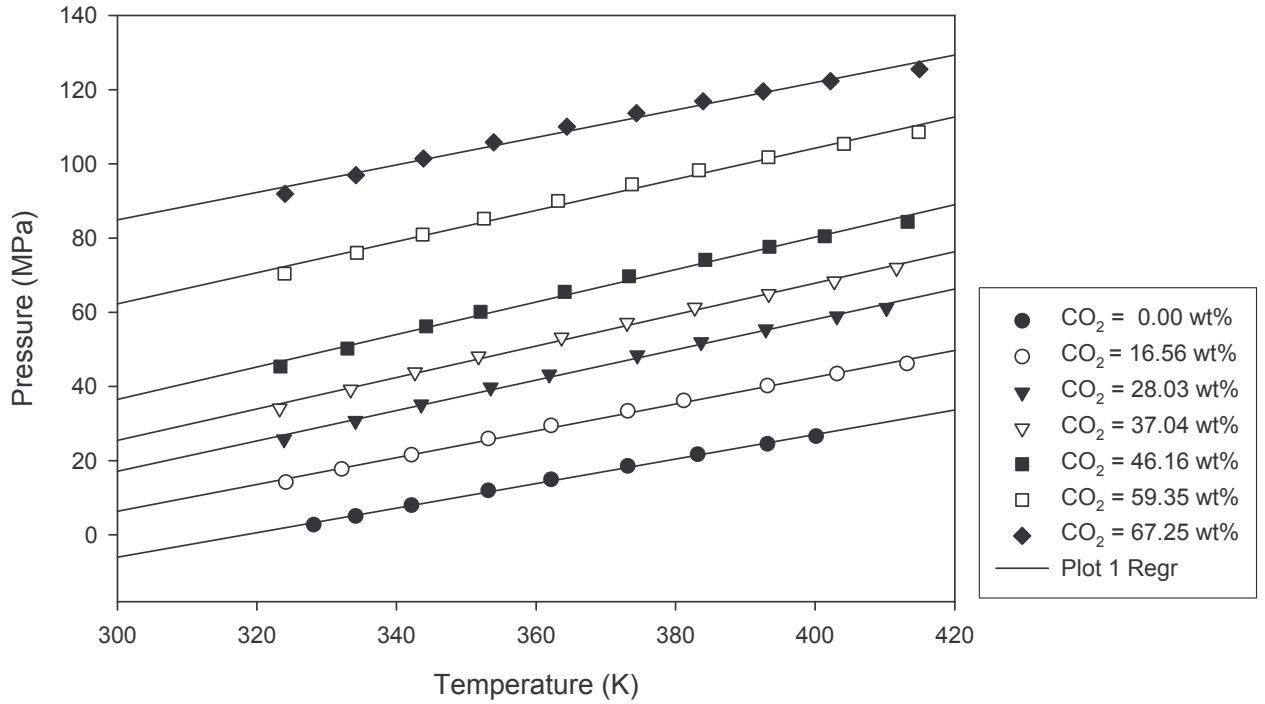
PCL (M_w=103,750) + DME + CO_2

P-T isopleths of cloud points of polycaprolactone
in DME + CO_2 mixed solvent. (CO_2 wt% is polymer free basis)



PCL (M_w=103,750) + HCFC-22 + CO_2

P-T isopleths of cloud points of polycaprolactone
in HCFC-22 + CO_2 mixture (CO_2 wt% is polymer free basis)



Conclusion

- The solubility of PCL was not concerned with concentrations of PCL (3, 5, 7 wt%)
- The phase behavior of PCL in each solvent exhibited LCST (lower critical solution temperature) behavior
- HCFC-22 was more powerful solvent than DME for dissolving PCL (The cloud point pressure of PCL in HCFC-22 was lower than in DME at the same temperature)
- CO_2 could be used as an Anti-solvent (As the proportion of CO_2 increased in each solvent, the solvent power was getting more weak)