CAP.C534

Advanced Supercritical Fluid Process

（超臨界流体プロセス特論）

3. Particle formation using SCF (II)

Department of Chemical Science and Engineering

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2018.10.11　Room 421 of South Buld. 4

Class Schedule

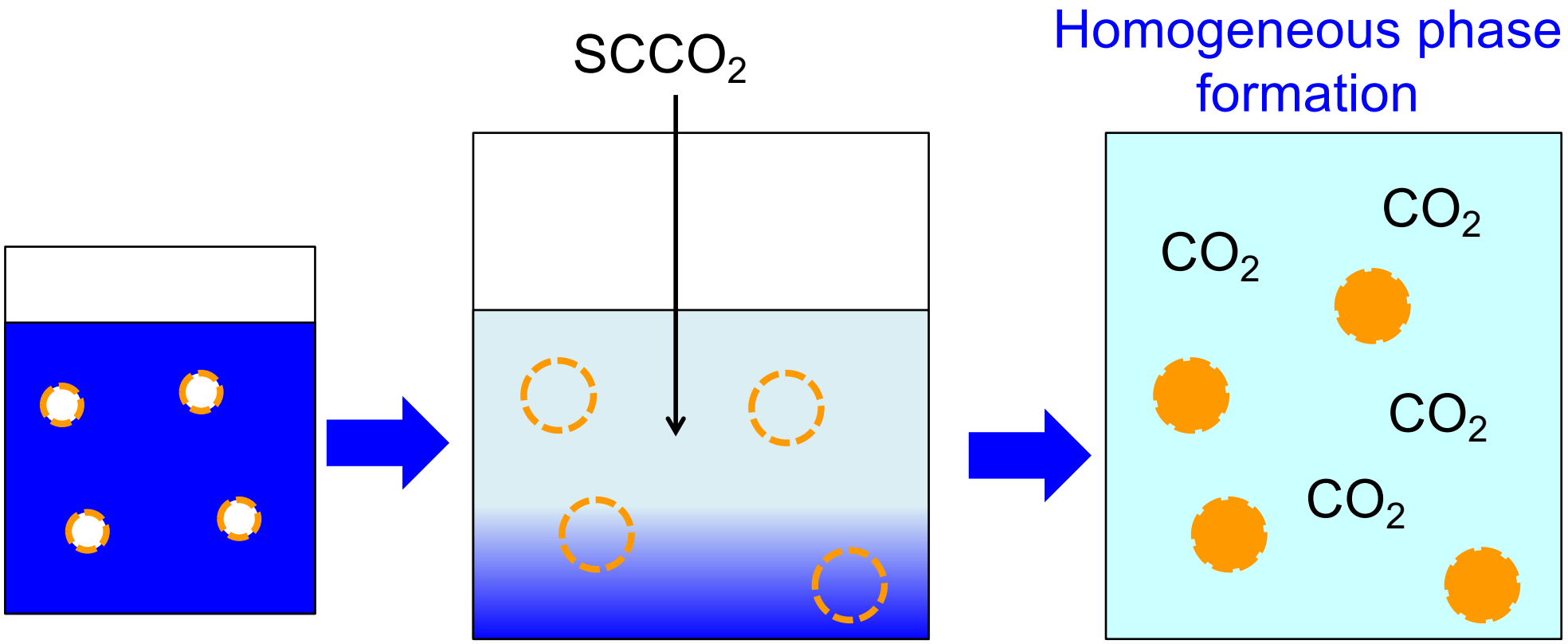
1. 9/27 Fundamental property of SCF
2. 10/4 Particle formation using SCF (I)
3. 10/11 Particle formation using SCF (II)
4. 10/18 Porous material formation using SCF (I)
5. 10/25 Porous material formation using SCF (II)
6. 11/1 Composite formation using SCF
7. 11/8 Film formation using SCF

11/22 Final report submission

Class document will be upload in OCW

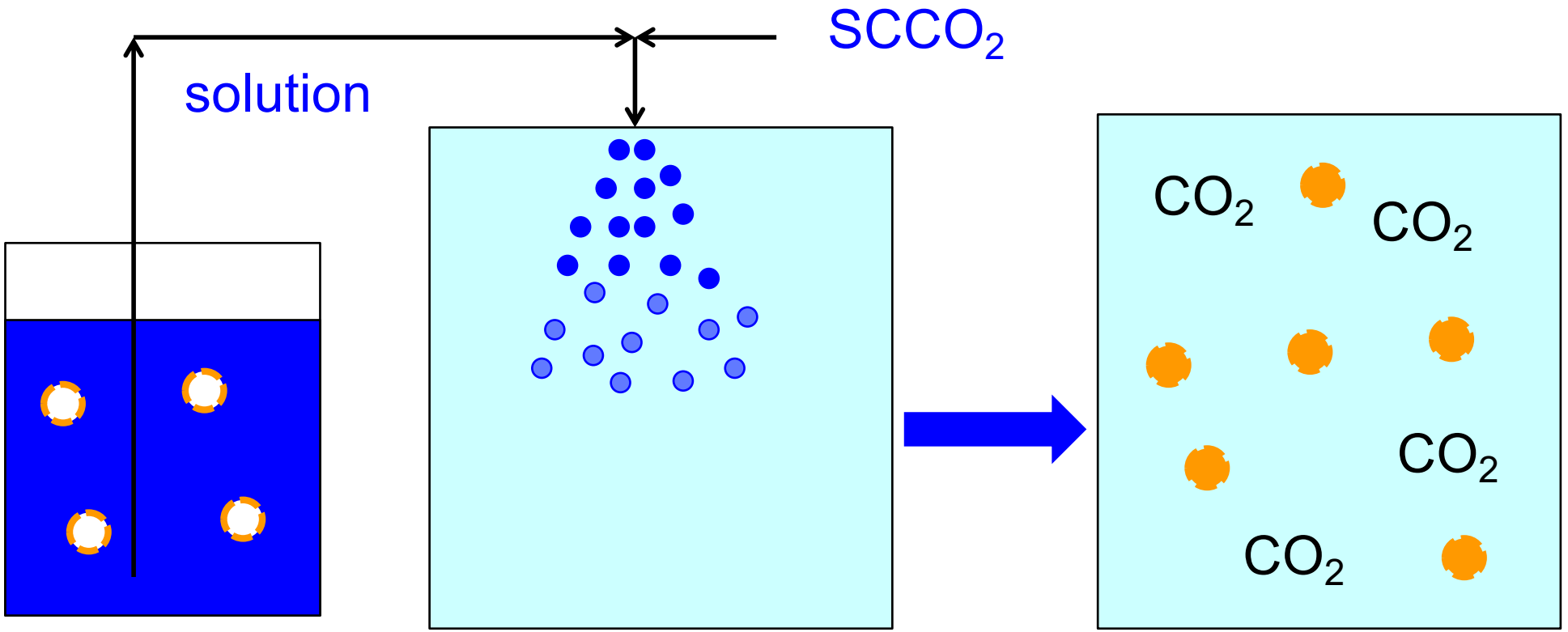
Particle formation using SCF (II)

- SAS method : Supercritical Anti-Solvent



Particle formation using SCF (II)

- SEDS method : Solution-Enhanced Dispersion of solids



Solute dissolved in solvent

Spraying solution and $SCCO_2$ via nozzle

Precipitation by solubility reduction

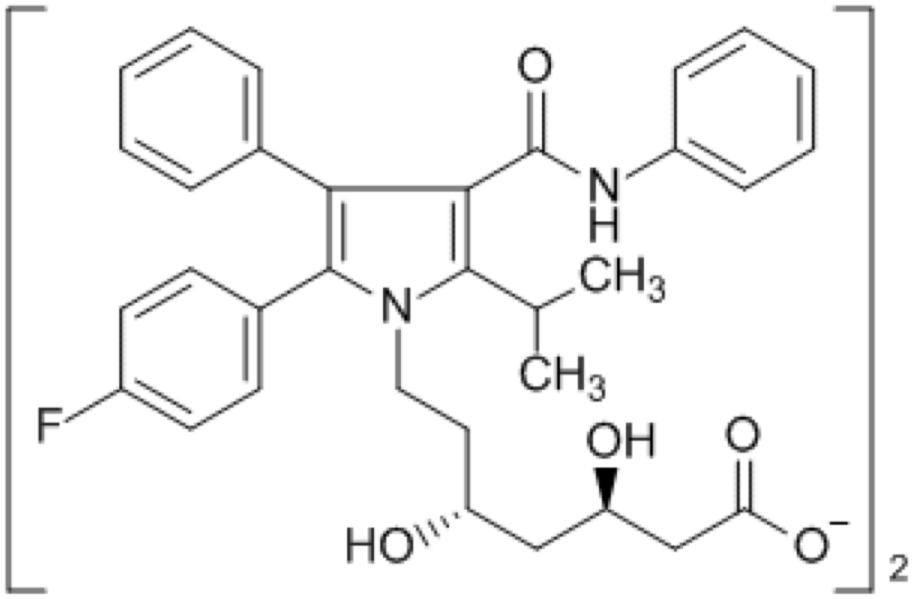
Particle formation using SCF (II)

➢ Micronization of Atorvastain Calcium (AC)

solvent : methanol

AC concentration :

25, 50, 100, 150 mg mL^{-1}



$Ca^{2+} \cdot 3H_2O$

$SCCO_2$ condition:

Temperature: 40, 50, 60 ℃

Pressure : 10 to 18 MPa

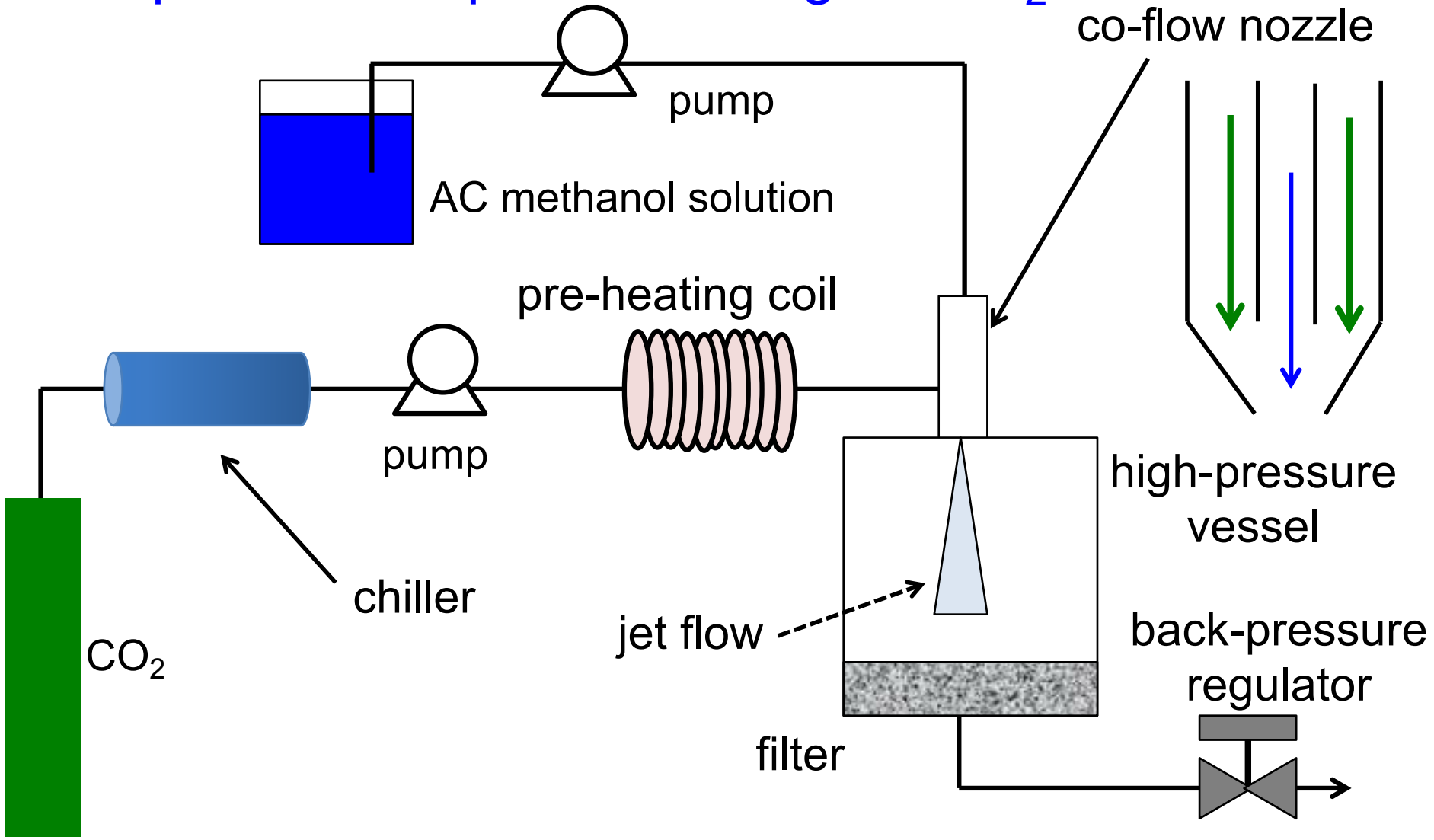
Feed rate ratio (CO_2 / drug solution):

45, 60, 90, 120 mg mL^{-1}

Eur. J. Pharm. Biopham., 69 (2008) 454-465.

Particle formation using SCF (II)

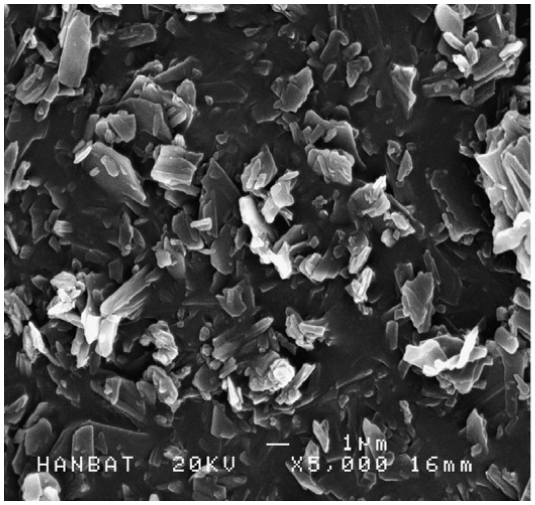
- Setup for SEDS process using $SCCO_2$



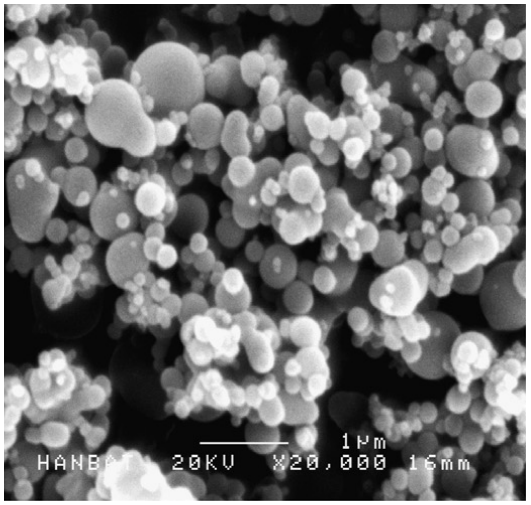
Eur. J. Pharm. Biopham., 69 (2008) 454-465.

Particle formation using SCF (II)

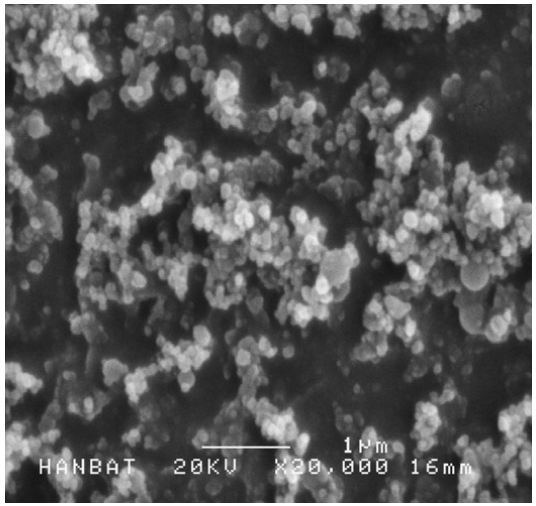
➢ Micronization of Atorvastain Calcium (AC) T = 40℃



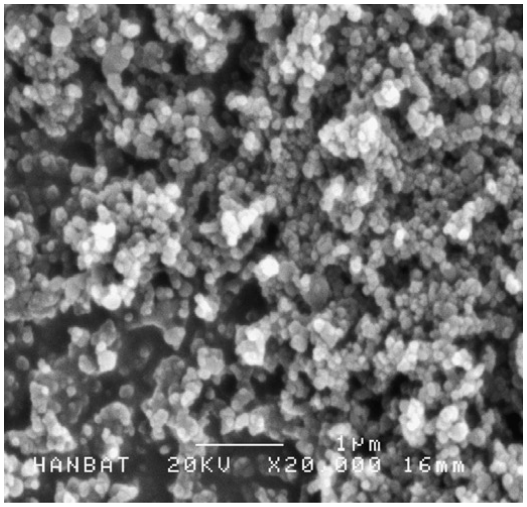
before



10 MPa



12 MPa



15 MPa

p /MPa	Particle size /nm
10	242
12	123
15	115
18	109

Eur. J. Pharm. Biopham., 69 (2008) 454-465.

Particle formation using SCF (II)

Q. 3.1

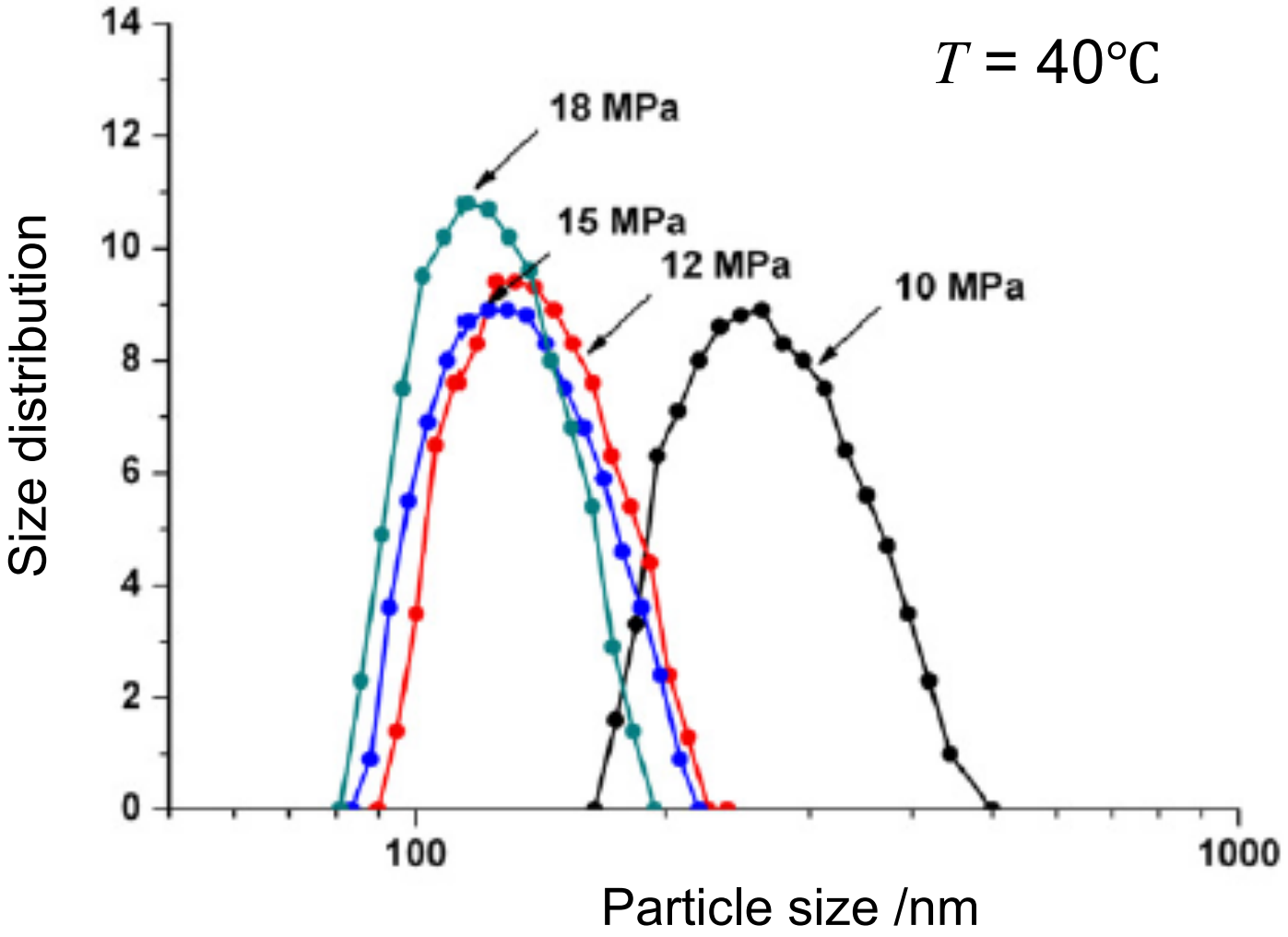
Give a reason why high pressure in spraying unit leads to the results of the smaller particle formation.

Particle formation using SCF (II)

A. 3.1（Discussion）

Particle formation using SCF (II)

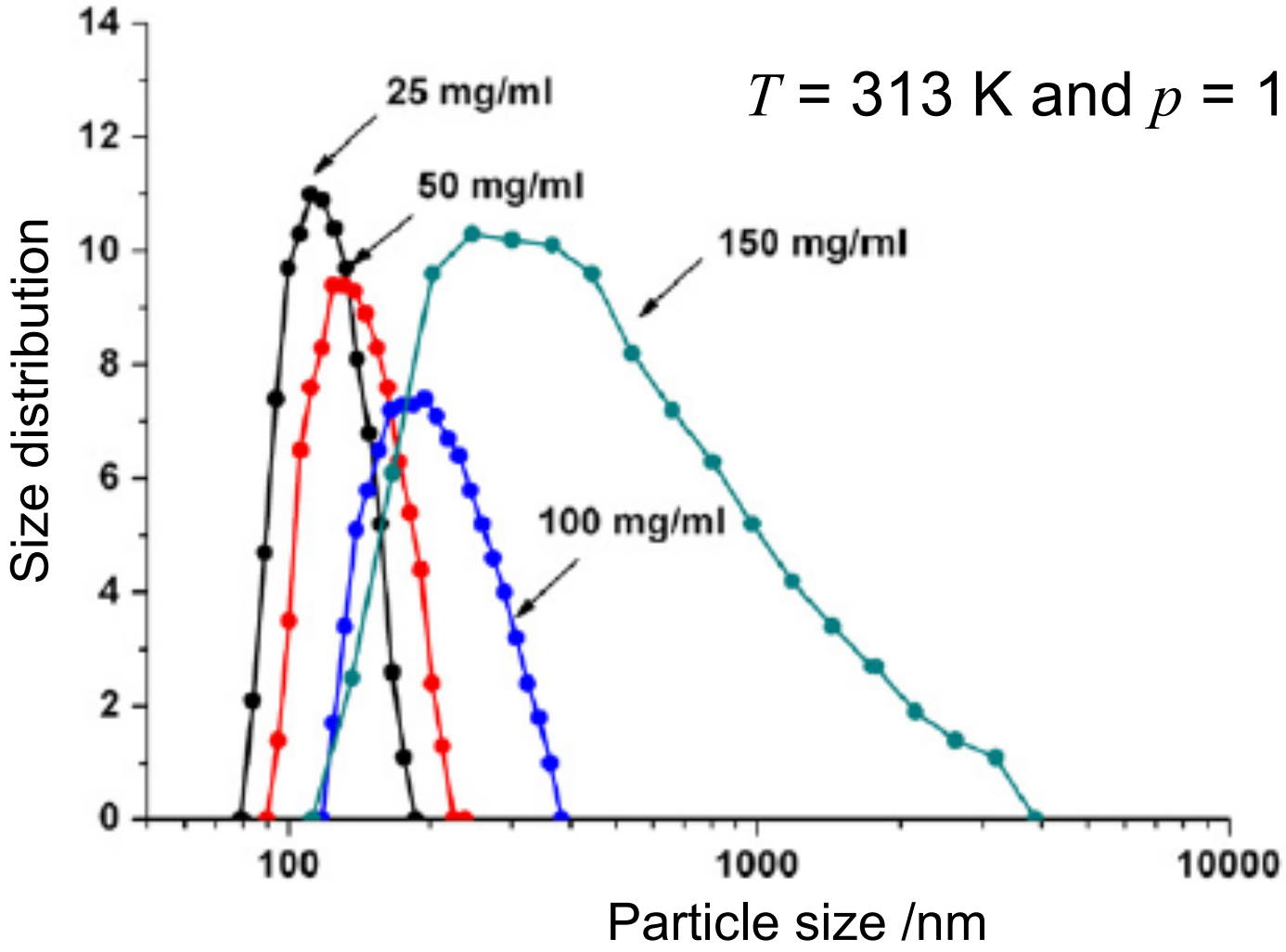
- Effect of pressure on particle size



Eur. J. Pharm. Biopham., 69 (2008) 454-465.

Particle formation using SCF (II)

- Effect of AC concentration on particle size



T = 313 K and p = 12 MPa

Eur. J. Pharm. Biopham., 69 (2008) 454-465.

Particle formation using SCF (II)

A, 3.2

Discuss the relation between AC concentration in solution and particle size formed in SEDS method.

Particle formation using SCF (II)

A. 3.2（Discussion）

Particle formation using SCF (II)

Micronization of β-carotene by SAS

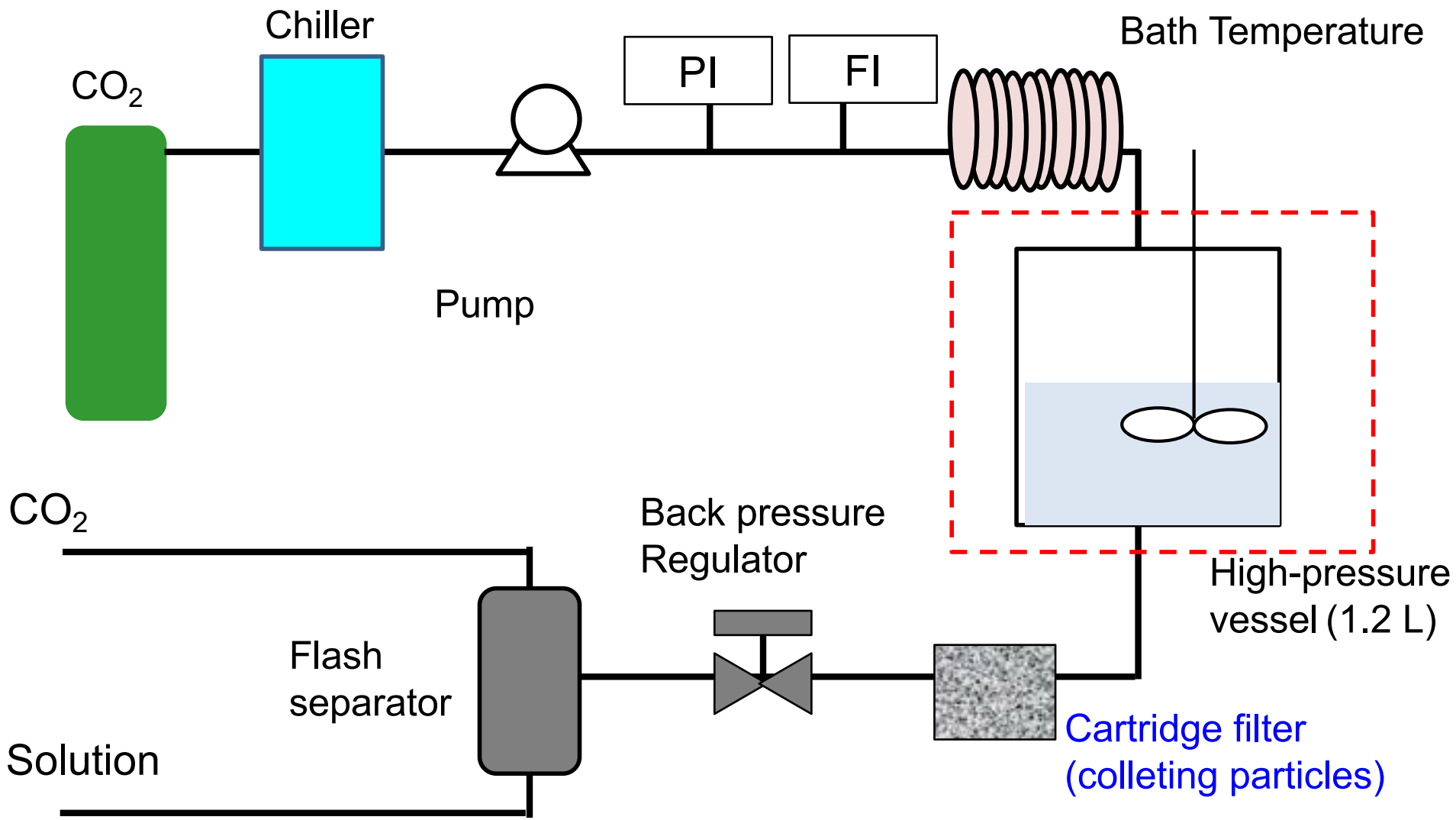
- Extraction of carotenoide from natural product
  - → solvent extraction using organic solvent
  - → further purification by crystallization or salting-out

- SAS using $SCCO_2$
  - → Effect of CO_2 flow rate and temperature
  - → Effect of solvent species
  - → Investigation on particle size and morphology

J. Supercrit. Fluids, 22 (2002) 237 – 245.

Particle formation using SCF (II)

Micronization of β-carotene by SAS



J. Supercrit. Fluids, 22 (2002) 237 – 245.

Particle formation using SCF (II)

Micronization of β-carotene by SAS

- Experimental condition in SAS process

Solute (particle) : β-carotene

Solvent : dichloromethane, ethyl acetate

$SCCO_2$ condition :

Temperature: 298, 333 K

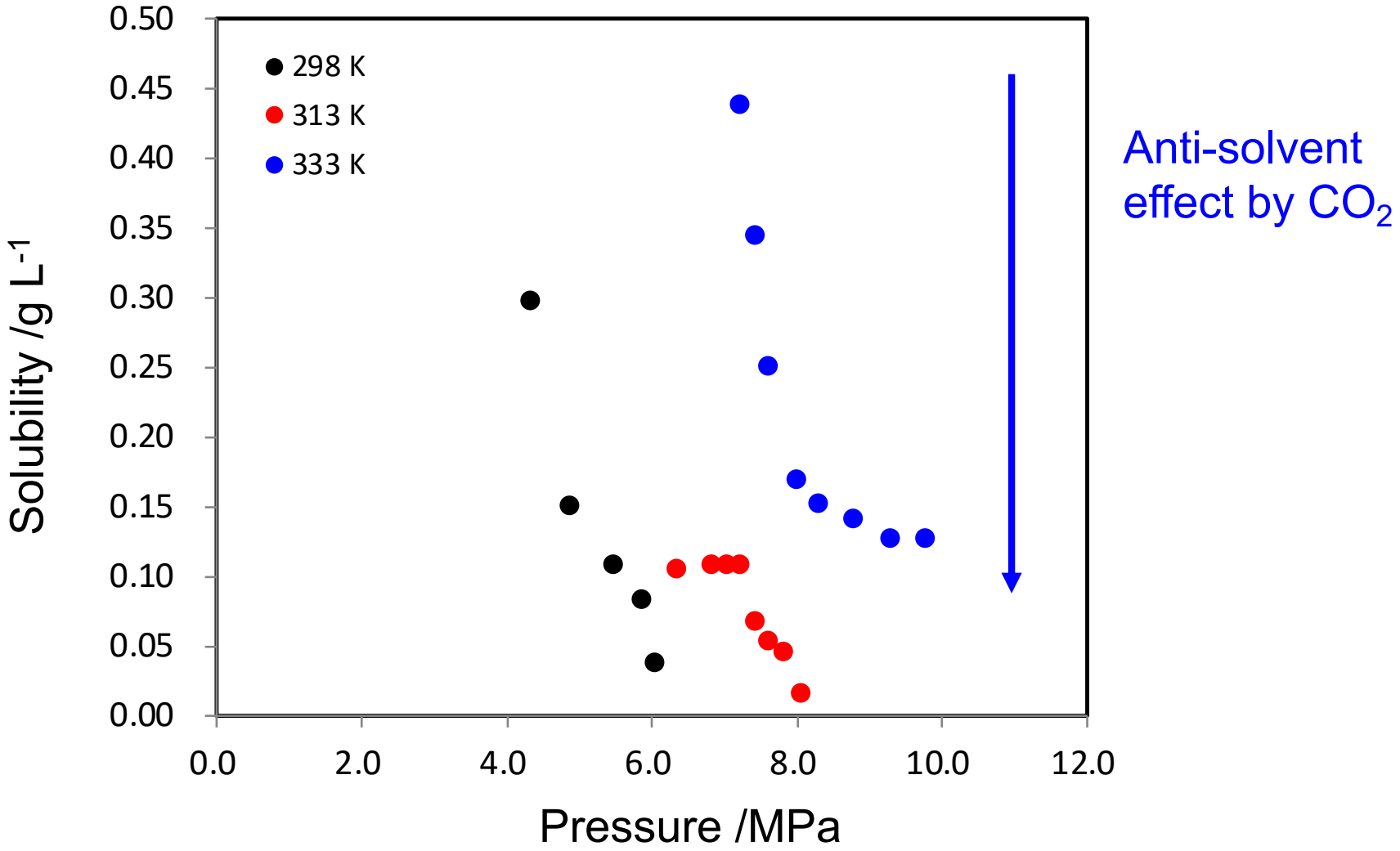
Pressure : 5.8, 7.8 MPa

Initial concentration of b-carotene: 1.0, 1.5, 2.0, 2.4 g L^{-1}

J. Supercrit. Fluids, 22 (2002) 237 – 245.

Particle formation using SCF (II)

Solubility of β-carotene in CO_2 + ethyl acetate



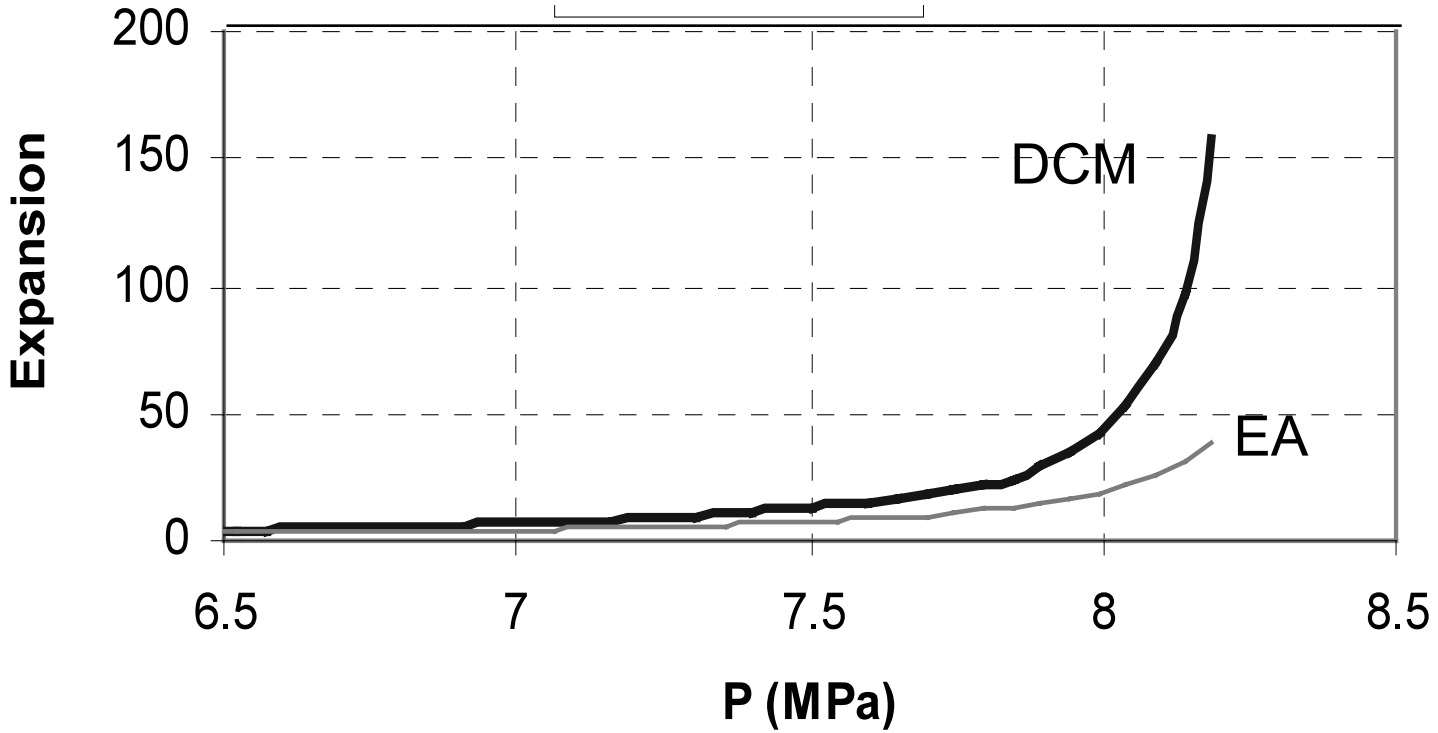
J. Supercrit. Fluids, 22 (2002) 237 – 245.

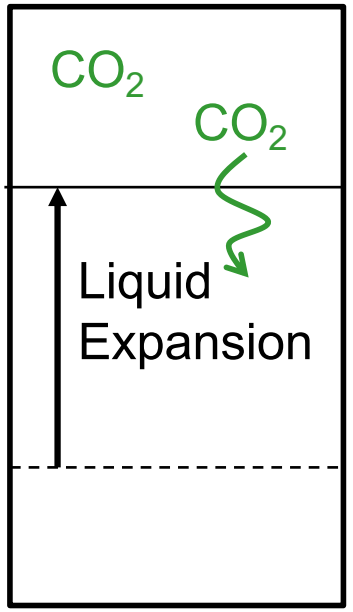
Particle formation using SCF (II)

➢ SASの条件

Solute (particle) : β-carotene

Solvent : dichloromethane (DCM), ethyl acetate (EA)



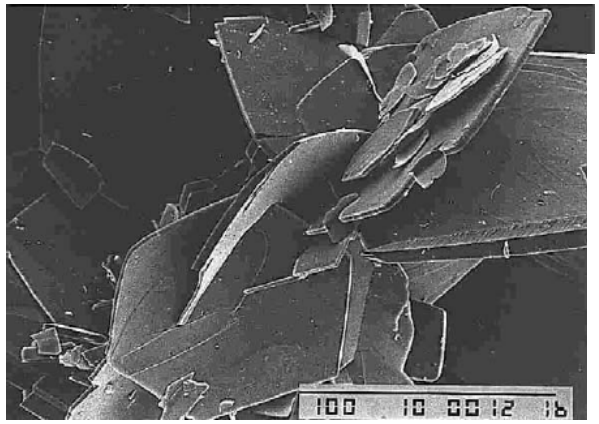


No effect on particle size

J. Supercrit. Fluids, 22 (2002) 237 – 245.

Particle formation using SCF (II)

Micronization of β-carotene by SAS



before

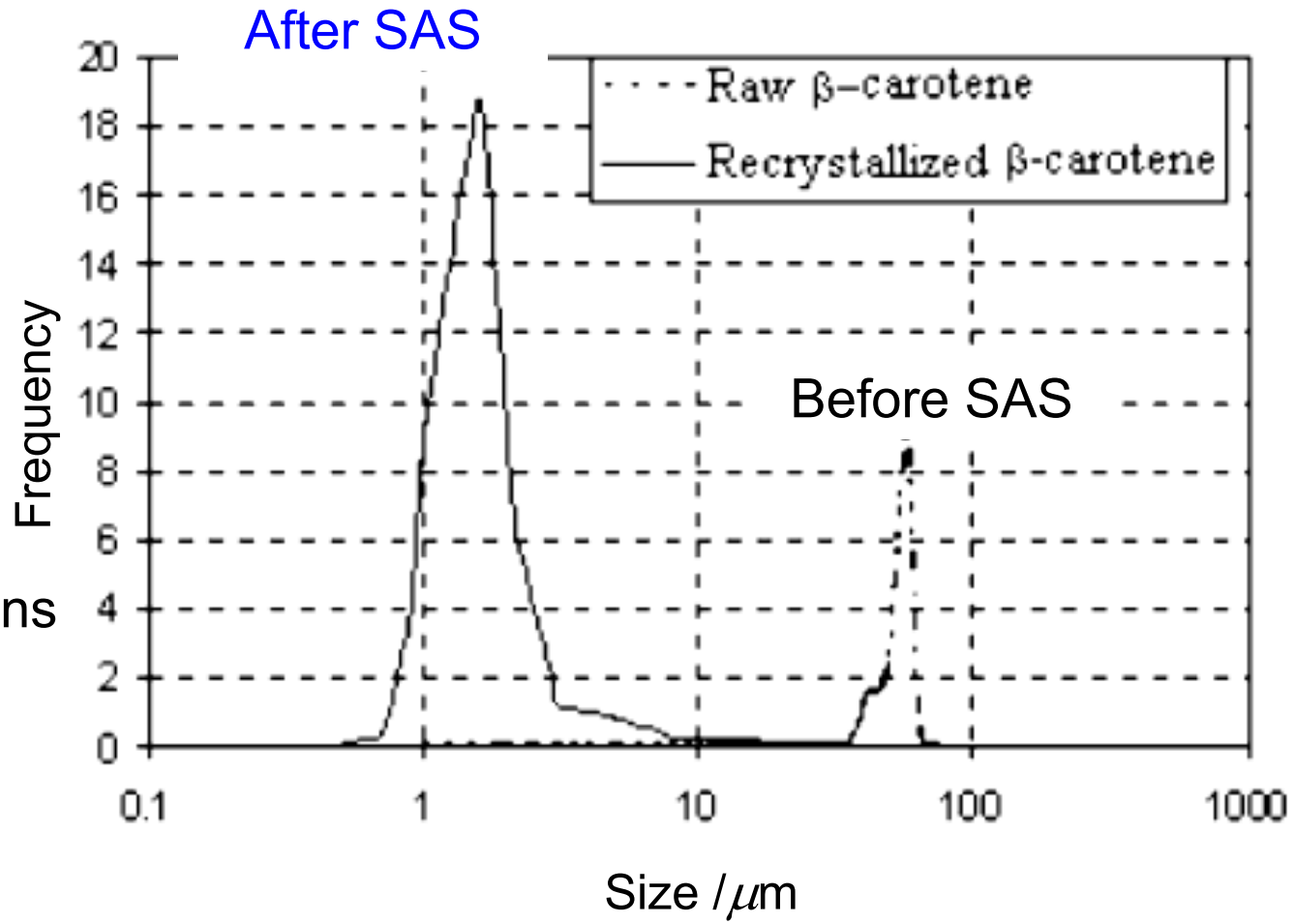
Crystallization conditions

T = 313 K

p = 7.8 Mpa

Solvent: ethyl acetate

Concentration: 1.5 g L^{-1}

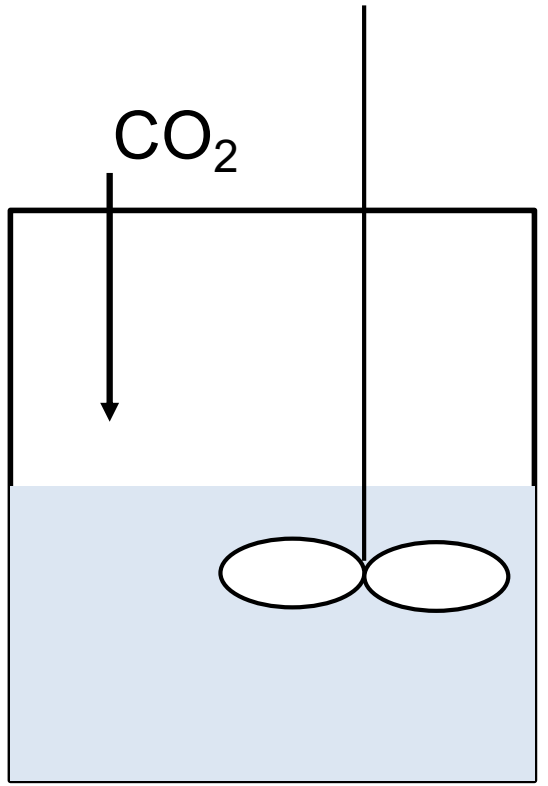


J. Supercrit. Fluids, 22 (2002) 237 – 245.

Particle formation using SCF (II)

Q. 3.3

How is the effect of stirring rate in precipitation vessel on particle size formed in SAS process?



Particle formation using SCF (II)

A. 3.3（Discussion）

Particle formation using SCF (II)

A. 3.3（Discussion）

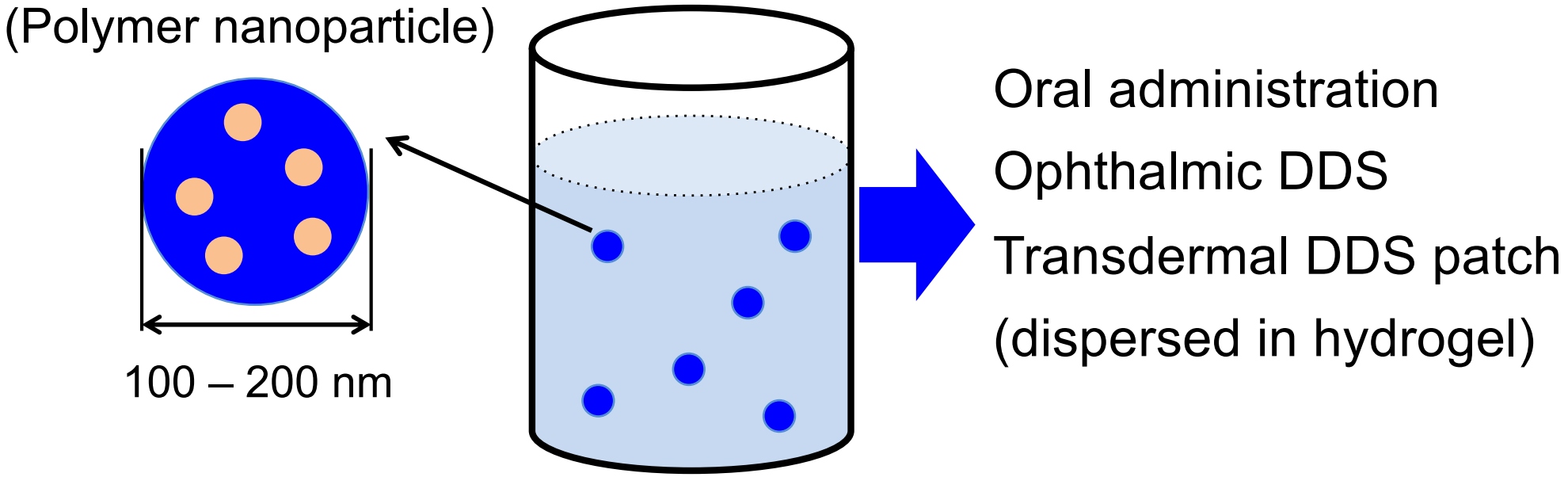
Particle formation using SCF (II)

➢ Nanosuspension production

>> Drug delivery system (DDS) application

>> Controlling drug release profile and drug amount

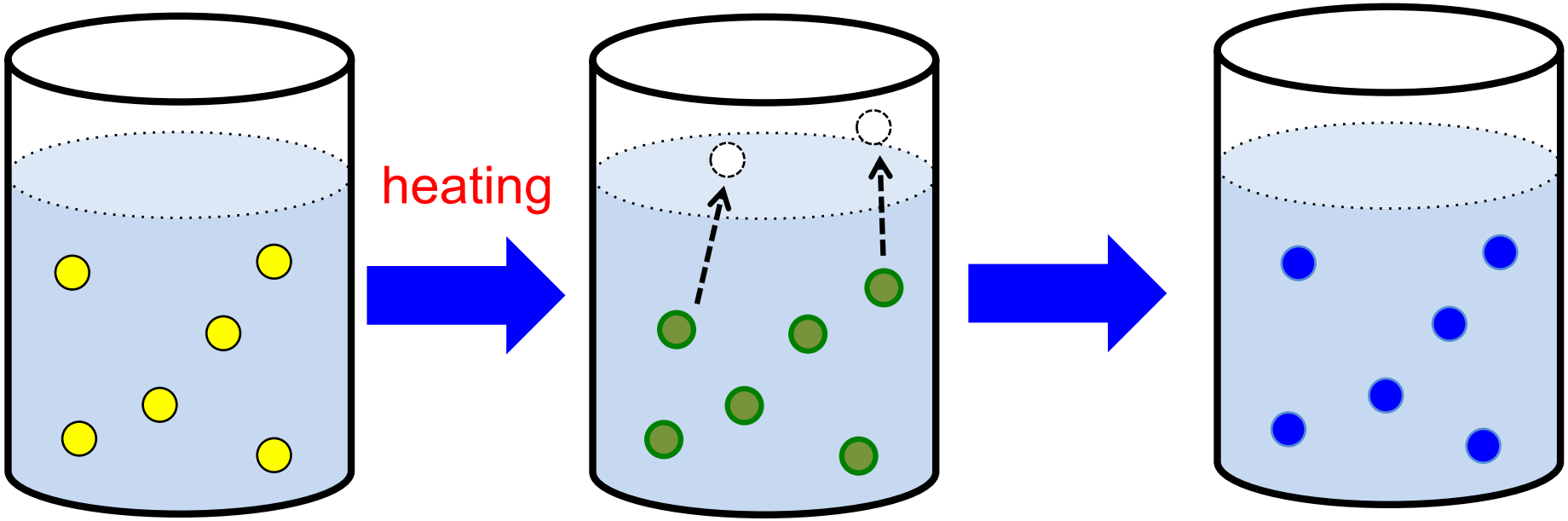
>> Polymer particle size and size distribution control



Particle formation using SCF (II)

➢ Extraction of emulsion

● Oil droplet dissolving polymer



(O / W emulsion)

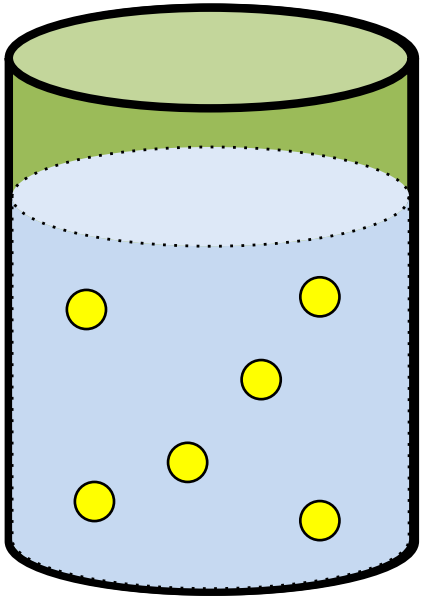
(Oil evaporation)

(polymer nanoparticle dispersed solution)

- ➢ Slow mass transfer of oil on evaporation
- ➢ Particle aggregation after oil evaporation

Particle formation using SCF (II)

➢ Supercritical Fluid Extraction of Emulsion



(Emulsion)

Supercritical CO_2

Campardell, R. et al., J. Supercrit. Fluids (2012)

- ➢ Enhanced extraction of oil phase
- ➢ Controlling polymer particle aggregation
- ➢ Batch operation

Slug flow in microchannel

- ➢ High contact probability between $SCCO_2$ and emulsion
- ➢ Continuous process

Particle formation using SCF (II)

➢ Supercritical Fluid Extraction of Emulsion

Carbon dioxide : purity over than 99.95 %

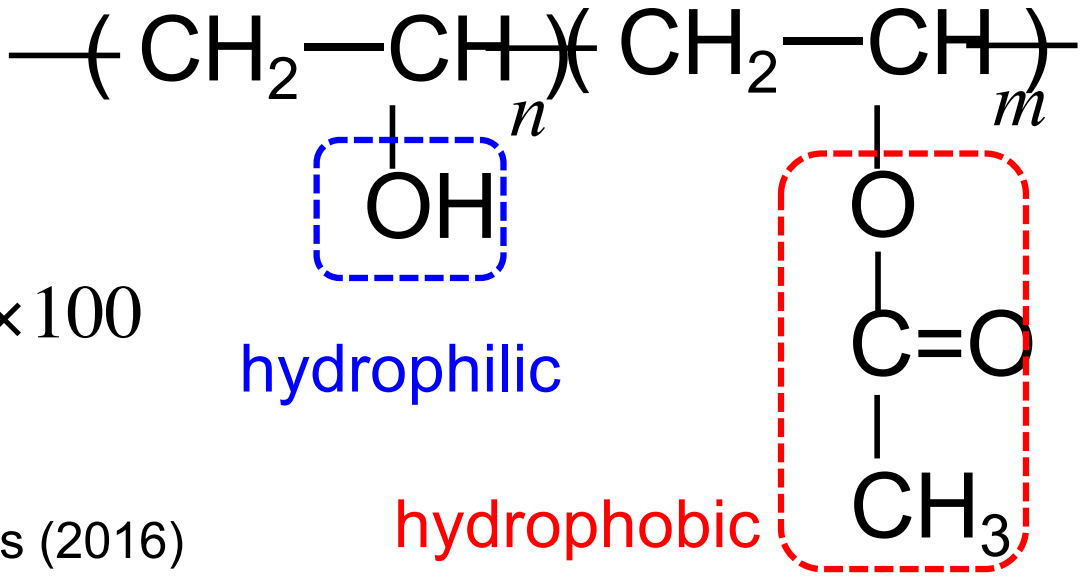
Oil phase : Ethyl acetate (EA), purity over than 99.5 %

Polymer and surfactant : Poly(vinyl alcohol) (PVA)

(1) Mw : 31000 – 50000, 98-99 % hydrolyzed (Sigma-Aldrich)

(2) Mw : 66000 – 79000, 78-82 % hydrolyzed (Wako)

(PVA)



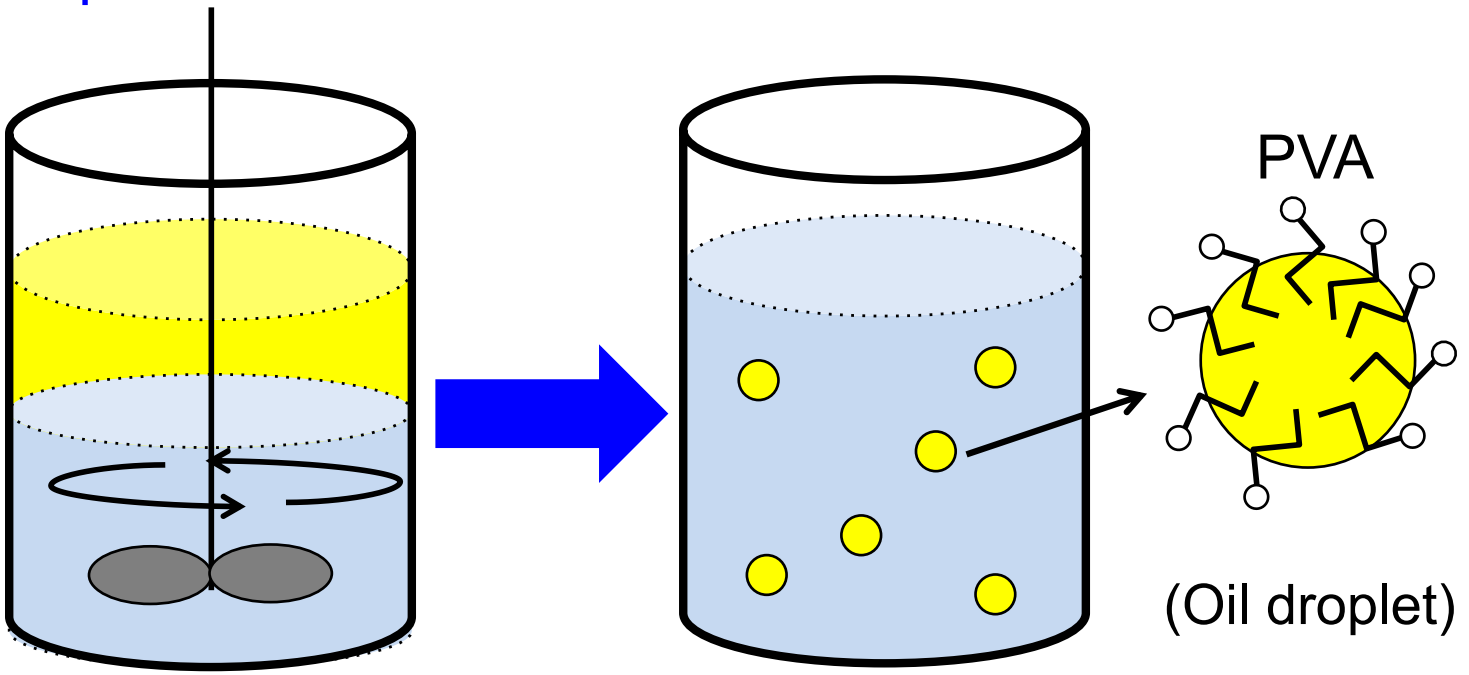
$$\text{hydrolyzed ratio} = \frac{n}{n+m} \times 100$$

Murakami, Y. et al., J. Supercrit. Fluids (2016)

Particle formation using SCF (II)

➢ Supercritical Fluid Extraction of Emulsion

PVA aqueous solution : 0.2 wt% and EA were mixed in 77 : 23 (mass)

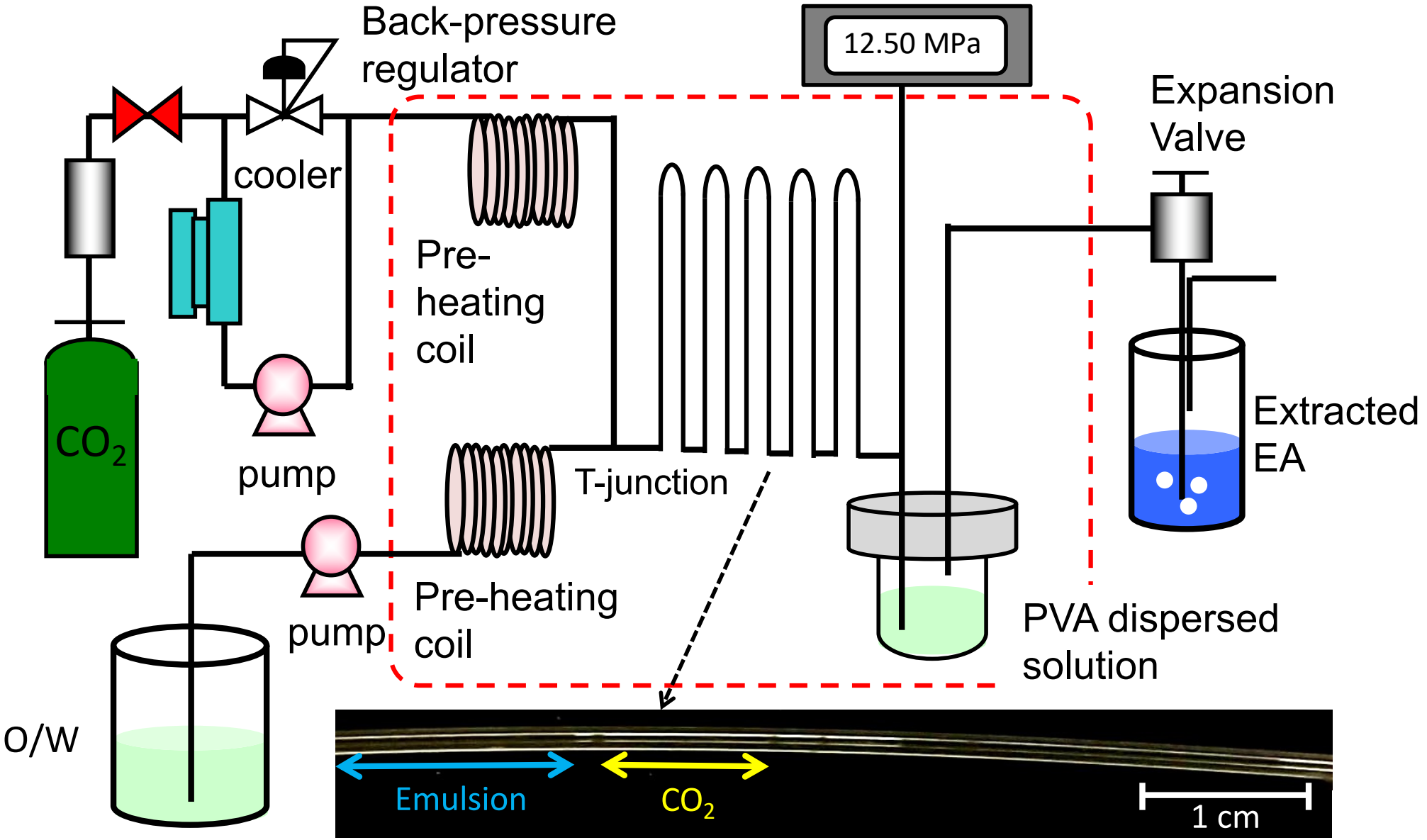


3,000 rpm for 30 min
at 10 °C

(O / W
emulsion)

Murakami, Y. et al., J. Supercrit. Fluids (2016)

Particle formation using SCF (II)



Murakami, Y. et al., J. Supercrit. Fluids (2016)

Microchannel : ϕ 0.5 mm × 1m

Particle formation using SCF (II)

➢ Supercritical Fluid Extraction of Emulsion

Condition

- Temperature and pressure : 37, 40 ^{o}C and 8 -12 MPa
- Residential time : 0.6 to 6.6 min
- CO_2 flow rate (at 1 atm) : 63 – 183 ml min^{-1}
- CO_2 and emulsion ration (mass) : 0.3 to 3.1

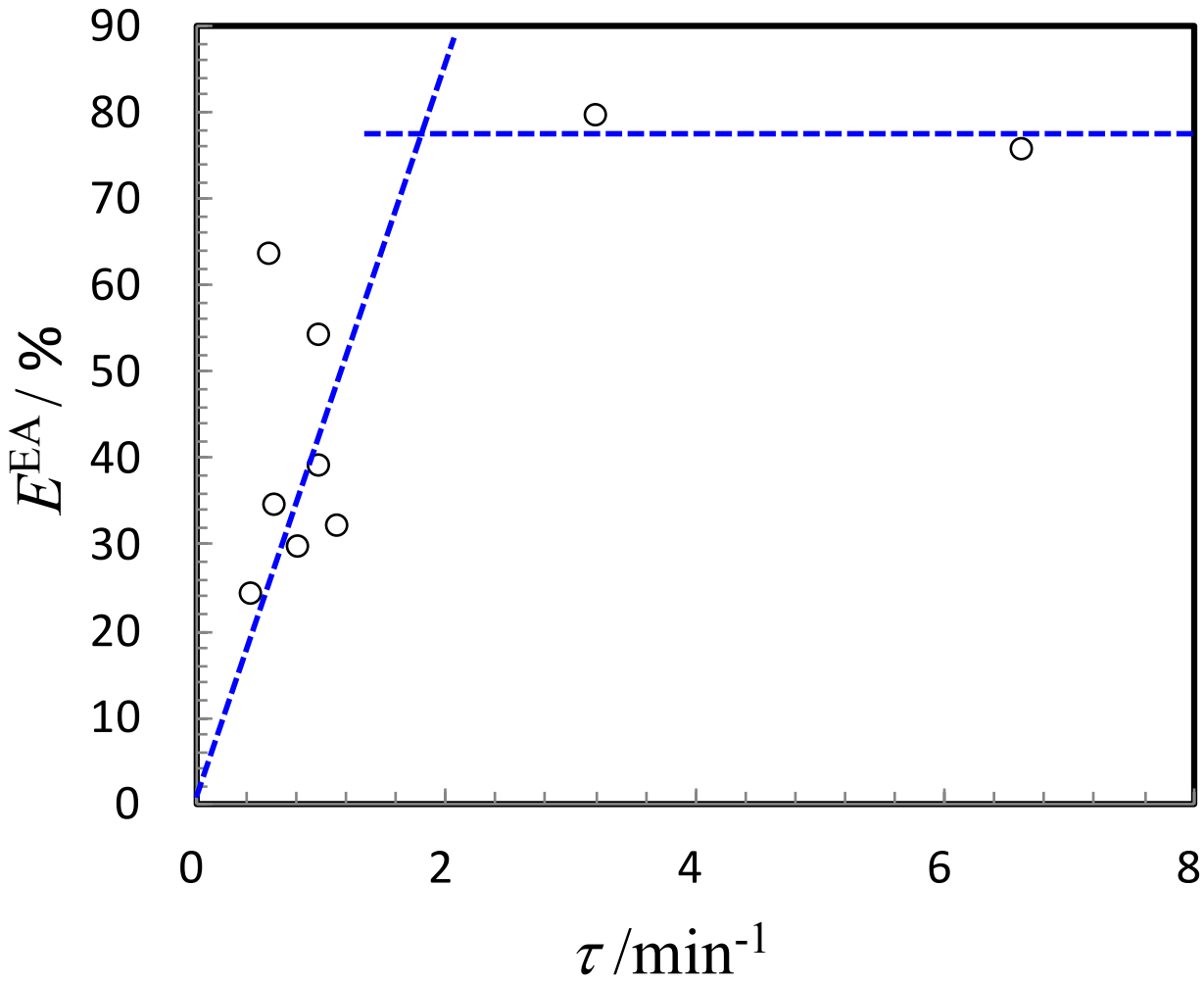
Characterization

- Gas chromatograph : Amount of extracted EA
- Dynamic Light Scattering (DLS) : particle size
- Fourier transform infrared spectroscopy (FT-IR):
  Residual EA in PVA dispersed solution

Particle formation using SCF (II)

➢ Supercritical Fluid Extraction of Emulsion

Effect of residential time on extraction efficiency



T = 37 °C, p = 8.5 MPa

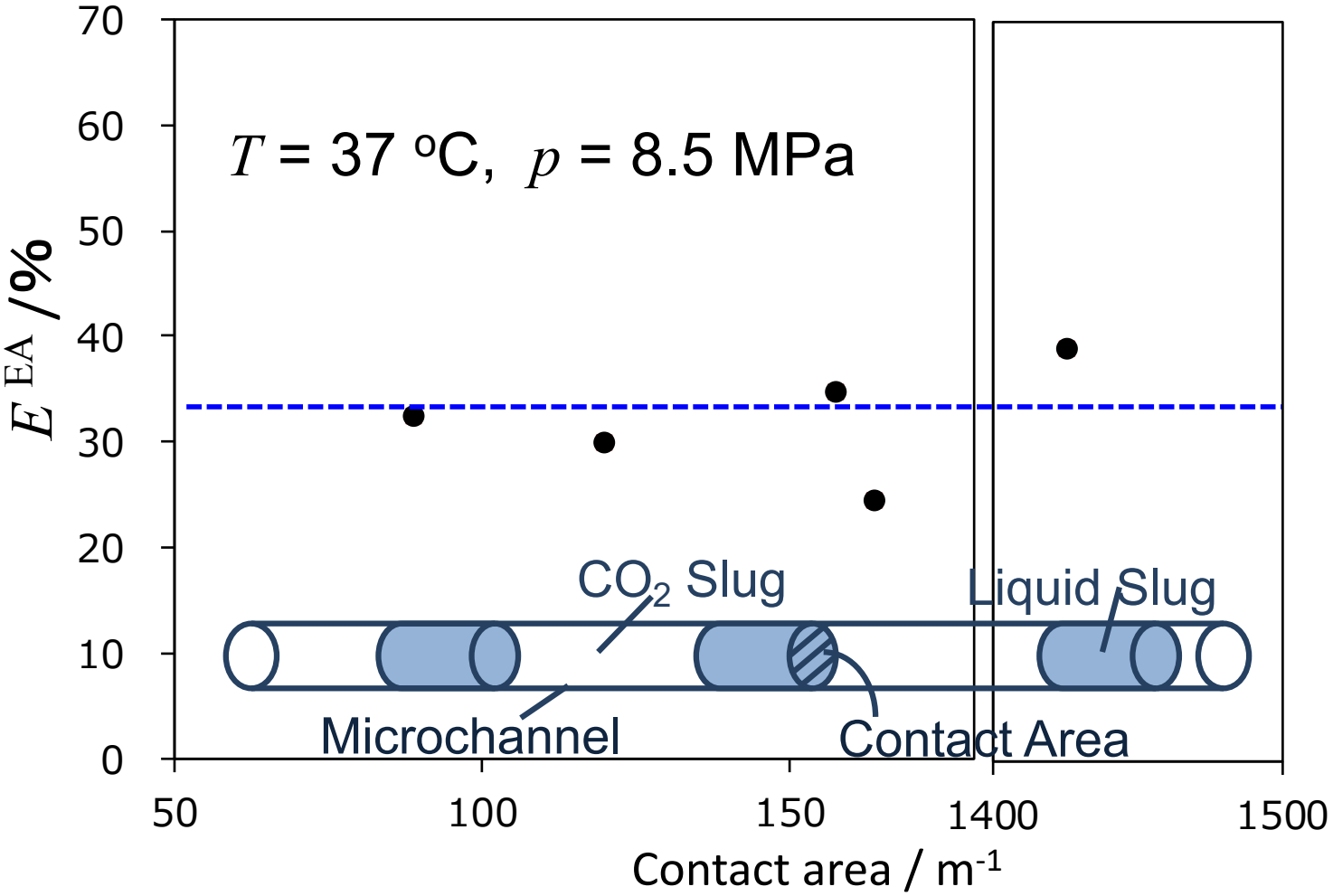
τ than 3 min

>> constant E^{EA}

Particle formation using SCF (II)

➢ Supercritical Fluid Extraction of Emulsion

Effect of contact area of CO_2/emulsion on extraction efficiency



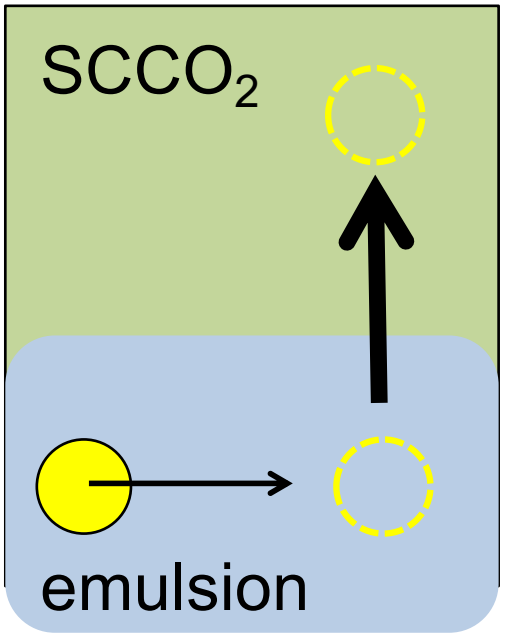
very small effect of contact area

Particle formation using SCF (II)

Q. 3.4

Discuss about (very) small effect of contact area of CO_2/emulsion on particle size formed in SFEE.

Mass transfer of EA



Particle formation using SCF (II)

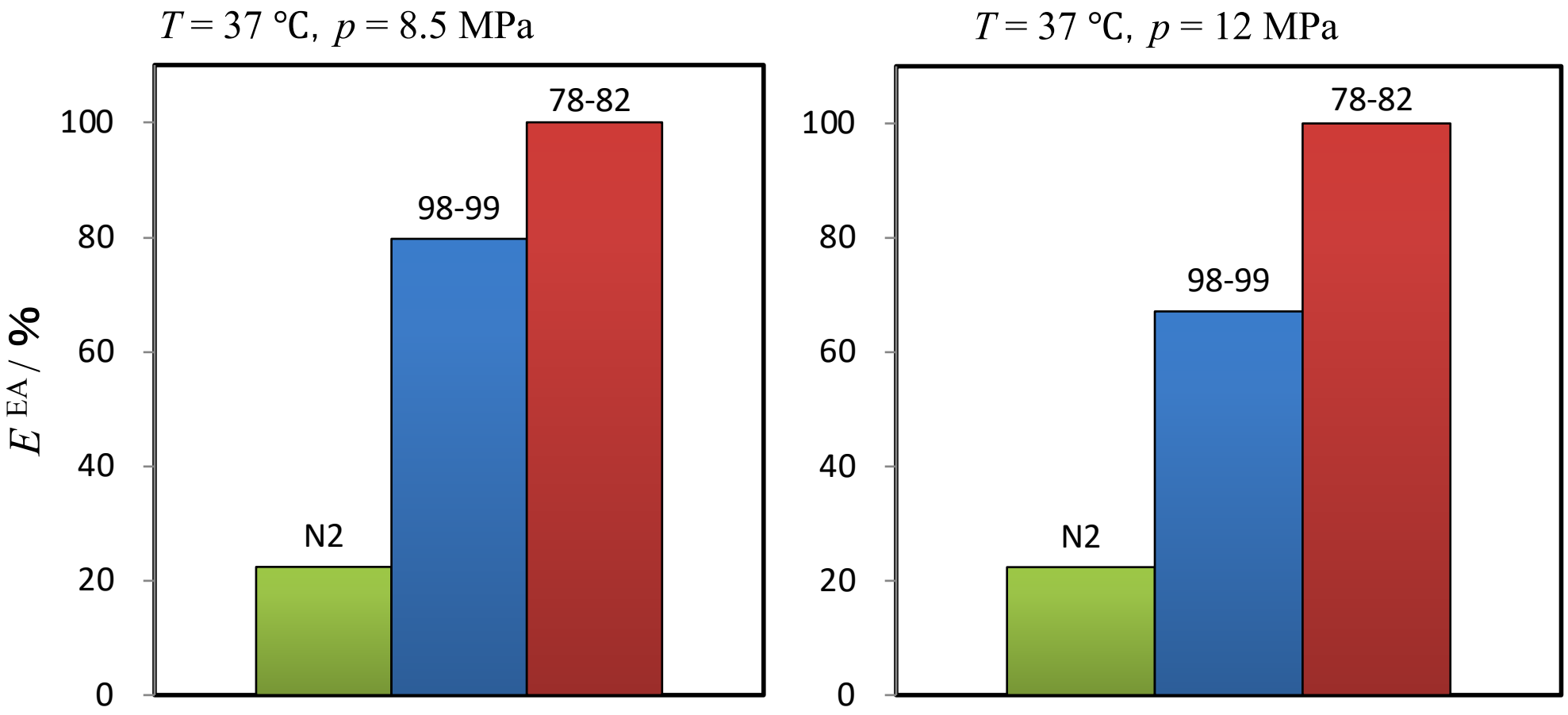
A. 3.4（Discussion）

Particle formation using SCF (II)

A. 3.4（Discussion）

Particle formation using SCF (II)

➢ Effect of surfactant hydrophobicity on SFEE



High hydrophobicity results in high extraction rate because of high affinity with CO_2. ⟶ CO_2 swelling effect on emulsion extraction

Particle formation using SCF (II)

➢ Results of particle formation via SFEE