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Solubility measurement of polyethylene glycol polymers in supercritical carbon dioxide at high pressures and temperatures

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SOLUBILITY MEASUREMENT OF POLYETHYLENE GLYCOL POLYMERS IN SUPERCRITICAL CARBON DIOXIDE AT HIGH PRESSURES AND TEMPERATURES

By

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A thesis
Presented to Ryerson University
In partial fulfillment of the
Requirement for the degree of
Master of Applied Science
In
Chemical Engineering

Toronto, Ontario, Canada, 2008
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ABSTRACT

Solubility Measurement of Polyethylene Glycol Polymers in Supercritical Carbon Dioxide at high Pressures and Temperatures

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Solubility and its measurement of different materials including polymers, drugs, proteins, peptides and many other organic or non organic compounds in supercritical fluids are of great importance in a wide variety of applications. These applications include: production of controlled drug delivery systems, powder processing, pollution prevention, spraying paints and coatings, and food processing.

Supercritical Fluids are getting more interest since the last two decades due to their abilities in replacing VOC solvents, and because of their tunable properties that could be achieved by varying their pressure and temperature in getting powerful solvents.

Supercritical fluid is a substance under pressure above its critical temperature. Under supercritical conditions the distinction between gases and liquids does not apply and substance can only be described as a fluid. Supercritical fluids have properties intermediate between those of gases and liquids, controlled by the pressure. They do not condense or evaporate to form a liquid or a gas. Fluids such as supercritical carbon dioxide offer a range of unusual chemical possibilities in both synthetic and analytical chemistry. Supercritical fluids have solvent power similar to a light hydrocarbon for most solutes.

Carbon Dioxide as supercritical fluid is the most common and useful solvent in dissolving different kinds of materials because of its unique features like non toxicity, inflammability, its low critical pressure and critical temperature values, and its low cost.

By adjusting the pressure and temperature of Carbon Dioxide above its P_c and T_c , we can modify its powerful to dissolve materials such as Polymers, Drugs, Proteins, and other organic and non organic materials.

Polyethylene Glycol polymers have a low toxicity and they are used in a wide variety of products. As a biodegradable polymer, PEG can be used alone or with other biodegradable polymers as a drug career into humans and/or animals bodies after getting dissolve with the compatible drugs or proteins in supercritical carbon dioxide.

The solubility of PEG of different molecular weights (PEG 600, PEG 1500, PEG 6000, and PEG 12000) in Supercritical Carbon Dioxide is measured at different pressures (from 15 to 50 MPa) and at temperatures (from 313 to 366 K). Also the saturation time that needed to reach the equilibrium state between the polymer and the supercritical fluid at the desired conditions is estimated. In general, the solubility of PEG in SC CO_2 increased with pressure and decreased with temperature due to the density effect of SC CO_2 which is increasing with pressure and decreasing with temperature. Almost PEG of different molecular weights is follow the same solubility pattern.

Static method is used to measure the PEG solubility and the measurement is analyzed by using a microgram scale and this method is compared with other methods.

Low molecular weight PEG polymers have higher solubility than that of high molecular weight polymers at the same supercritical conditions of P, V, and T. Mixing process was found to have a strong effect in reaching the two phase equilibrium state and in getting polymer dissolved properly. Best fitting empirical equation is used to figure out the solubility pattern and its relationship to pressure and temperature.

Acknowledgment

I would like to extend my abundant thanks to my supervisors Dr. A. Lohi, Dr. S. Upreti and Dr. J. Wu who gave me the creative ideas, precious instructions and creative advices.

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This modest work is dedicated to my lovely wife Hadeel Al Neddaff and to my dearest kids Aya and Hussien.

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Nomenclature

- p Absolute pressure (N/m²)
- c Concentration of the solute in a gas (mol/cm³)
- ρ Density (g/cm³)
- d Density of a gas (g/cm³)
- η Dynamic viscosity (g/cm.s)
- K Equilibrium constant (dimensionless)
- ϕ Fugacity coefficient (dimensionless)
- f^s, f^v Fugacity of solid and of vapor phases (N/m²)
- $\Delta H_{Solvation}$ Heat of solvation (J/g.K)
- $\Delta H_{Vaporization}$ Heat of vaporization (J/g.K)
- $H_{g,l}$ Henry's constant (N.m/mol)
- K_T Isothermal Compressibility factor (mol/cm³)
- ν Kinematic viscosity (m²/s)
- $[AB_k]$ Molar concentration of a solute in a gas (mol/cm³)
- v Molar volume (cm³/mol)
- M_A, M_B Molecular weight of the solute and of the gas (g/mol)
- θ, b Peng-Robinson Equation of state parameters.
- x_g Solubility of a gas in a liquid (wt. fraction)
- y_s Solubility of solid component in the gas phase (wt. fraction)
- $[A], [B]$ Molar concentration of a gas (mol/cm³)
- E Enhancement factor (dimensionless)
- T Absolute temperature (K)
- Z Compressibility factor (dimensionless)

(1) Introduction

(1.1) Supercritical Fluids are the Replacement of VOC

Solvents, defined as substances able to dissolve or solvate other substances, are commonly used in manufacturing and laboratory processes and are often indispensable for many applications such as cleaning, fire fighting, pesticide delivery, coatings, synthetic chemistry, and separations. Organic solvents are an important component of many industrial processes. Unfortunately, many of these solvents have adverse environmental and health effects. For these reasons, organic solvents such as halogenated hydrocarbons (e.g., chloroform and dichloromethane) are being phased out and benign replacements are being developed. Billions of pounds of solvent waste are emitted to the environment annually, either as volatile emissions or with aqueous discharge streams. Many of these solvents are known to upset our ecosystems by depleting the ozone layer and participating in the reactions that form tropospheric smog. In addition, some solvents may cause cancer, are neurotoxins, or may cause sterility in those individuals frequently exposed to them. While contained use of these solvents would be acceptable from both an environmental and a health perspective, such operations are difficult to achieve, and alternative solvents are currently being sought to minimize the problems inherent in solvent release to the environment. Many commonly used solvents and extractants are hazardous materials. [1]

The most novel substitutes are supercritical fluids as solvents in replacing volatile organic compounds and also to remove organic compounds from hazardous mixtures and contaminated materials. Using supercritical carbon dioxide as a solvent offers several advantages over conventional organic solvents including minimizing of organic liquids and gases waste generation. SC CO₂ solvent strength and its low viscosity dependence on temperature and pressure make SC CO₂ attractive for organic compounds replacement.

Figure 1.1, represents the fields that can be used in replacing hazardous organic compounds. [1]

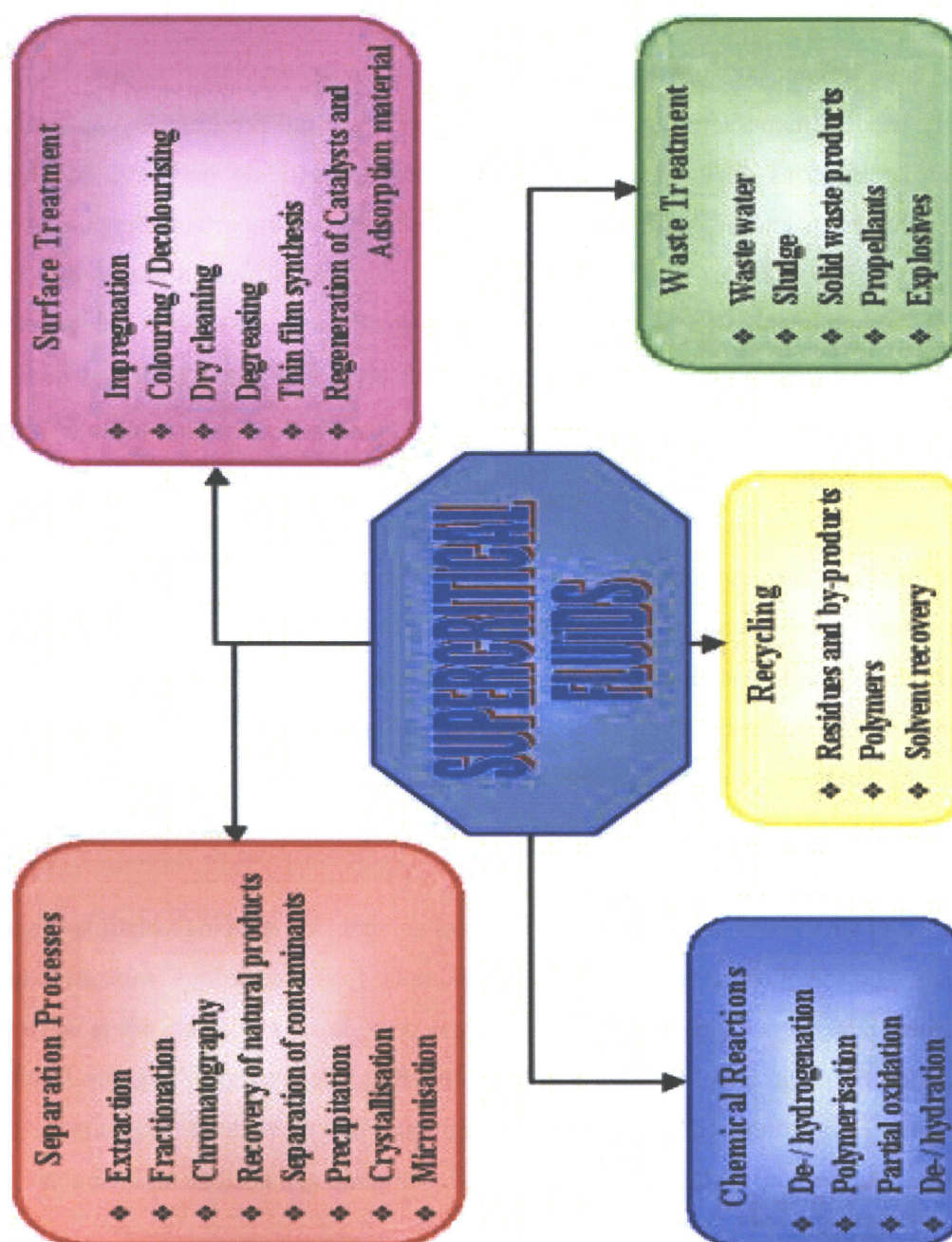


Figure (1.1) Supercritical fluids usage fields. [1]

One approach to the prevention of pollution and the reduction of worker exposure from conventional solvents is the use of less hazardous substitutes. In the supercritical state, fluids exhibit unique solvent properties. Separation of the supercritical fluid from the extracted materials can be accomplished by pressure reduction, adsorption onto activated carbon, or with a membrane process, e.g., decaffeination of coffee. Supercritical fluid extraction has been studied extensively on a laboratory scale to remove organic compounds from hazardous mixtures and contaminated waters. Many such systems have been employed commercially.

Supercritical fluid is any substance above its critical temperature and critical pressure. In the supercritical region there is only one state-of-the-fluid and it possesses both gas- and liquid-like properties. It is a gas above its critical temperature that has free mobility of the gaseous state but with increasing pressure its density will increase towards that of a liquid. Supercritical fluids are such high compressed gases and as such they combine valuable properties of both liquid and gas.

Supercritical fluid exhibits physicochemical properties intermediate between those of liquids and gases. Characteristics of a supercritical fluid are: dense gas, solubilities approaching liquid phase, diffusivities approaching gas phase. Supercritical fluid represents the phase of a compressible gas that is found beyond the critical temperature in which a gas will not compress to a liquid, even with the application of high pressures. Below the critical temperature, a gas will compress to its liquid state if enough pressure is applied.

Mass transfer process is rapid with supercritical fluids. Their dynamic viscosities are closer to those found in normal gaseous states. In the vicinity and beyond the critical point, the diffusion coefficient is more than ten times that of a liquid. As is the case for density, both the viscosity and diffusivity are dependent on temperature and pressure. Changes in viscosity and diffusivity are more pronounced in the region of the critical point. [2]

Thus we can say that:-

- Under supercritical conditions, there are no limits between gases and liquids and then the substance can only be described as fluid.
- Supercritical fluids have properties intermediate between those of gases and liquids, controlled by the pressure.
- They do not condense or evaporate to form a liquid or a gas.
- Supercritical fluids have tunable solvent power due to their sensitive density with changes in pressures and temperatures.
- The supercritical fluids (SCF) are completely miscible with industrial gases (e.g. N_2 or H_2) and this leads to a much higher concentration of dissolved gases than can be achieved in conventional solvents.

Supercritical fluids offer advantages in textile processing as they combine the unique properties as solvents of both gas and liquid. The solvating power of supercritical fluid is proportional to its density, whereas its viscosity is comparable to that of a normal gas. Such a combination leads to highly remarkable penetration (penetration of supercritical fluids in solutes) properties. Increasing the supercritical fluids solvation power by increasing their density is desirable in the polymer processing processes.

Liquids and gases have uniform density in a given system, whereas supercritical fluids have clusters of molecules with high local density that is much greater than the bulk density of the system. This clustering of the molecules allows supercritical fluids to have some important liquid-like physical properties that result in liquid-like solubility for many solutes (like polymers) in supercritical fluid solvents. The distance between clusters allows for important gas-like physical properties in terms of viscosity, surface tension, and diffusivity. [2]

(1.2) Carbon Dioxide as Supercritical Fluid

The process that makes supercritical fluids useful as solvents should be processed at high pressures and some times at high temperatures. The solvents are frequently chosen on the basis of suitability of the temperatures and pressures corresponding to the supercritical region of the substance. There are some other factors that will limit the use of supercritical fluids as solvents; these factors include toxicity, cost, availability, and environmental effects.

According on the above factors, supercritical carbon dioxide is the most preferable solvent. Carbon dioxide is a readily available, cheap, recyclable and is non-toxic and non-flammable. Above the temperature of 31.1°C and pressure of 73.8 bar carbon dioxide exhibits physical properties which they are intermediate between those of gases and liquids. Figure 1.2 explains the phase diagram of carbon dioxide and shows the triple and critical points. The supercritical conditions are readily achievable using commercially available equipment. Supercritical carbon dioxide is able to dissolve a range of chemical substances including organic substrates, catalysts, and light gases. Its main advantage however comes from the fact that this solvent can be easily turned into a gas by simply releasing the pressure leaving no solvent residues and requiring no evaporation or separation.

SC CO_2 is widely used as an alternative to conventional solvents (such as volatile organic solvents) with numerous applications such as: extraction and purification of specialty chemicals and useful natural products (such as biopolymers and biomaterials), an alternative solvent in coatings industry, (replacing 40-90% of volatile solvents), degreasing and dry cleaning applications. It is also increasingly applied as a solvent in synthetic industrial processes (such as synthetic polymers and biodegradable polymers).

[4]

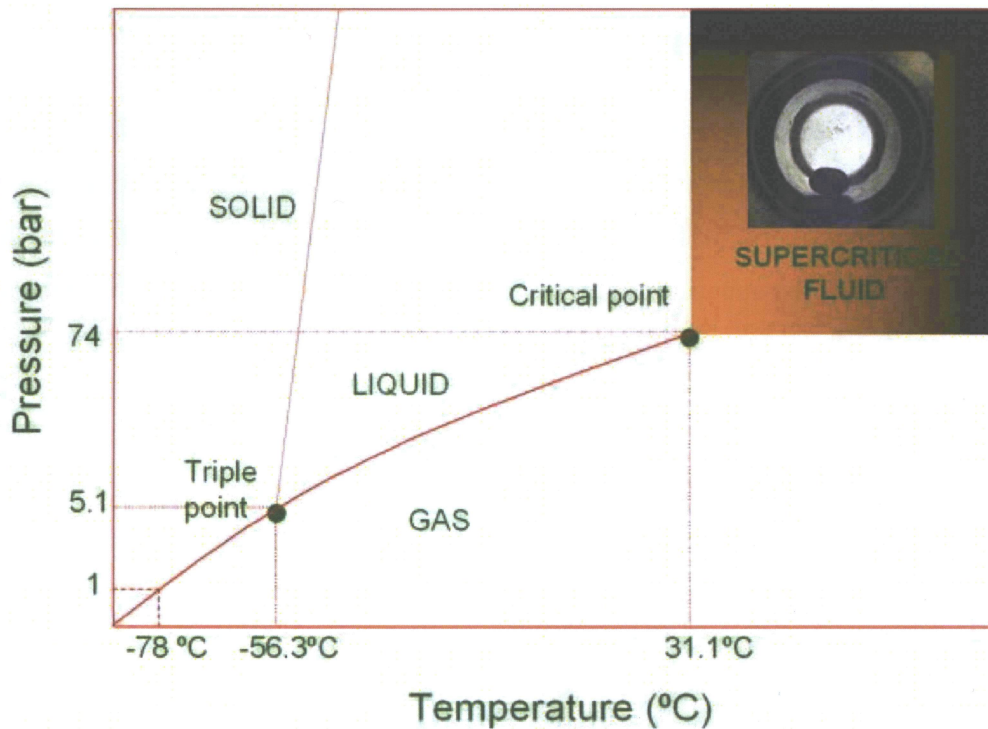


Figure (1.2) Carbon Dioxide Phase Diagram, [3]

Carbon dioxide is frequently used as a solvent because of its special properties: -

- Carbon dioxide does not affect the edibility of foodstuffs and will have toxic effects at extremely high concentrations.
- It is produced on the commercial scale and is readily available together with the necessary logistics.
- No disposal problems. It is recovered from the process in the form of an uncontaminated gas and can be reused.
- Being easy to handle and combustible.
- The critical point of the carbon dioxide is within the range which is readily manageable by technical means(31.1 °C and 73.8 bar)
- It is non-toxic, non-hazardous and has low cost.
- It is nonflammable and non-corrosive
- Processing with supercritical carbon dioxide often generates no waste stream.
- Maintenance and running cost for wastewater treatment and drying process is not necessary.

(1.3) Producing Nano-Particles using Supercritical Fluids

The basis of nanotechnology is the ability to form nano-sized particles, which are solid particles, usually comprised of three to five molecules together.

Nano powders have been of extreme interest in the pharmaceutical field. Drug delivery has been impacted in several ways due to the advances in nano powder technology. Smaller particles are able to be delivered in new ways to patients, through solutions, oral or injected, and aerosol, inhaler or respirator. New production processes allow for encapsulation of pharmaceuticals which allow for drug delivery where needed within the body. Dosing of pharmaceuticals had also improved. Smaller particles mean better absorption by the body therefore less drug is needed. Because of a combination of these, side effects are lessened due to better use of pharmaceuticals.

Particles formation process is the biggest challenge that the chemical engineers and pharmacutists faced in the last decade to use supercritical fluids as solvents or non solvents to precipitate a very fine particles with specific shapes.

In recent years, SC CO₂ techniques have emerged as a promising method for precipitating particles from solution with the traditional environmental and tunable solvent advantages while also leaving particles solvent-free. In particular, these novel methods provide a feasible and clean way to process thermal-labile or unstable biological compounds, such as the promising application in the development of drug-delivery systems. [5] One of the most important applications of supercritical fluid technology for the last two decades is particle formation. Methods for particles formation using supercritical fluids include rapid expansion of supercritical solutions (RESS) and the supercritical anti-solvent (SAS) process.

CO₂ is a great choice for processing pharmaceutical products due to its relatively accessible critical point and its low toxicity. Since most organic solvents are miscible with supercritical CO₂, a low residual solvent content can be achieved in the final product. Measuring the solubility of biodegradable polymers and comparing it with the solubility of active materials (e.g. drugs and proteins), is the key to use the proper process and proper supercritical fluid in producing nano particles of drug career systems.

(1.4) Solubility of Polymers in Supercritical Fluids

Solubility of polymers in supercritical fluids has a unique mean toward finding the proper process (such as rapid expansion of supercritical solution, gas anti-solvent, supercritical anti-solvent and particles from gas saturated solution) in affecting polymers processing, and also in investigating how the supercritical fluid will serve as solvent, anti-solvent or solute. Solubility can be the most affecting property on the rate, yield, design and economy of processing polymers using supercritical fluids. Many factors may affect the solubility of polymers in supercritical fluids, including; polarity of the polymer, polymer chain length, end functional groups, polymer molecular weight, and polymer-SC Fluid interaction. In addition to all these factors the supercritical conditions of pressure and temperature are playing the rule of thumb in modifying the solubility. In addition to the advantage of controlling the solvent power by adjusting its density, there are other advantages in using supercritical fluids as solvents. High diffusivity and low viscosity of supercritical fluids give them a unique ability to penetrate into polymers in an efficient way much better than other traditional liquid solvents. [6]

Affecting the properties of polymers when they process with supercritical fluids is an important issue. Several supercritical fluids-based processes take full advantage of the change in melting point of crystalline polymers especially when forming coated particles.

The pressures and temperatures needed to dissolve a given polymer in a supercritical fluid solvent depend intimately on the polymer architecture, which fixes both the strength and type of intermolecular interactions and the free volume of the polymer. Branching of such polymers increases the free volume of the polymer which makes it easier to dissolve in a supercritical fluid solvent and also, branching reduces the intermolecular interactions between polymer segments. Since branching has an impact on the polymer phase behavior, end groups can have a significant effect on the phase behavior of polymers in supercritical fluids (when they used as solvents), especially when the chemical structure of the end group differs from the groups in the main chain.

(2) Theoretical Background

In this chapter there is an explanation of supercritical fluids phase behavior represented by P-V-T Figure 2.1, and also the behavior of polymers solubility in supercritical fluids. By understanding the pattern of polymer solubility, we can figure out the pressure and temperature impacts on this specific solubility.

(2.1) Phase Behavior of Supercritical Fluids

The common and typical P-V-T phase diagram of a pure component can be drawn as shown in Figure 2.1. At triple point all three phases can coexist at same temperature and pressure, also at this point there will be a phase-equilibrium of fusion, vaporization and sublimation. The boiling point line starts from triple point and ends at critical point. Along this curve, both temperature and pressure increase continuously, and they are equal for the two phases (liquid and vapor) in equilibrium.

Other thermodynamic properties such as volume, enthalpy, entropy and internal energy are vary along the vaporization curve but they also not equal for the liquid and vapor phases when they are in equilibrium. As the critical point is approached, all of thermodynamic properties of the two phases (liquid and vapor/gas) gradually become equal. At the critical point all of the properties of the two phases are equal and these phases become a single continuous phase.

In equilibrium systems the critical point is reached only by tuning a control parameter, which is the pressure mostly. In supercritical systems, pressure has the most dominant and direct effect in tuning the supercritical fluid density. [6]

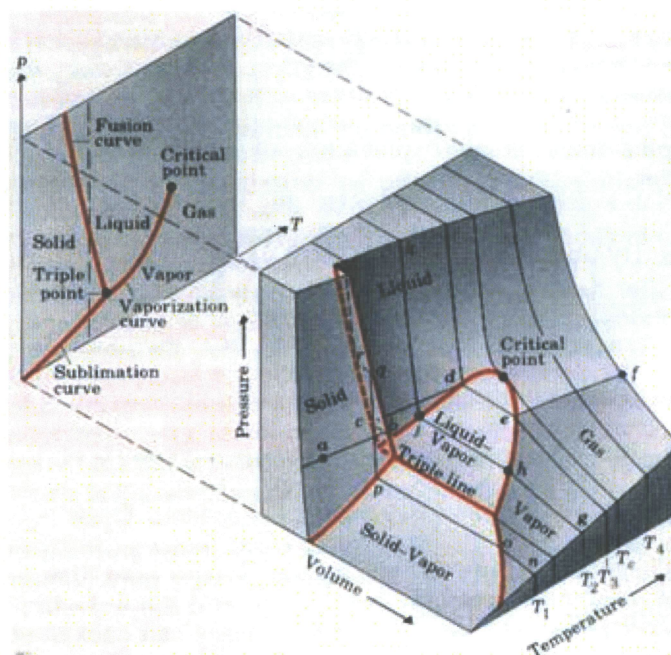


Figure (2.1) P-V-T Phase Diagram for a pure component. [7]

The lines above the critical point are continuous and monotonic with a negative slope $(\partial p / \partial v)_T$. Below the critical point, horizontal lines which represent the isotherms and the length of these lines represent the difference between molar volume of liquid and of gas phases when they are at equilibrium. As the temperature is raised toward the critical temperature, the properties of the phases approach each other, and finally becoming identical at the critical point (in equilibrium). The isotherm at the critical temperature is characterized by a horizontal inflection point at the critical point. Thus, at the critical pressure the compressibility of the pure component at constant temperature becomes infinite. Above the critical temperature and pressure, the region will follow the supercritical conditions (temperature and pressure will be higher than the critical ones). [6] As shown in table 2.1, the properties of supercritical fluids are in between of liquids and gases. The density of supercritical fluids will be less than that of liquids but much more than that of gases.

Table A.1 in Appendix A, shows the critical properties (temperature, pressure and density) of the most common solvents.

The diffusivity of supercritical fluids is significantly higher than that of liquids, while it is lower than that of gases as shown in Table 2.1. The combination of these two properties (density and diffusivity), makes supercritical fluids much better solvents than would be expected. This quite true when the temperature and pressure of supercritical fluids are not too far above the critical conditions. [6]

Table (2.1) Physical properties ranges of gases, supercritical fluids and liquids. [6]

Property	Density (kg/m ³)	Viscosity (cP)	Diffusivity (mm ² /s)
Gas	1	0.01	1 – 10
SCF	100 – 800	0.05 – 0.1	0.01 – 0.1
Liquid	1000	0.5 – 1.0	0.001

At the critical point, there will be:

- One phase,
- Divergence of Isothermal Compressibility K_T (is a measure of the relative volume change of a fluid or solid as a response to a pressure change at constant temperature).

At critical point $(\partial P / \partial V) = 0$, the isothermal compressibility is $K_T = (-1/V)(\partial V / \partial P)_T$. At the critical point, if the temperature of the fluid has been raised just above its critical value, the isothermal compressibility of this fluid K_T will be much higher than that of real gas. So, at the critical point we can generate high densities of fluids at low cost. The evolution in isothermal compressibility K_T is related to the pressure variation ΔP which is induced by a 1% volume reduction of a closed system. The relationship between K_T and ΔP for the supercritical fluid shows that supercritical fluid is not much compressible and can be used as a reactive or mass-transfer fluid for materials processing. The difference in behavior of fluid density and viscosity induces that the relative importance of natural convection (as measured by the ratio of buoyancy to inertial forces) is two orders of magnitude higher in supercritical fluid than in a liquid (at constant Reynolds number). Also, the kinematic viscosity ν (dynamic viscosity η /density ρ of fluid) is very low in supercritical region which is important for mass transfer applications. [2]

(2.2) Solubility of Solids and Liquids in Compressed Gases

The most important and remarkable property of gases when compressed to above their critical pressures is their ability as solvents which is directly related to their high density. The higher mass transfer characteristics, related to high diffusion coefficients at low viscosity are other favorable property of dense gases. The extent at which solids and liquids can be dissolved in compressed gases (i.e. supercritical fluids) is varying enormously according to the small changes in pressure and/or temperature that will affect the gases density and also related properties such as solvent power.

Understanding the solubility pattern of solids and liquids in dense gases requires well knowledge of high pressure phase behavior of the mixtures (solutes + solvents) especially when we deal with low volatile liquids and solids as solutes in high pressure gases as solvents.

It is very difficult to predict P-V-T phase data at high pressure because of highly complex systems which differ significantly according to molecular size, shape, structure, and polarity which is giving a shift in phase behavior. Because of the diverge in partial molar properties of most solutes at the critical point, the properties of the system (solute + high pressure gases) will be very sensitive to any change in temperature and/or pressure which leads to serious difficulties in system description and of solubility prediction. Understanding and measuring the solubility of solids and liquids in compressed gases, and studying the effects of temperature and pressure on this solubility can not be dealt as a classical thermodynamic problem.

The difficulties in predicting the solubility of pure solvents in dense gases are due to the absence of accurate equations of state that can express the fugacity coefficients over ranges of inherent as a function of temperature, pressure and composition. It can be seen that at relatively low pressures, the solubility falls off by an order of magnitude for rising temperature, whereas at high pressures, the solubility will increase with increasing temperature. [8]

There are two basic motivations to measure experimentally the solubility of solids and liquids in supercritical fluid solvents; first is to get the data of direct use for systems of such a degree of complexity that any prediction is difficult or impossible. Secondly, there is a great need for accurate experimental data on equilibrium properties of well defined dense fluid mixtures involving different types of molecular interactions. These data are prerequisites for developing and verifying the new theoretically based accurate and possibly predictive thermodynamic models. [8]

Fugacity and Fugacity Coefficient:

Fugacity f is a measure of chemical potential in the form of adjusted pressure. Fugacity relates directly to the tendency of a substance to refer one phase (liquid, solid or gas) over another. As well as predicting the preferred phase of a single substance, fugacity is also useful for multi-component equilibrium involving any combination of solid, liquid and gas equilibrium. It is useful as an engineering tool for predicting the final phase and reaction state of multi-component mixtures at various temperatures and pressures without doing the actual lab test. Fugacity could be considered a “corrected pressure” for the real gas, but should never be used to replace pressure in equations of state (or any other equations for that matter). Fugacity is strictly a tool, conveniently defined so that the chemical potential equation for a real gas turns out to be similar to the equation for an ideal gas.

Fugacity coefficient is defined as the ratio fugacity/pressure. For gases at low pressures (where the ideal gas law is a good approximation), fugacity is roughly equal to pressure. Thus, for an ideal gas, the ratio f/P is equal to one. In order to understand the solid solubility in supercritical fluids, it is necessary to understand the fugacity coefficient evolution as a function of composition and density. For solubility of both solids and liquids in supercritical fluids, it is necessary to calculate the fugacity coefficients for the pure component in supercritical fluids. This calculation requires use of equation of state to describe the phase behavior in the supercritical region. Peng-Robinson cubic equation of state is one of the most famous equations that have been used to describe the phase behavior of the solubility of pure or mixture in supercritical fluids. [9]

Solubility of Solids in Compressed Gases:

In any phase equilibrium calculation and when one of the phases is gas under high pressure, it is necessary to consider the calculation of vapor-phase fugacity coefficients. Vapor-phase fugacity coefficients are particularly important for calculating the solubility of a solid in dense gases because in such cases failure to include corrections to gas-phase non-ideality can lead to big errors. For the solubility of solids in compressed gases, we can assume that the solubility of this gas in the solid is negligible; therefore we can consider the solid in this case is pure.

In general, the solubility of pure solids (or any heavy component) in gas phase can be represented as: [8]

$$Y_2 = \frac{P_2^s}{P} E \dots\dots\dots (A)$$

$$\text{Where: } E \equiv \frac{\phi_2^s}{\phi_2} \exp \left(\int_{P_2^s}^P \frac{v_2^s}{RT} dp \right) \dots\dots\dots (B)$$

Where: Y_2 is the solubility of solid in gas phase,

ϕ_2^s is the fugacity coefficient at saturation pressure P_2^s , where subscript 2 stands for solid component,

v_2^s is the solid molar volume.

E is called the **enhancement factor**, it is always greater than unity, and it is considered as correction factor that must be applied to the simple (ideal gas) expression valid only at low pressures. The enhancement factor provides a measure of the extent that the pressure enhances the solubility of solids in the gas; as $P \rightarrow P_s^s, E \rightarrow 1$. It is a dimensionless measure of solvent power because it is the ratio of the observed solubility to the ideal-case solubility. E factor increases with the size of the solute molecule, which indicates that the solvation forces are in relation to the molecule number in interaction with the solute. E is very sensitive to the nature of the solvent and may vary up to 8 orders of magnitude as a function of density. [8]

Solubility of Liquids in Compressed Gases:

This situation is more complicated than the solubility of solids in compressed gases case, because gas is soluble to an appreciable amount in liquids. So, we can not here consider the liquid is free of gas as we did with solid phase. [8]

In general, the solubility of heavy liquids in dense gases can be expressed as:

$$Y_2 = \frac{(1 - X_1)P_2^s \varphi_2^s \exp\left(\int_{p_2^s}^p \frac{V_2^l}{RT} dp\right)}{\varphi_2 P} \dots\dots\dots (C)$$

Where X_l is the solubility of a gas 1 in a liquid 2 (where subscript 1 stands for gas component and subscript 2 stands for liquid component) and it can be calculated from:

$$X_1 = \frac{Y_1 \varphi_1 P}{H_{1,2} \exp\left(\int_{p_2^s}^p \frac{V_1^\infty}{RT} dp\right)} \dots\dots\dots (D)$$

Where: Y_l is the solubility of a gas in a liquid,

φ_1 is the fugacity coefficient of the gas,

\overline{V}_1^∞ is the partial molar volume of the gas in the liquid phase,

$H_{1,2}$ is the Henry's constant.

when the gas is partially soluble in the liquid Henry's Law can be used to estimate the liquid-phase fugacity of the liquid. [8]

It is necessary to use trial-and-error to solve equation (C), because all X_g, φ_g and φ_l are depend on the composition of the vapor. Henry's Constant must be determined experimentally, or can be estimated by using a suitable correlation. [8]

Due to the Peng-Robinson equation of state, the fugacity coefficient can be calculated as follows: [9]

$$\ln \hat{\phi}_i = \frac{\hat{b}_i}{b} (Z - 1) - \ln [Z(1 - b/V)] + \frac{\theta}{bRT} \left(\frac{\hat{b}_i}{b} - \frac{\hat{\theta}_i}{\theta} - 1 \right) * \frac{1}{2\sqrt{2}} \ln \left[\frac{1 + (1 + \sqrt{2}) * b/V}{1 + (1 - \sqrt{2}) * b/V} \right]. \quad (\text{E})$$

$$Z = \frac{1}{1 - b/V} - \left(\frac{\theta}{bRT} \right) * \frac{b/V}{1 + 2(b/V) - (b/V)^2} \dots\dots\dots (\text{F})$$

Where: Z is the compressibility factor and the quantities θ, b represent the equation of state parameters.

Where:

$$\hat{\theta}_i = \left[\frac{\partial(n\theta)}{\partial n_i} \right]_{T,V,n_j}, \quad \hat{b}_i = \left[\frac{\partial(nb)}{\partial n_i} \right]_{T,V,n_j}$$

The calculation of solubility of solids and liquids in supercritical fluids is still problematic. The most commonly used equations of state, cubic equations of state, are well known to be inadequate to the proper description of the critical region. [9]

(2.3) Modeling Solubility in Dense Gases at Equilibrium State

Chastill, in 1982 [10] formed a new model to describe and to predict the solubility of pure components in dense gases, this model is related the solubility directly to the density (concentration) of the gas avoiding the complexity of the equations of state. The assumptions that he used are:

- The molecules of a solute associate with the molecules of a gas in formation solution complex are in equilibrium with the gas.
- The equilibrium concentration can be calculated from the mass action.

In an ideal case if one molecule of a solute A associates with k molecules of a gas B to form one molecule of a solution complex AB_k in equilibrium,

We can write: $A + kB \leftrightarrow AB_k$

$$\text{So, } K = \frac{[AB_k]}{[A][B]^k} \dots\dots\dots (G)$$

$$\text{And } \ln K + \ln[A] + k \ln[B] = \ln[AB_k] \dots\dots\dots (H)$$

Where: $[A]$ is the molar vapor concentration of a solute,

$[B]$ is the molar concentration of a gas, and

$[AB_k]$ is the molar concentration of a solute in a gas,

K is the equilibrium constant, which can be expressed as:

$$\ln K = \frac{\Delta H_{\text{solvation}}}{RT} + q_s \dots\dots\dots (I)$$

Where: $\Delta H_{\text{solvation}}$ is the heat of solvation, and q_s is a constant.

The vapor concentration of the solute $[A]$ can be approximated by the Claperon-Clausius

$$\text{equation: } \ln[A] = \frac{\Delta H_{\text{vaporization}}}{RT} + q_v \dots\dots\dots (J)$$

Where: $\Delta H_{\text{vaporization}}$ is the heat of vaporization of the solute, and q_v is a constant.

Usually $[A] \ll [AB_k]$, when we combine all of the above relations we will end up with:

$$\frac{\Delta H}{RT} + q + k \ln[B] = \ln[AB_k] \dots\dots\dots (K)$$

Where: ΔH is the total heat of reaction $\Delta H = \Delta H_{\text{Solvation}} + \Delta H_{\text{Vaporization}}$, and $q = q_s + q_v$.

It is convenient to express the concentration and the density as:

$$[AB_k] = \frac{c}{(M_A + kM_B)}, \text{ and } d = [B] * M_B$$

Where: c is the concentration of the solute in a gas, d is the density of a gas.

M_A, M_B Are the molecular weights of the solute and of the gas respectively.

So, we can get:

$$\frac{\Delta H}{RT} + q + k \ln d - k \ln M_B = \ln c - \ln(M_A + kM_B) \dots\dots\dots (L)$$

And thus we can write the (L) relation as:

$$c = d^k * e^{\left(\frac{a}{T} + b\right)} \dots\dots\dots (M)$$

Where: k is an association number, $a = \frac{\Delta H}{R}$ and $b = \ln(M_A + kM_B) + q - k \ln M_B$.

Because the approximation of $\ln[A] = \frac{\Delta H_{\text{Vaporization}}}{RT} + q_v$ is not quite accurate over a wide

range of temperatures T , it can cause an error in solubility calculations.

Constant b depends on the molecular weight of both the gas and the solute and on their melting points. [10]

(3) Literature Review

In this chapter, the latest studies that dealing with supercritical fluids/polymers systems in general, and SC CO₂/PEG systems in specified are listed.

(3.1) Bio- and Biodegradable Polymers

Biopolymers are a class of polymers that can be produced by living organisms. There are many examples of biopolymers like starch, DNA, RNA, and proteins, in which the monomer units are sugars, nucleic acids and amino acids. Biopolymers have a well defined structure, chemical composition, and the sequence in which their units are arranged in what is called the primary structure. They miss their molecular mass distribution because they all alike when they made of same kind of protein (for example) and they all contain the same sequence and number of monomers and thus they all have the same mass distribution. This phenomenon is called mono-dispersity which is in contrast to the poly-dispersity that encountered in other polymers. [11]

Some biopolymers, such as poly-lactic acids can be used as plastics, replacing the need for polystyrene or polyethylene based plastics. Some of the biodegradable polymers can break down with exposure to sunlight (e.g. Ultra-Violet Radiation), water (or humidity), bacteria, enzymes, wind and some instances rodent pest or insect attack or any other environmental degradation. [11]

The earliest of these polymers were originally intended for other, non-biological uses, and were selected because of their desirable physical properties, for example:

- Poly (urethanes) for elasticity.
- Poly (siloxanes) or silicones for insulating ability.
- Poly (methyl methacrylate) for physical strength and transparency.
- Poly (vinyl alcohol) for hydro-philicity and strength.
- Poly (ethylene) for toughness and lack of swelling.
- Poly (vinyl pyrrolidone) for suspension capabilities.

To be successfully used in controlled drug delivery manufacturing, a material must be chemically inert and free of leachable impurities. Some of the materials that are currently being used or studied for controlled drug delivery include: Poly (2-hydroxy ethyl methacrylate), Poly (N-vinyl pyrrolidone), Poly (methyl methacrylate), Poly (vinyl alcohol), Poly (acrylic acid), Poly-acrylamide, Poly (ethylene-co-vinyl acetate), Poly (ethylene glycol), and Poly (methacrylic acid).

However, in recent years additional polymers designed primarily for medical applications have entered the arena of controlled release. Many of these materials are designed to degrade within the body, among them: poly-lactides (PLA), poly-glycolides (PGA), poly-(lactide-co-glycolides) (PLGA), poly-anhydrides, and poly-orthoesters. Originally, poly-lactides and poly-glycolides were used as absorbable suture material, and it was a natural step to work with these polymers in controlled drug delivery systems. The greatest advantage of these degradable polymers is that they can break down into biologically acceptable molecules that are metabolized and removed from the body via normal metabolic pathways.

Polymers with low molecular weight or composed of shorter hydrophobic blocks are more soluble in water than high molecular weight polymers or composed of longer hydrophobic blocks. In general, degradation time will be shorter for low molecular weight, hydrophilic polymers and amorphous polymers.

The biodegradable polyesters are all strongly hydrophobic polymers, and this causes some limitations in practical drug formulations. To add hydrophilic and other physico-chemical properties, polyethylene glycol, PEG, has been incorporated into biodegradable polyesters. [11]

PEG is a non-toxic, water soluble polymer with proven biocompatibility. Block copolymers consisting of hydrophobic polyester segment and a hydrophilic PEG segment have attracted large attention due to their biodegradability and biocompatibility.

A wide variety of drug formulations, such as micro/nano-particles, micelles, hydro-gels, and injectable drug delivery systems have been developed using poly(lactic-co-glycolic-acid) – polyethylene glycol block copolymers. [11]

(3.2) PEG in Drug Delivery Systems

It is interesting to combine components such as commercially established proteins or drugs that have pharmaceutical problems (e.g. low solubility in water, side effects or non-specific drug action) and a polymer with suitable properties for controlled drug delivery.

Tremendous research effort has been extended for selective drug delivery using polymeric devices to increase therapeutic effects and to decrease undesirable side effects of the drugs.

Recently, colloidal carries using biocompatible blocks copolymers to form micelles have been studied extensively for selective drugs delivery [14]. It is well established that block copolymers composed of PEG as the hydrophilic part and the appropriate hydrophobic part has been shown to self associate in an aqueous medium to form spherical micelles that have a dense core materials consisting of hydrophobic blocks and a corona surrounded by hydrated outer PEG segments. [11]

As one component of the amphiphilic blocks, PEG's (different molecular weights of polyethylene glycol polymer) have been extensively used in drug delivery systems due to their ideal properties such as non-toxicity, approved for internal use, relatively high water solubility, non-immunogenicity, and non-thrombogenicity.

For drug targeting, polymeric carriers have several advantages in pharmaceutical applications. One of these advantages is the accumulation of macromolecular drugs and their vehicles more effectively and remaining in tumor tissue for a much larger period than in normal tissue with little drainage, following both the direct injection into tumor and the indirect accumulation from the blood stream. [12]

(3.3) Supercritical Fluids Technology in Drug Delivery

Supercritical fluids technology is present in many pharmaceutical industries and operations including crystallization, particle size reduction, preparation of drug delivery systems, coating, and product sterilization. This technology has been also well known and viable in the formulation of particulate drug delivery systems, such as micro-particles and nano-particles, liposome, and inclusion complexes, which control drug delivery and/or enhance the drug stability. The advantages of using supercritical fluids technology include use of mild conditions for pharmaceutical processing, use of environmentally benign nontoxic materials, minimization of organic solvents use, narrow size distribution, and production particles with controllable morphology. The properties of supercritical fluids, such as polarity, viscosity, density and diffusivity can be altered several times by varying operating temperature and/or pressure during the process. This flexibility is enabling the use of supercritical fluids for various applications in the pharmaceutical industries, and with the drug delivery system design being a more recent addition. The most critical point for drug delivery industries is producing small particles with a narrow size distribution, because particles size affects the solubility, dissolution rate, target-ability, and bioavailability.

Drug delivery using supercritical fluids technology is gaining more attention due to the limitations of using conventional methods such as crushing, grinding, milling, and spray drying. These conventional techniques require using extensive amounts of organic solvents which may cause toxic effect, using mechanical forces (during crushing, grinding and milling) which may degrade pharmaceuticals, and spray drying may cause thermal stress to some products. Using supercritical fluids techniques, particles of either drug alone or a mixture of drug and its carrier (polymer or lipid carrier) can be formed. More interest has been found when the drug and its carrier can be simultaneously precipitated by using supercritical fluids techniques. For example, supercritical carbon dioxide has been used to dissolve Lovastatin and Naproxen as drugs, and Poly-Lactic Acid (PLA) as a carrier to produce a saturated solution and then precipitate the particles of drugs and polymer when expand the mixture through a nozzle. [13]

There are three factors that will affect the particles produced and hence the drug delivery process using supercritical fluids, these factors are:

1. The solutes (drugs, peptides, polymers, lipids, drug carriers, etc.) properties.
2. The nature and type of supercritical fluids.
3. The process characteristics (such as flow rate of solute and solvent, the supercritical conditions which include temperature and pressure, expansion process conditions, nozzle geometry, etc.).

Drug properties, such as their solubility in supercritical fluids will determine the characteristics of the particles formed similarly, polymers properties such as its concentration, crystallinity, glass transition temperature, nature of polymer chain, presence of active groups and polymer composition are the most important factors that determine the morphology of the formulated particles. In another way, supercritical fluids act as plasticizers for polymers by lowering their glass transition temperatures (T_g). Therefore, polymers with a low transition temperature tend to form sticky and aggregated particles. Polymer chain and its length and the use of different chain composition can alter polymer crystallinity and hence the particles morphology. [14]

Formation of Polymer/Ingredient Particles using SCF as Solvents:

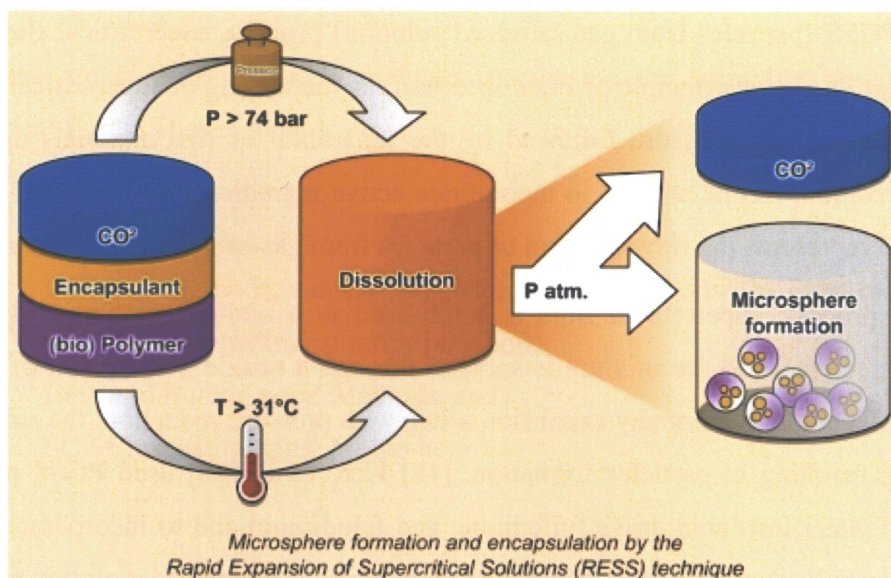
The co-precipitation process using particles coating together with impregnation methods, employing supercritical fluids as solvents, has been used to produce polymer particles loaded by an active ingredients. The typical co-precipitation of polymer and active ingredient can be achieved by using RESS (rapid expansion of supercritical solution) process when both compounds are soluble in supercritical fluid as shown in Figure 3.1A. RESS is the most recommendable process that can bring simultaneous size reduction and impregnation without the worry over residual organic solvents. This application is limited for the materials (polymers and active ingredients) that are soluble in supercritical fluid to a reasonable amount at the given experimental conditions. In co-precipitation by RESS process, it is very difficult to control the concentration of the active ingredient inside the polymer phase, because it is very rapid particles forming process. [17]

The major limitations of using co-precipitation process (low solubility of components in supercritical fluid) could be overcome by employing organic supercritical solvents. [17]

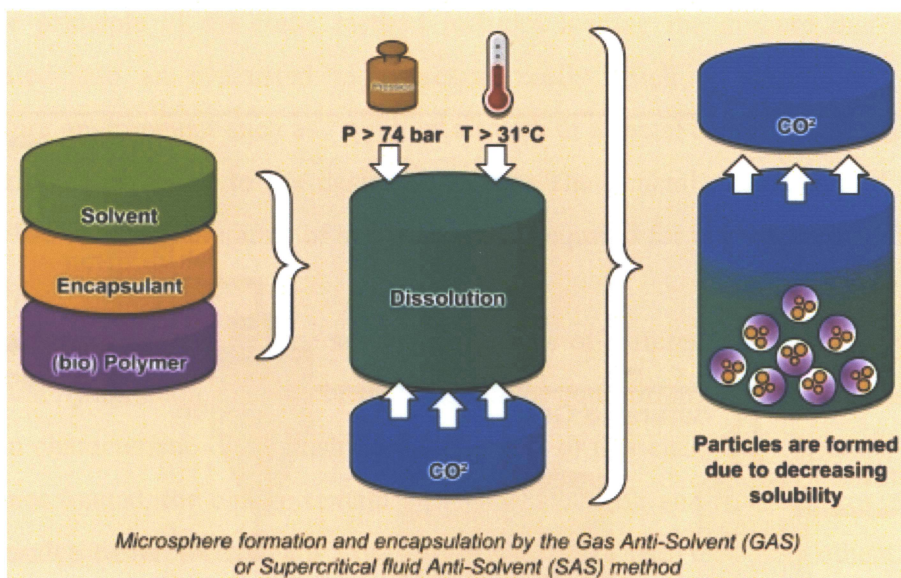
Mashima et al. [16] conducted RESS process to produce biopolymers micro-particles containing proteins by using particles coating method. A suspension of lysozyme and lipase as proteins has been dissolved with the polymer (PEG, PMMA, L-PLA, and D,L-PLGA) in supercritical carbon dioxide by the aid of alcohols as co-solvents. The study takes advantage of the solubility difference of proteins and polymers in supercritical carbon dioxide and co-solvent mixture. The authors controlled the polymer coating thickness by changing the feed compositions.

Formation of Polymer/Ingredient Particles using SCF as Anti-Solvent:

Polymer particles loaded with active ingredients, employing supercritical fluids as anti-solvents, can be produced by three different methods: (A) Polymer and an active ingredient can be dissolved in an organic solvent, and the solution of binary compounds is being in contact with supercritical anti-solvent. This method is feasible when both compounds are soluble in a single organic solvent. (B) Polymer solution containing suspended active material is contacted with supercritical anti-solvent. This method can be used when the polymer is soluble and the active compound is not in a particular organic solvent. (C) Polymer and an active ingredient are separately dissolved in two different solvents and both solutions simultaneously contacted with supercritical anti-solvent. [18] Organic liquid solvent, water and another supercritical fluid can be used as solvents for each of the compound. Elvassore et al. [19] encapsulated insulin in L-PLA particles using the SAS process. A mixture of DMSO (dimethyl sulfoxide) and methylene chloride with 50% ratio was used as a solvent giving the homogenous solutions of the two compounds. These processes are therefore basically solvent-induced physical mixing processes; the degree of mixing of two different materials strongly depends on the similarity of the compounds. Polymer and drug are often chemically dissimilar systems, and supercritical anti-solvent technology may be not applicable to every pair of polymer/drug composites to achieve a desired level of drug loading in polymer. Figure 3.1, represents the RESS, GAS and SAS processes and their characteristics in a simple diagram.



(A) Rapid Expansion of Supercritical Solutions Process.



(B) Gas Anti-Solvent or Supercritical fluid Anti-Solvent Processes.

Figure (3.1), RESS, GAS and SAS processes and their operational principles. [15]

Formation of Polymer/ Ingredient Particles using SCF as Solute:

In PGSS (particles from gas-saturated solution) process, supercritical fluid is used as a solute. The basic principle of PGSS process, i.e. the mixing of supercritical fluid and polymer under high pressure followed by the separation of two materials upon rapid depressurization, can be applied to incorporate active ingredients into polymer particles. Figure 3.3 represents the flow diagram of particles from gas-saturated solution process.

In PGSS process, supercritical fluid is solubilized in a molten solution (polymer and active ingredient), and the mixture is sprayed through a nozzle. As a result of the large cooling effects that accompany expansion along with pressure reduction, the substance is solidified, resulting in particles formation. [18] Kerc et al. [20] used PGSS process to micronize water insoluble drugs (nifedipine and felodipine) and to incorporate the drug particles in polyethylene glycol polymer with the aim to increase dissolution rate of the drugs. The inclusion efficiency is increasing with contact time and operating pressure, which is due to the increase of active materials solubility in supercritical fluid.

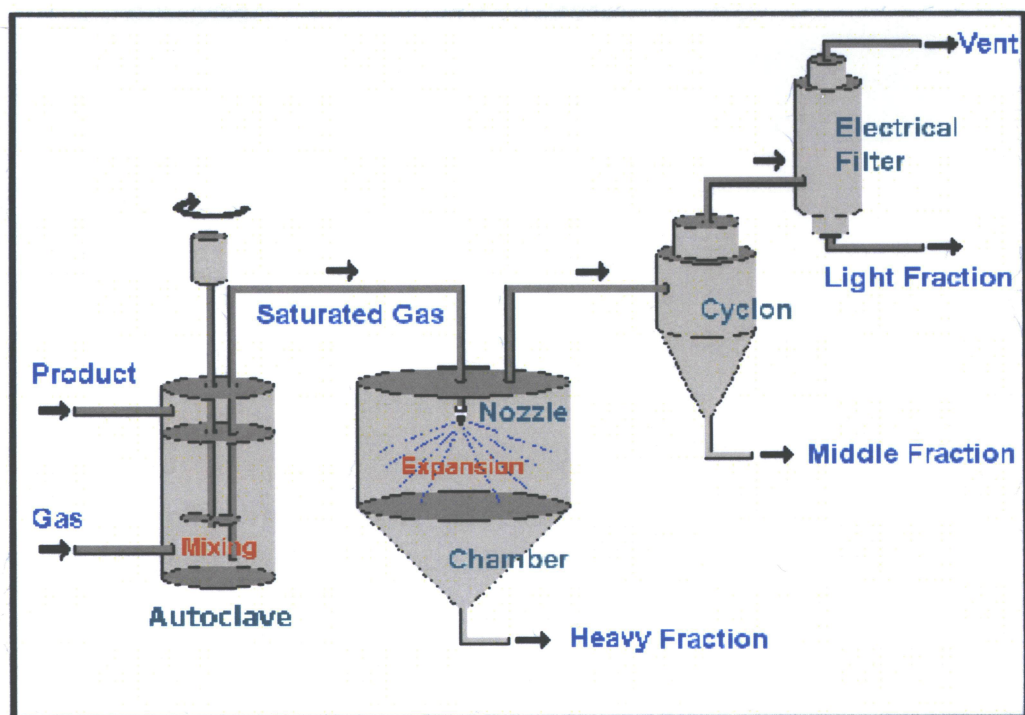


Figure (3.2), PGSS process flow diagram. [21]

(3.4) Measuring the Solubility of Polymers in SCF

There are different types of methods to measure the solubility of polymers in supercritical fluids. These methods include:

- (i) Static Methods,
- (ii) Dynamic methods, namely: (a) Recirculation methods, (b) Flow methods and (c) Saturation (or transpiration) methods.
- (iii) Dew and Bubble point Methods, and
- (iv) SCF Chromatographic Methods.

Static Methods

The principle of the static method includes loading the mixture that should be investigated into an evacuated high pressure cell, which is placed in a constant temperature environment such as liquid, or air bath or a metal block thermostat and then pressurizing the mixture to the desired pressure. The general advantages of the static methods are the small amounts of substances that required for the measurements and the simplicity of this method.

The contents of the cell, i.e. the segregated phases of different density, are brought to equilibrium by agitation, shaking or stirring, and the equilibrium pressure is measured.

The main characteristic distinguishing the methods of this class from dynamic methods, is that once loaded, the charge remain enclosed in the cell and no phase (or part of the system) undergoes a mechanically driven translatory flow with respect to others. [22]

In the static method, determination of compositions of the equilibrium phases can be accomplished by one of the two ways either synthetic or analytic method.

Synthetic Methods:

In these methods, the overall composition of the mixture contained in the cell is known from the beginning of measurement. The compositions of the coexistent equilibrium phases may then be recalculated from the known equilibrium temperature and pressure data, provided that at the system state conditions, the pressure-temperature-volume behavior as a function of composition is known for the phases present in the system. In most cases, the above conditions are satisfied at low and normal pressures, where the amounts of constituents present in the light (gaseous) phase are so small that the appropriate corrections can be evaluated by using the rough-state behavior (as a function of composition) predictions yielded by any simple equation of state. When dealing with the systems at high pressures, the conditions of having an accurate P-V-T-Composition prediction method at hand is barely satisfied. This means that some additional, experimentally determined, information is required. For determining the composition of only one of the coexistent phases (such as the solubility of a low volatile solute in supercritical fluids) in binary systems, this method is completely sufficient and no analysis is needed. [22]

Analytic Methods:

In these methods, the samples of one or both equilibrium phases formed in the system may be withdrawn and analyzed, are employed in high pressure investigations much more frequently. In this case, the initial composition of the mixture charged into the cell needs to be known only to the extent corresponding to the requirement of pre-determining the location of the measured equilibrium data point in the phase diagram. The approach is facilitated by the fact that, at high densities of phases encountered at high pressures, sufficiently representative samples of one or more phases may usually be taken without excessive risk of equilibrium state. If for a given system the sampling can be achieved in a tractable and reproducible way, the method represents a well suited and relatively inexpensive means to acquire very accurate phase equilibrium and solubility data. [22]

On the other hand, the major difficulty with the analytical method still resides with the withdrawal of the samples of equilibrium phases from the cell without disturbing the system equilibrium and with their transport to analytical devices while avoiding any changes in their homogeneity and composition. The static methods employ equilibrium cells of constant or variable volume; where the pressure may be continuously adjusted and controlled (at fixed composition and temperature) by a movable piston, adding flexibility to the operation and avoiding additional costs of a more complicated construction. This facility may be used to detect the bubble and/or dew point pressures and also to locate the critical points. The advantage of the view cells is that any possible phase transitions and phase inversions may be immediately detected visually and hence the important solid-liquid-vapor and liquid-liquid-vapor phase border curves as well as critical loci may be determined. [22] Table 3.1 represents the bibliography of the most considerable published papers that have used static methods to measure the solubility of valuable materials in supercritical fluids.

Table (3.1), Bibliography of Static Method

Scientists	Solvents	Solutes	References
Diepen & Scheffer	SC Ethylene	Naphthalene	[23]
Warzinski, Lee and Holder	SC CO ₂	Molybdenum	[24]
Yonker & Smith	SC Ammonia	Caffeine & Theophylline	[25]
Suppes & McHugh	SC CO ₂	Aromatic Materials	[26]
Fernandez & Fernandez-Prini	Sub- & SC Xenon	Iodine	[27]
Tuma & Schneider	SC Fluids	Dyes	[28]

Recirculation Methods

The main part of the recirculation apparatus is a thermo-stated equilibrium cell similar to the cells used in static experiments. The main advantage and principal characteristic of the recirculation apparatus are that the equilibrium cell can be mechanically driven circulation through external loops of either the lighter or the heavier phases. The circulation is usually achieved by magnetically operated high-pressure pumps. There are two main reasons for introducing external circulation of phases, (1) is to make the stirring and contacting of the phases to be equilibrated more efficiently and then to improve the process of equilibration and reduce the period required. (2) Is the sampling of the equilibrium phases can be substantially facilitated. After reaching the equilibration, the phase circulated through an external loop is a steady-state regime already which represents a separated equilibrium phase. The best way is to do the analysis without disturbing the phase stream in the circulation loop by using continuous refractometry, densitometry, UV/vis monitoring, etc. [29]

Flow Methods

By this method, a preheated mixture of constant overall composition flows continuously to the equilibrium cell, wherein it separates into two phases differing in density. Flow methods have been developed primarily for systems containing thermally unstable compounds and also for reacting systems. The purpose of design these methods are: (1) to reduce the time required to attain the required state conditions. (2) To reduce the residence time of the studied mixture in the high temperature compartment of the apparatus. The reduction of these both periods of time is necessary to minimize the changes in composition due to possible proceeding reactions, in particular to minimize the extent of thermal decomposition of thermally unstable constituents in the studied system. High pressure pumps should be used here to deliver, in a continuous manner, the components in a fluid state to form a steady mixture of constant composition at a desired system pressure, which may be either liquid or gas or a blend of both. [30]

The main disadvantages of using the flow methods are: (1) A relatively large consumption of the studied substances. (2) Pressure fluctuations can be suppressed completely, which makes precise pressure control somewhat more difficult. [30]

Saturation Methods

Experimental apparatus belonging to this technique are most frequently applied for determining the solubility of solids and high viscous heavy liquids in supercritical fluids. These methods include using the simple technique by loading the non-volatile heavy phase (either liquid or solid) batch-wise in a saturator (equilibrium cell) and staying there as a stationary phase during the entire experiment. SC Fluid will pass at a constant pressure through a pre-heater, where it reaches the desired temperature, and then continuously fed to the saturator through its bottom, strips the solutes from the stationary heavy phase and the mixture (SCF and the solutes) leaves the saturator from the top. Saturation method is often used to study the co-solvent effects, in which a stream of solvent and co-solvent mixture of known composition is fed to the saturator, so that the ratio of the concentrations of the volatile components is now in priori. There are few points in this technique that should be noticed: (1) There is no way to detect the phase transition or any phase change in the saturator. (2) Should avoid any entrainment of the particles or drops of the stationary heavy phase with the stream of SCF-rich phase. (3) The SCF-rich phase should be in equilibrium with the stationary phase during the entire period of sampling or sample collection. It should avoid any precipitation or condensation of the extracted solutes from the effluent stream during the expansion process, so it is prefer to heat the expansion valve to a sufficient temperature. [31]

Dew and Bubble point Methods

In these methods, a mixture of known composition (solutes and SC Fluid) is isothermally (constant temperature) expanded or isobarically (constant pressure) heated till a phase change is detected. The equipment used in this technique is very similar to that of static cells (variable volume static cells are mostly dew and bubble point cells). The dew and bubble point method can be used to locate visually the phase transition state, i.e. a pressure value is found at which the composition of one of the present phases is equal to the known total composition at a given temperature. [32]

The main advantage of these methods is that no sampling or analysis is required whereas the main difficulty in running apparatus lies in the preparation of the mixture of known composition in the cell. This phase synthetic method has no complicated analytical devices and procedures, and is therefore relatively inexpensive, but the most important advantage is it doesn't disturb the equilibrium conditions. On the other hand, the phase boundary is not detected directly, but as a consequence of the formation of a new phase. At high pressures, these methods are preferred because: (a) Complete depressurization process is less critical, (b) There is no need to very high volume differences in phase change detection, and (c) The volumetric properties as a function of pressure are by-products of interest.

It should be noticed that this method is not applicable to systems whose coexisting phases have similar refractive indices or in those cases in which the liquid phase doesn't condense as a mist, but as a thin layer on the walls of equilibrium cell. [32]

Supercritical Fluid Chromatography Methods

Chromatography is a family of laboratory techniques for the separation of mixtures, it involves passing a mixture dissolved in a "mobile phase" through a stationary phase, which separates the analyte to be measured from other molecules in the mixture and allows it to be isolated. The chromatographic technique is widely used in analysis and for the separation of complex mixtures in a wide range of pressure and temperature. By analogy with the low pressure applications GLC-LLC, it is possible to obtain thermodynamic properties, and hence solubility in dense gases, from chromatographic data. This approach is very promising because chromatographic measurements are rapid, require small amount of solute, and it can separate impurities from the solute.

Most of the commercially available supercritical fluid chromatographs can be modified by including an extractor before the equilibrium cell, through which the supercritical fluid flows and is saturated by the substratum. [33]

(3.5) Literature Review of PEG/SC CO₂ System

Daneshvar et. al. [36] found the phase equilibrium data of different molecular weight polyethylene glycol-carbon dioxide mixtures and they correlated these data using a lattice-model-based equation of state. The data that have been collected were at temperature of 313 K and at 323 K over a pressure up to 29 MPa. The experimental apparatus used to obtain the vapor-liquid composition data were countercurrent circulation system. Equilibrium was achieved by circulating both the liquid and vapor phases, the SC CO₂ phase was drawn from the top and driven to the bottom of the equilibrium vessel while the polymer phase was drawn from the bottom and driven to the top. They used high pressure valves to take samples from both phases at equilibrium. The equilibrium time was approximately 30 minutes. Their conclusions were:

- The solubility of PEG in supercritical carbon dioxide is a strong function of molecular weight.
- The threshold pressure above which the solubility is corresponding to the solubility limit is about 15 MPa for PEG 600.
- The decrease in PEG 600 solubility upon heating is governed by the decrease in CO₂ density or its solvation power.

Courgouillon et. al. [37] presented the phase equilibrium data of three polyethylene glycol of molar mass 200, 400, 600 with supercritical carbon dioxide over the temperature range 313-348 K and pressure up to 26 MPa. They used static analytical apparatus to conduct their results.

Their conclusions are summarized below:

- An increase in temperature or in PEG molecular weight reduces the solubility in SC CO₂.
- The analytical method that used was different from that of Daneshvar et. al. [36] and this explains the difference in solubility measurements of both of them.

Hao J. et. al. [34] used PGSS (particles from gas-saturated solution) process to precipitate PEG polymer particles of different molecular weights by using supercritical carbon dioxide as a solute and in the absence of any organic solvents.

They realized that the performance of the PGSS process is strongly influenced by:

- PGSS process conditions of pressure and temperature,
- Type of the polymer,
- Molecular weight and distribution of the polymer, and
- The type of spray nozzle.

Their conclusions were:

- The optimum conditions for processing PEG into precipitated micro-particles using PGSS process are 110 bar pressure and 50 °C temperature.
- The smaller the diameter of the nozzle, the higher percentage of spherical or near-spherical particles produced.
- Increasing the temperature and decreasing the pressure favor the production of spherical particles.

Finally, the latest study of the phase behavior of PEG/SC CO₂ has been done by Hun-Soo Byun [38], where he measured the cloud-point data of PEG/CO₂ system in the temperature range from 35 to 195 °C and pressure up to 2360 bar. The molecular weights of PEG covered were 200, 300, 400, 600, 1000, 2000, and 4000.

His conclusions were:

- The phase behavior of PEG/CO₂ system show negative slopes with dissolution at temperatures ranging from 35 to 195 °C and pressures up to 2360 bar.
- All of the curves show rapid increases at the upper critical solution temperature.

(3.6) Objectives and Motivations of Study

The most important objectives of this study are:

1. Measuring the solubility of polyethylene glycol polymers in supercritical carbon dioxide using a wide range of pressure and temperature. Polyethylene glycol polymers are often used in medical and health industries as a drug carrier and in cosmetic and beauty industries as an essential additive, so it is interesting to investigate their solubility in supercritical carbon dioxide in order to decide what are the best conditions and processes to produce these utilized and valuable polymer particles.
2. Investigating the best operating conditions of supercritical fluids (pressure and temperature) to reach high solubility values and studying how these conditions will enhance the supercritical carbon dioxide density. Modifying the solubility of PEG by increasing SC CO₂ density and studying the opposite effect of PEG vapor pressure on the solubility will provide us with clear and useful ideas in producing this kind of polymers in a nano size with uniform shapes.
3. Detecting the proper process in producing polyethylene glycol polymer particles and figuring out how successful the supercritical carbon dioxide will process PEG.
4. Conduct an empirical equation to describe the solubility pattern at different supercritical conditions. A new empirical equation of best solubility fitting is necessary to describe the solubility pattern and to predict its behavior at high supercritical conditions. Depending on the regression values, the empirical equation will show how successful and reliable using this kind of equations that can replace in some times using the equations of state.

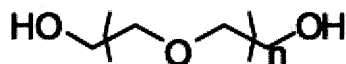
(4) Materials and Apparatus

The materials and apparatus chapter is divided into two sections, materials section which is describing polyethylene glycol polymer and carbon dioxide gas and the apparatus section which is describing the experimental set up.

(4.1) Materials

Polyethylene Glycols:

This well known polyether polymer is composed of repeating subunits that have identical structure, and it is produced mainly by polymerization of ethylene oxide. This oligomer (which is consist of a finite number of monomer units) with the polyethylene oxide polymer (PEO) are liquids or low melting solids, depending on their molecular weights. Most PEG's and PEO's include molecules with a distribution of molecular weights, i.e. they are poly-disperse polymers.



Chemical Formula: $C_{2n} H_{4n+2} O_{n+1}$
Molecular Mass: $44n + 18$ g/mol.
Density: $1.1 - 1.2$ g/cm³

Polyethylene glycol polymers are non-toxic, water soluble and they are main media of many products:

Skin creams (like Cetomacrogol), laxatives (e.g. Macrogol, Miralax, Glycolax), bowel preparation before surgery or colonoscopy and drug overdoses, treatments for hepatitis C (PEG-Interferon Alpha), repairing nerve, fusion B-cell (with Myeloma cells) in monoclonal antibody protection, preventive agent against colorectal cancer (PEG Mw 8000), mask antigens on red blood cells, making tooth paste as a dispersant, osmotic pressure creature (in Bio-Chemistry), heat transfer fluid in electronic testers, anti-foaming agent in soft drink. [39]

Table 4.1, shows some physical and chemical properties of polyethylene glycol polymers.

Table (4.1) PEG physical properties.

PEG Mw.	State/Color	Density (g/cm ³)	Melting Point, °C	Comments
600	Oily liquid/white	1.12 at 25 °C	17-23	Aqueous sol. pH is 5-7; Viscosity 135 cp at 25 °C; Pour point 17 °C.
1500	Solid/white	1.18 at 25 °C	44-48	pH of 1% aqueous sol. is 5-7; water content 0.3%; Flash point (open cup) 285 °C.
6000	Solid/white	1.027 at 20 °C	60-63	pH of 5% aq. sol. is 4-7; Freezing point 56-63 °C; Viscosity at 100 °C and 50% sol. is 100 cp.
12000	Solid/white	1.2 at 20 °C	64-65	pH of 1% aqueous sol. is 5-7; water content 0.3%.

Carbon Dioxide:

We received CO₂ as liquefied gas under a pressure of ~ 120 bars from BOC/CANADA, with a purity of 99.95%. The gas has been used as is and without any purifications.

The P-V-T properties of CO₂ and their relation to its density are listed in Appendix A.

(4.2) Apparatus

The apparatus that used in study experimental work are:

SFT Phase Monitor II:

The SFT (supercritical fluid technology) phase monitor II (made by Supercritical Fluid Technology Incorporation) is specially designed high-pressure view cell for liquid and supercritical phase equilibrium and solubility studies. It includes a view cell with precise temperature and pressure control, continuous temperature and pressure readouts, a manual operated pump, and integral mixing.

SFT phase monitor can be used in different areas including solubility determinations, extracting monomers from polymers matrices using SCF, infusion of materials into a polymer matrix, improving reaction yields in SCF, infusion drugs into delivery systems, and extraction of selected compounds. SFT phase monitor contains the following main parts: (see Figure 4.1)

Pressure Vessel (cell)

A 316 stainless steel, 3 to 30 ml variable volume cylindrical high pressure vessel which can work under a maximum pressure of 689 bar and under a maximum temperature of 150 °C. The vessel can retain the high pressure with ½” thick and 7/8” diameter quartz windows which allow the operator to view the phase changes inside the cell. There are two windows on both sides of the vessel, one for light supply and the other to observe the phase changes using video camera. The temperature can be raised inside the vessel by using an electric heater with a 200 Watts of heating band power which is attached directly to the vessel. A thin insulation is surrounded the vessel to minimize the heat losses. Pressure cell volume is checked experimentally (see B.2 in Appendix B).

Inside the cell, sample scoop is used to hold Pyrex tube which comprises the polymer sample as show in Figure 4.5.

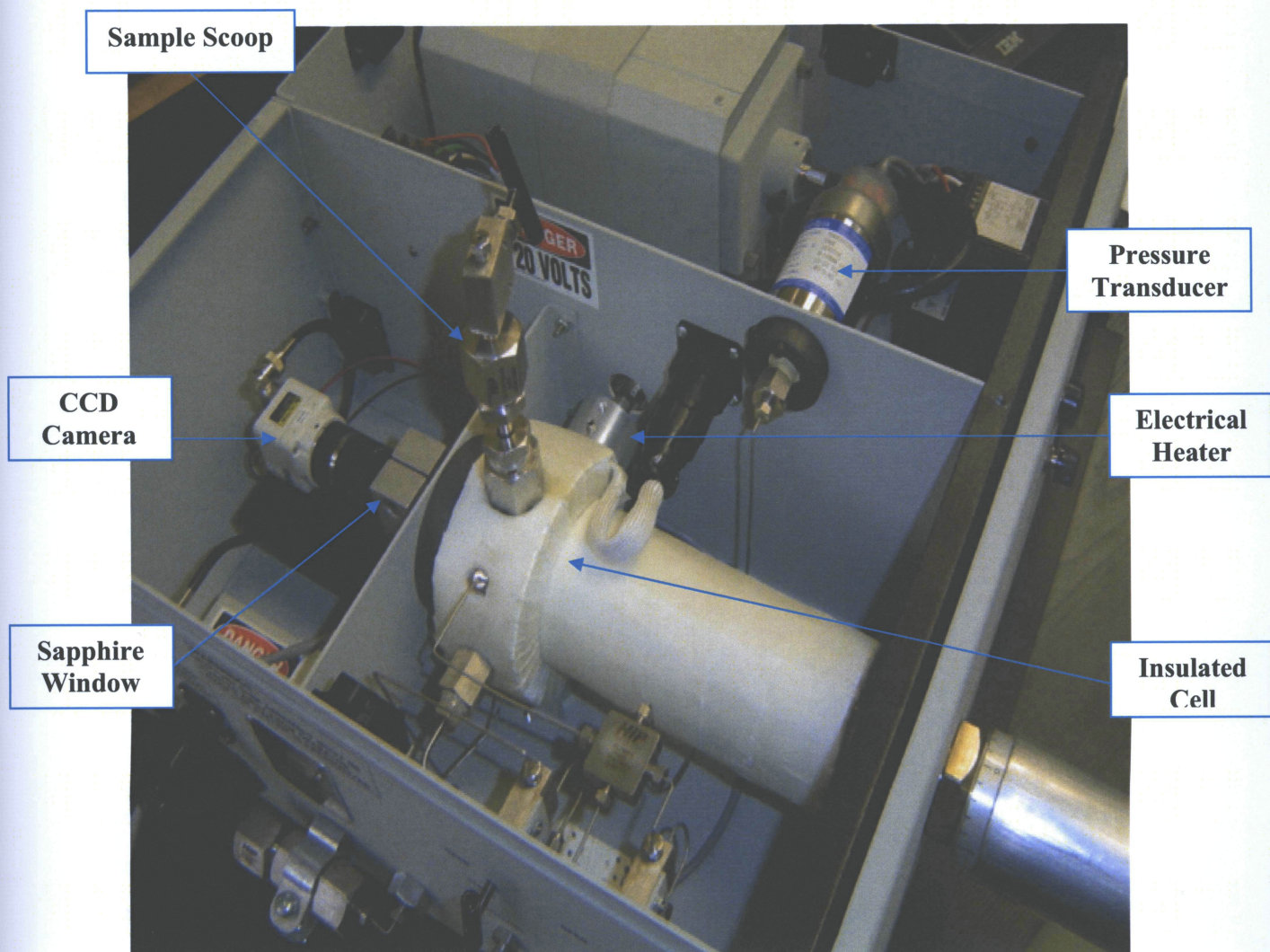


Figure (4.1) SFT Phase Monitor II.

Manual Displacement Pump

Pressure inside the cell can be controlled up to 689 bar using a manual displacement pump which is used to increase the pressure inside the cell by reducing its volume (i.e. piston and cylinder system). The piston is driven forward at a rate of 14 turns per inch displacing 0.36 ml/turn. The minimum volume of the cell that can be reached using this manual pump is 3 ml.

Programmable Electric Heater

A heating rate and dwell time can be achievable by using a Fuzzy Logic Control (FLC) which is maintaining the main job of the heater. Temperature is monitored and controlled by an internally mounted RTD.

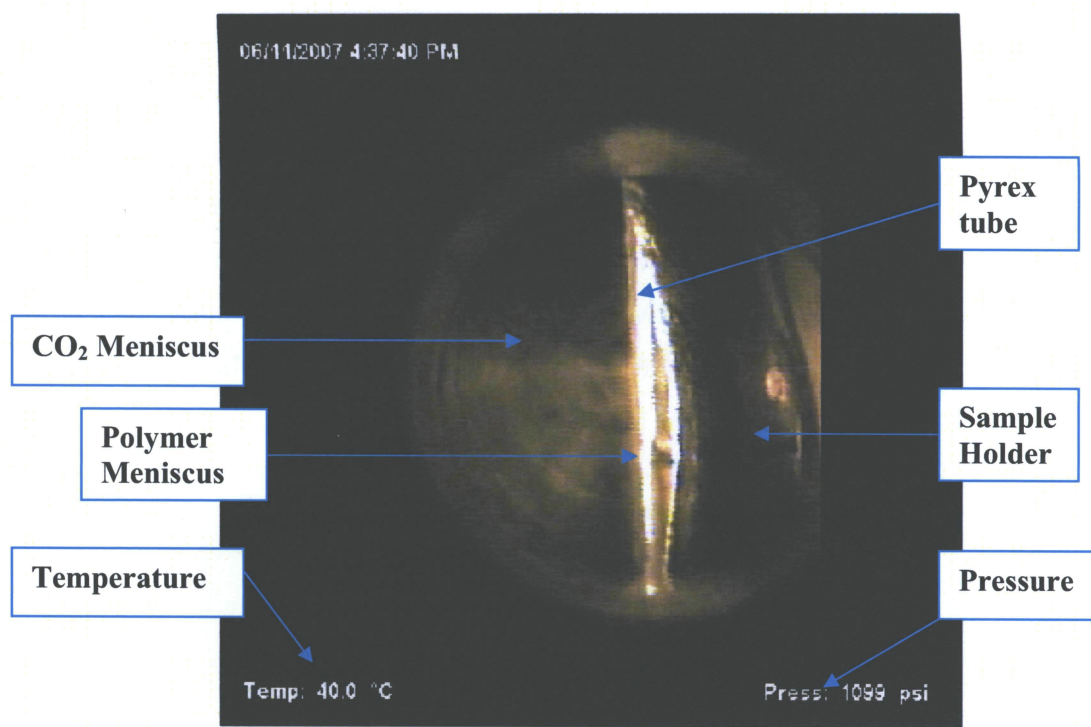
Temperature range that can be covered is from room temperature and up to 150 °C.

Viewing Apparatus

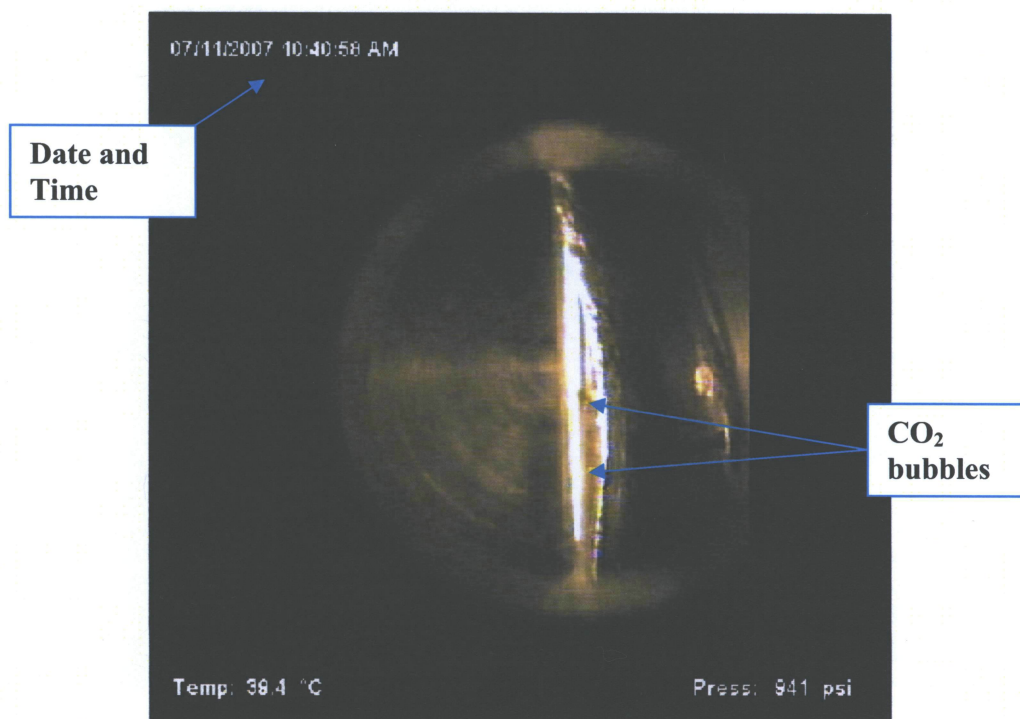
A variable focus, color CCD camera is used, which is attached directly to a quartz window. The second window is used to supply illuminated, variable intensity, fiber optic light.

Data Acquisition Package

The DAP system provides real time image and data capture from the SFT monitor directly to a PC computer. The video image, along with the temperature and pressure data, is displayed on the PC monitor. The experimental data, current date and time can be recorded and saved directly in the PC hard drive. Figure 4.2 shows pictures of video images that are collected from DAP system during measuring PEG polymer solubility runs. [35]



(A) Pressurization Process image.



(B) Depressurization Process image.

Figure (4.2) DAP system images of pressurization and depressurization processes.

260 D Syringe Pump:

The 260D syringe pump is used for filling the high pressure cell with liquid carbon dioxide and then pressurize it to reach the high pressure supercritical conditions, and also it can provide a pressure programming system to handle supercritical fluids. With pressure control up to 517 bar and a flow rate range from sub-micro-liter and up to 107 ml/min, the 260D offers a convenient versatility for polymer solubility measurement in supercritical CO₂ and other fluids. Figure 4.2, represents syringe pump photo.

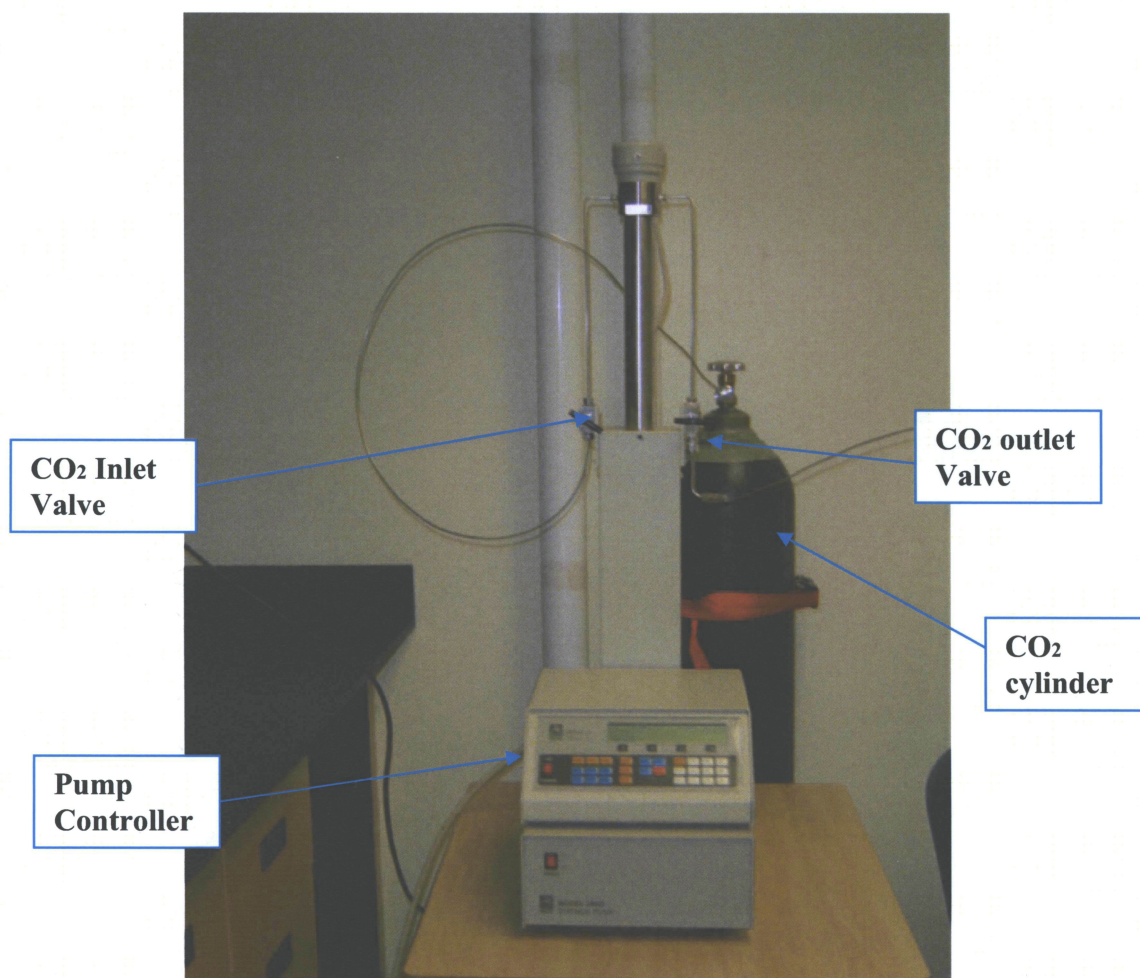


Figure (4.3), Syringe pump.

Figure 4.4, represents the schematic diagram of the experimental set up showing the main devices used.

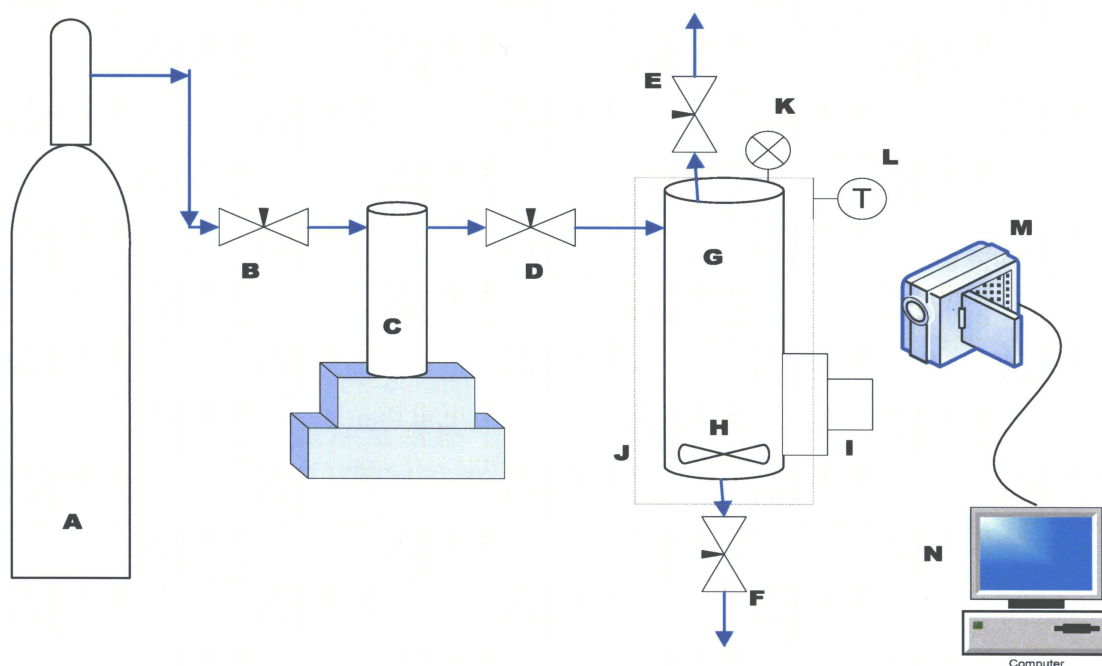


Figure (4.4) Schematic Diagram of the main apparatus.

A: CO₂ cylinder; B, D, E and F: are high pressure needle valves; C: syringe pump; G: cell (which contains sample scoop); H: mixer; I: electric heater; J: insulation; L: temperature control unit; K: pressure transducer; M: camera.

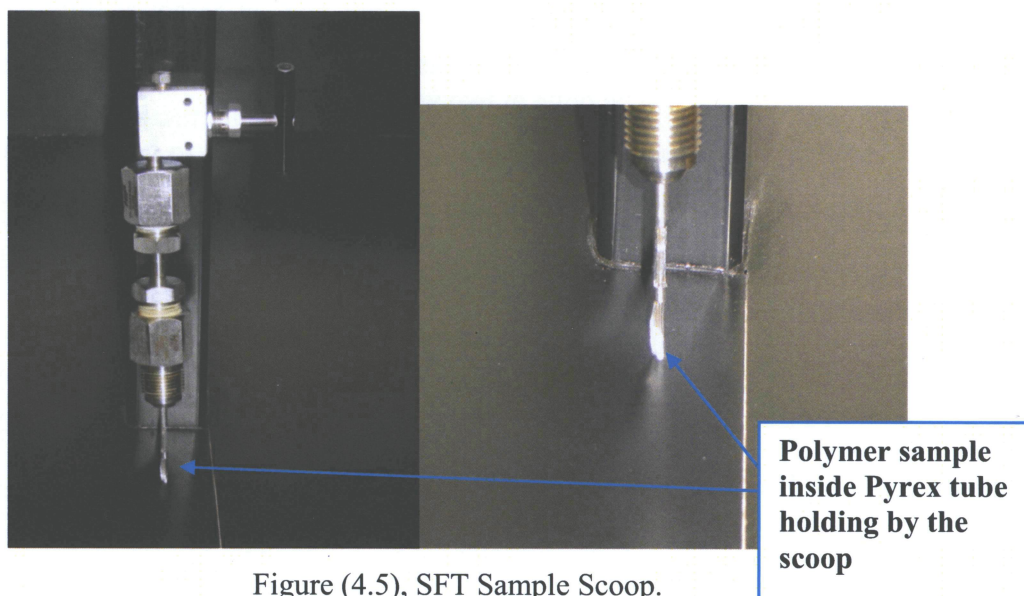


Figure (4.5), SFT Sample Scoop.

(4.3) Experimental Procedure

The following steps represent the experimental procedure that we followed in measuring the solubility of polyethylene glycol polymers in supercritical carbon dioxide:

- A. Test the cell to be sure there is no leakage or loss of gas at given value of pressure (up to 500 bar) and during period of 35 hr.
- B. Start the light source and then start video camera in order to view the entire cell and also to see the experimental readings (pressure, temperature, date and time) which referring to the conditions inside the cell.
- C. Load PEG sample into the cell by inserting a measured weight of PEG inside Pyrex capillary tube (1.2-1.5 mm diameter) and then place the loaded tube to the sample scoop followed by closing the valve assembly. We could not fix the PEG polymer amount that has been inserted in the Pyrex tube because of the high accuracy required (10^{-6} g). See appendix C to see the amounts of PEG polymer inserted.
- D. Vacuum the cell, which is necessary to be sure there is no air inside the cell.
- E. Load the cell with liquid CO₂ through the bottom inlet valve. The maximum rate of increasing pressure of CO₂ entering the system is 1 bar/s.
- F. Fill the cell with liquid CO₂ (we can see that through the monitor), then set the temperature to the desired value. It takes more than one hour to reach steady state fixed temperature.
- G. pressurize the cell can be done in two ways:
 1. Pressurize the cell using pump piston system (manually) to pressurize the cell by reducing its volume (from maximum volume of 33 ml to minimum volume of 3 ml); the pressurizing rate here should not exceed 1 bar/s. See Appendix B for actual cell volume calculation.
 2. Pressurize the cell using 260D syringe pump to pressurize the cell by pumping liquid CO₂ continuously to the cell to reach the desired pressure using specified flow rate (1 μ l/min to 107 ml/min at any pressure up to 517 bar).

The second method is used in pressurizing the cell because it provides a constant pressure without need to change the cell volume (as required in first method) which may give some unexpected errors. Also it is hard to fix the pressurizing rate manually (using the first method) whereas syringe pump provides this facility. The only limitation of using syringe pump in pressurizing the cell is that one needs to watch the CO₂ flow rate continuously to prevent the reaching of high level (more than 10 ml/min); high and fluctuated flow rate will affect the cell temperature stability.

- H. Use the syringe pump to keep the system at constant pressure by pumping CO₂ continuously at almost constant flow rate.
- I. Estimate the saturated time (period required to reach the equilibrium state between supercritical CO₂ phase and the polymer phase) by measuring the amount of polymer dissolved in SC CO₂ at different periods till reach the saturation when the amount of polymer dissolved does not affect by time any more (constant amount dissolved with increasing time). This happened when SC CO₂ phase is saturated with polymer phase and the period to reach this called saturation time.
- J. Depressurize the cell (after saturated time consuming) through the top exhaust valve. The depressurizing step should be done very slowly (should not exceed 3-4 bar/min) in order to give the CO₂ bubbles that dissolved inside PEG sample enough time to release without pushing any amount of polymer outside the Pyrex tube. Depressurizing rate depends on the pressure applied and on the PEG molecular weight.
- K. Weigh the Pyrex tube that containing PEG sample to get the difference in weight which represents the polymer dissolved in SC CO₂. The solubility (as wt. fraction) is estimated (See Appendix B).
- L. Measure the solubility at each single pressure starting from the lower value; we repeat that for each PEG molecular weight. The temperature and pressure values are chosen depending on PEG molecular weights and on what have been done in the literature. See Appendix B to see a sample of calculations.

(5) Results and Discussion

(5.1) Evaluating the Saturation Time of PEG/SC CO₂ Systems

Saturation time can be defined as the period of time that required in reaching the equilibrium state between the polymer and supercritical carbon dioxide. In this study, we measured the saturation (equilibrium) time by measuring the solubility of different molecular weights of polyethylene glycol polymer in supercritical carbon dioxide in different periods of time and at different conditions (pressure and temperature). For PEG 600, the saturation time estimation curve at pressure of 200 bar and at temperature of 323 K is shown in Figure 5.1.

Also, for PEG 1500, the saturation time estimation curve at pressure 300 bar and at temperature 323 K is conducted as shown in Figure 5.2. It is clear that the measured saturation time represents the period from 24 to 25 hr at which constant PEG amount dissolved in SC CO₂.

By the same way we measured the saturation time for PEG 12000 at pressure of 300 bar and at temperature of 338 K as shown in Figure 5.3. When the amount of polymer dissolved in SC CO₂ is getting constant with increasing time, means these phases are in equilibrium (or SC CO₂ phase is saturated with polymer phase).

The saturation time required for PEG 12000 (little bit more than 25 hr) is close to that of PEG 1500 at the same pressure and at different temperature. The saturation time of both PEG 1500 and PEG 12000 behaved almost in the same way, whereas its behavior is different from that of PEG 600, and this may be due to the difference in state between PEG molecular weights (PEG 1500 and PEG 12000 are solids whereas PEG 600 is liquid at ambient temperature).

Since the operating conditions and polymer molecular weights were varied and the saturation time did not affected (24-25 hr), so we can say the operating conditions and polymer molecular weights have a limited effect on saturation time estimation.

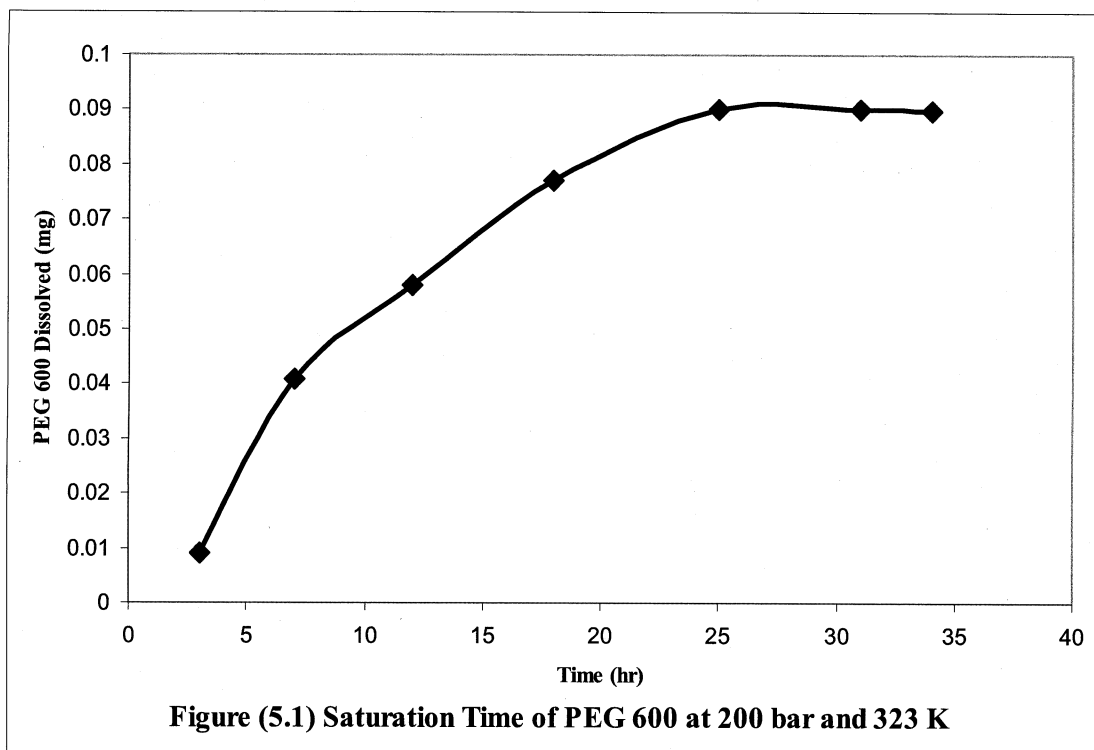


Figure (5.1) Saturation Time of PEG 600 at 200 bar and 323 K

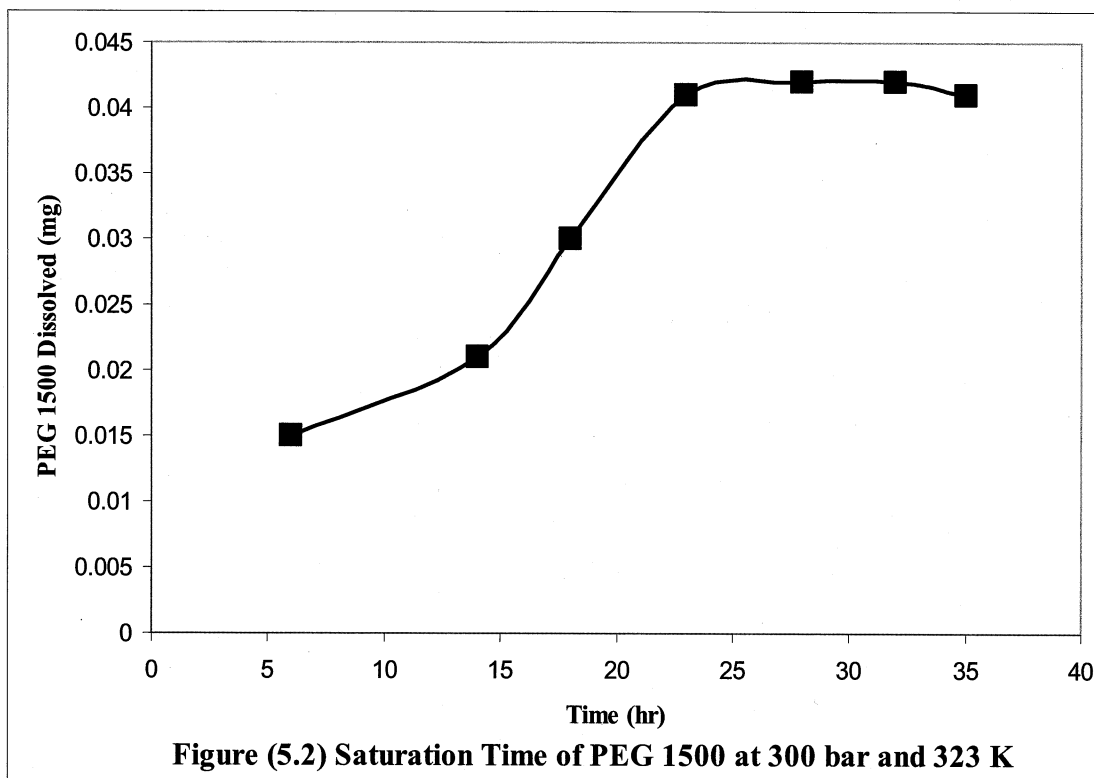
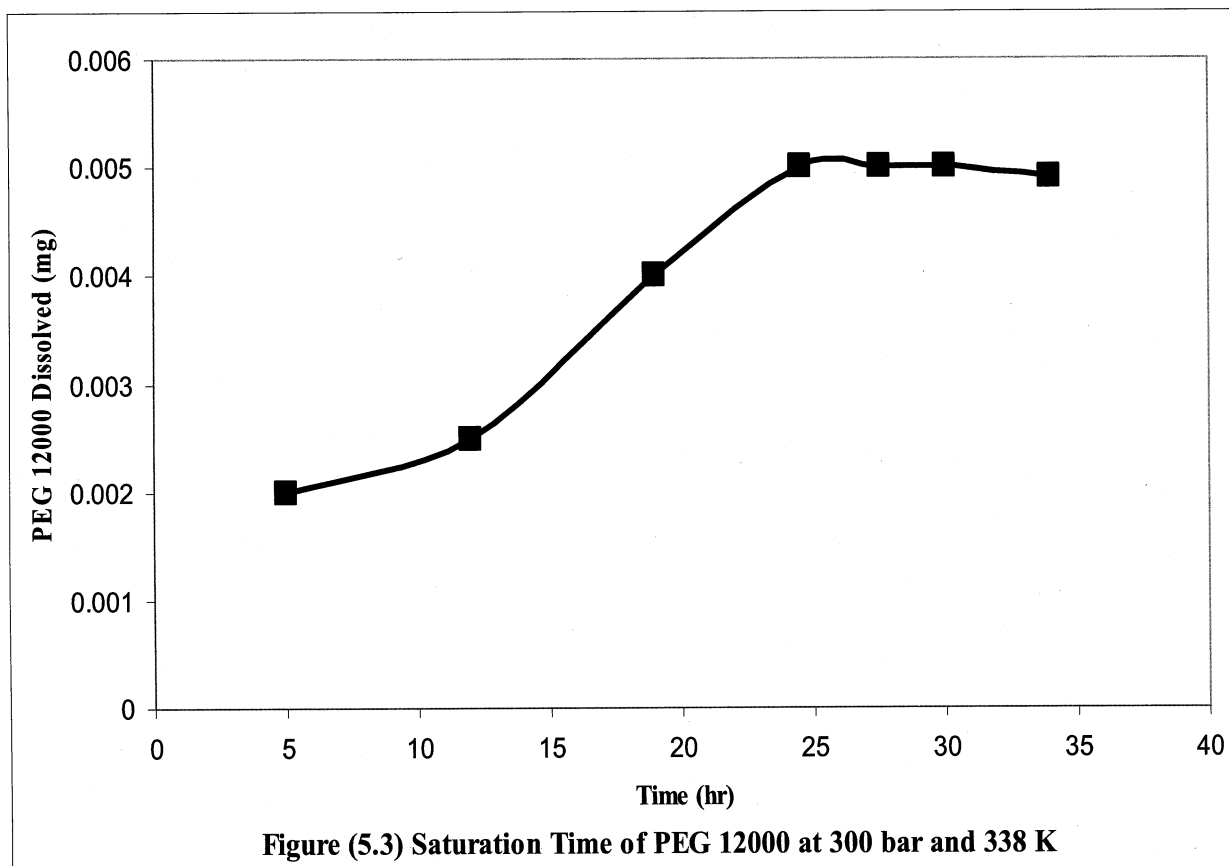


Figure (5.2) Saturation Time of PEG 1500 at 300 bar and 323 K



(5.2) Mixing Impact on Saturation Time and Equilibrium State

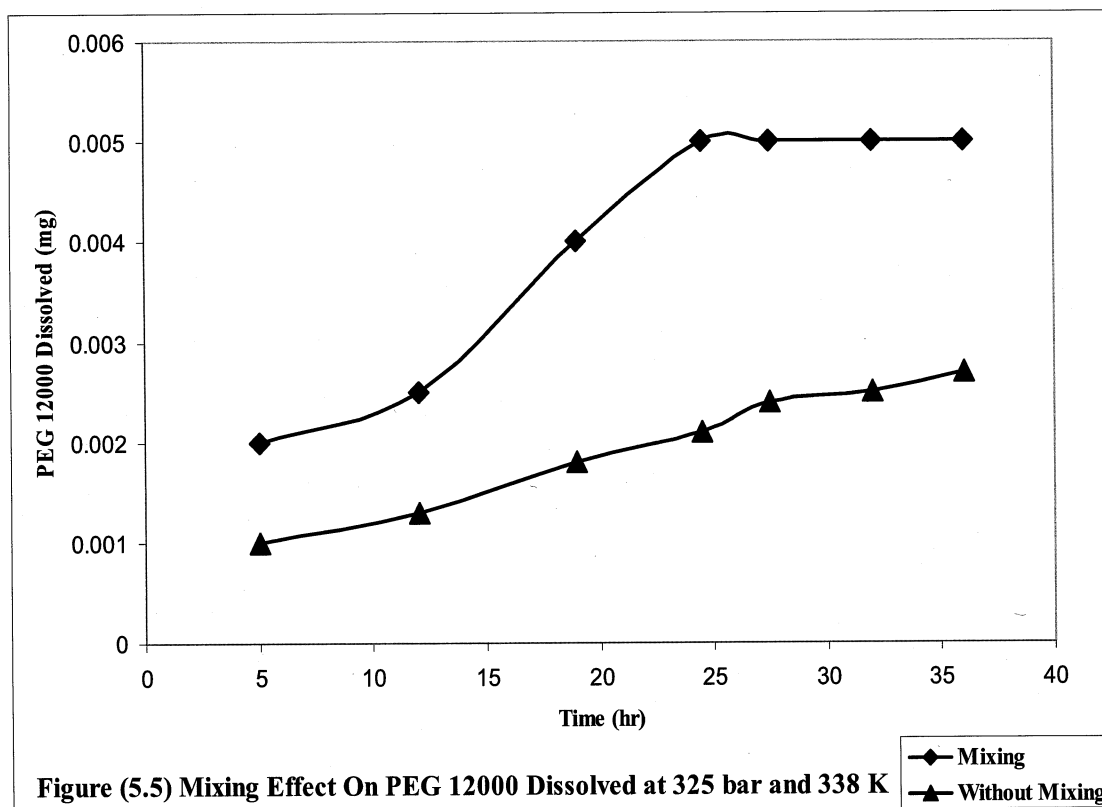
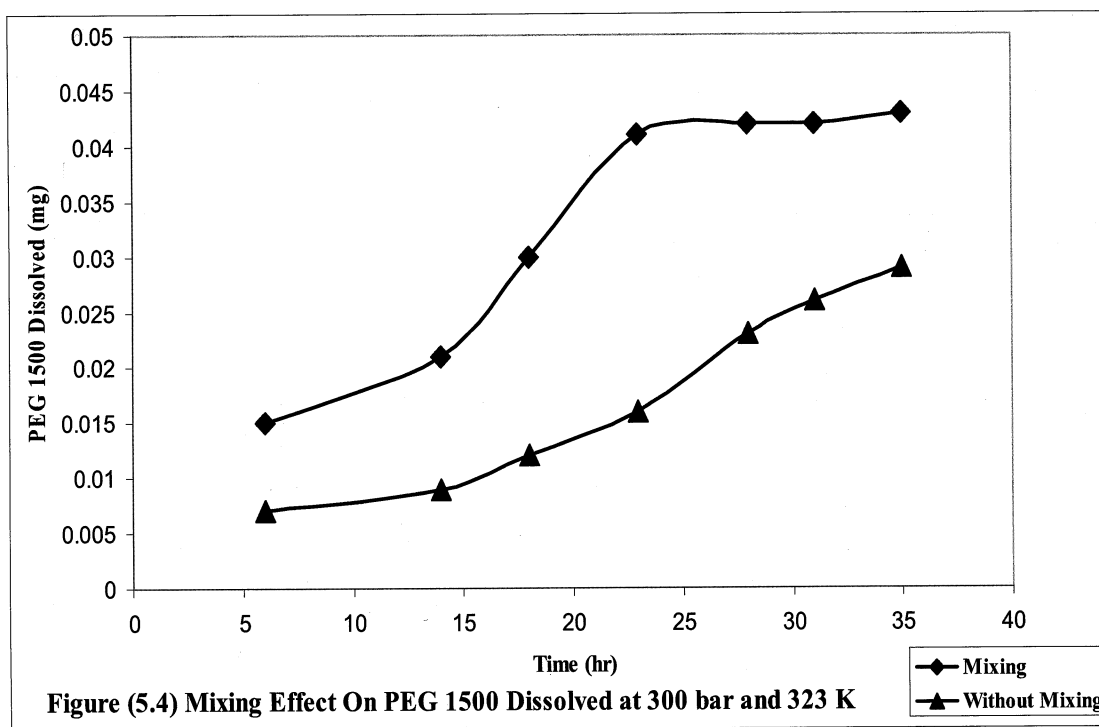
It is found that mixing process has direct effect on the way in reaching the equilibrium state between polymer phase and supercritical carbon dioxide phase in saving time and in modifying the system equilibrium conditions.

Figures 5.4 and 5.5 are showing a comparison in solubility values and in its behavior between measuring the solubility using mixing process and measuring it without using mixing process.

Without mixing, the system needs more time to reach the steady equilibrium state between the two phases. Usually with closed high pressure cells like the one used in this study, it is preferable to use magnetic mixer with speed regulator, otherwise a continuous moving cell can be used to keep both phases in better contact. Also, by modifying the surface contact area between the two phases can be used to save more time toward the equilibrium state.

A magnetic mixer with a regulator is used in this study, and the mixer speed is fixed on the maximum value to keep this speed constant during all experiments.

For systems at elevated pressures, the rotational speed is limited to not exceed the laminar regime (viscosity driven regime), and hence the SC CO₂ viscosity does not subject to a big change when the pressure and temperature change (from $\mu=0.069$ mPa.s at 150 bar & 313 K to $\mu=0.085$ mPa.s at 500 bar & 366 K), so the SC CO₂ viscosity has a limited effect on mixer speed. (See Figure A.1 in Appendix A for SC CO₂ viscosity)



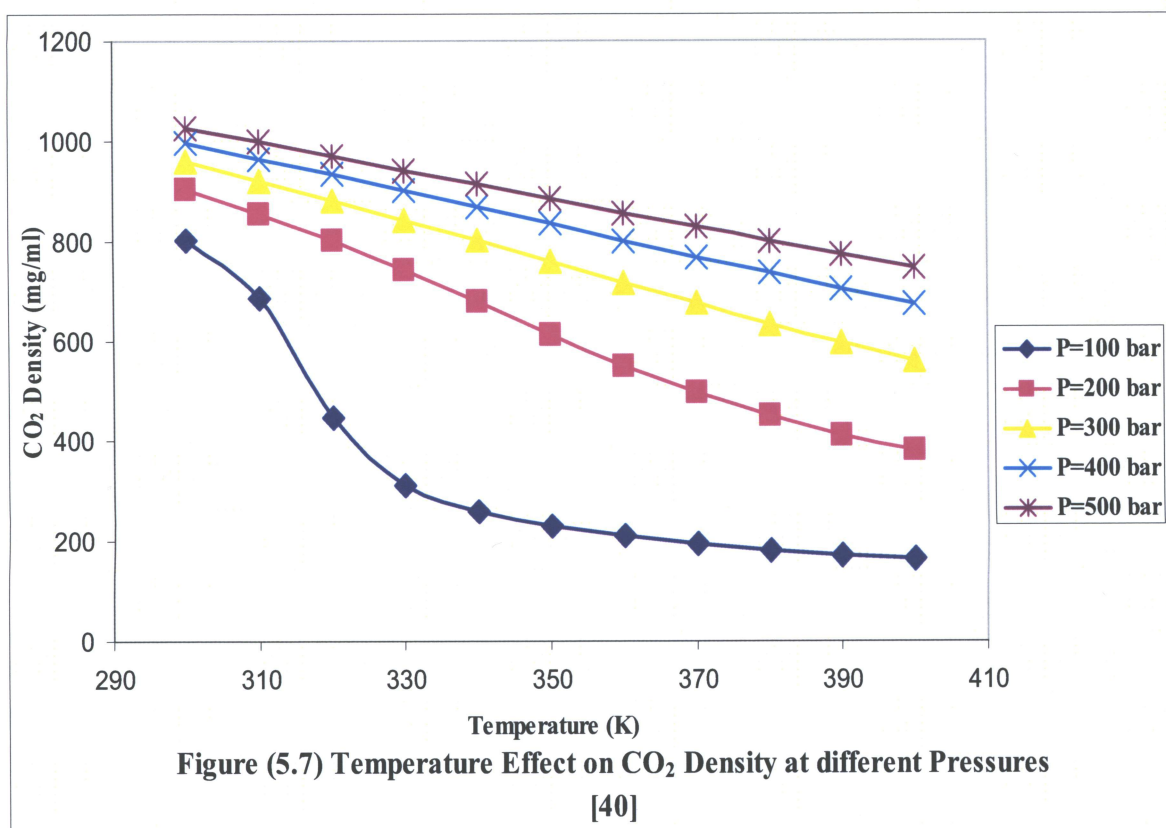
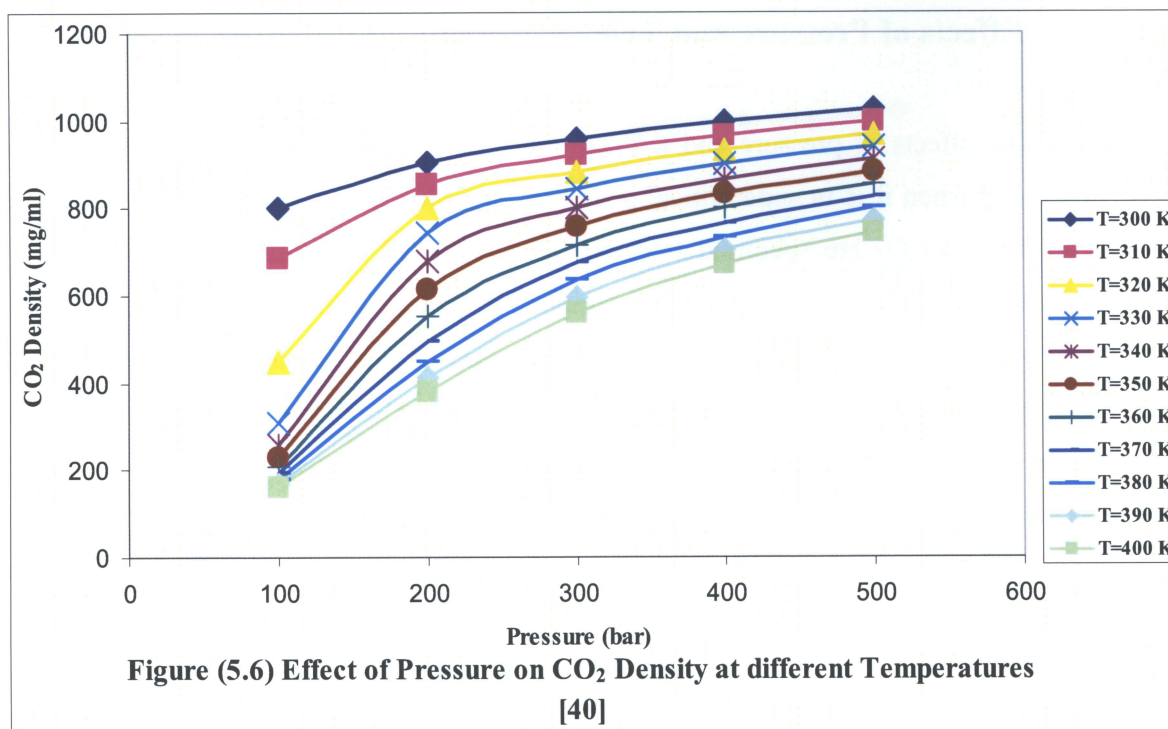
(5.3) Effects of Pressure and Temperature on CO₂ Density

The effects of pressure and temperature on the density of CO₂ when it is in gas phase and when it is in supercritical phase are presented and analyzed. Thermodynamic properties of CO₂ are specified from the literature [40] and the relationships of CO₂ density versus pressure and versus temperature are drawn as shown in Figures 5.6 and 5.7 respectively. As shown from these Figures, carbon dioxide density increases with pressure and decreases with temperature, so the density of supercritical carbon dioxide can be enhanced by increasing pressure and by decreasing temperature. There is another important issue that should be realized from these two figures; the density of carbon dioxide is very sensitive to the changes in pressures and in temperatures just above its critical points (P_C and T_C).

Density increases sharply with pressure in between of two values, 100 bar and 200 bar which they are just above carbon dioxide critical pressure P_C (74 bar) as we see in Figure 5.6. On the other hand, carbon dioxide density decreases sharply with temperature in between two values, 310 K and 330 K which they are close to carbon dioxide critical temperature T_C (305 K) as shown in Figure 5.7. So, the best conditions at which carbon dioxide can be a super tunable supercritical fluid are:

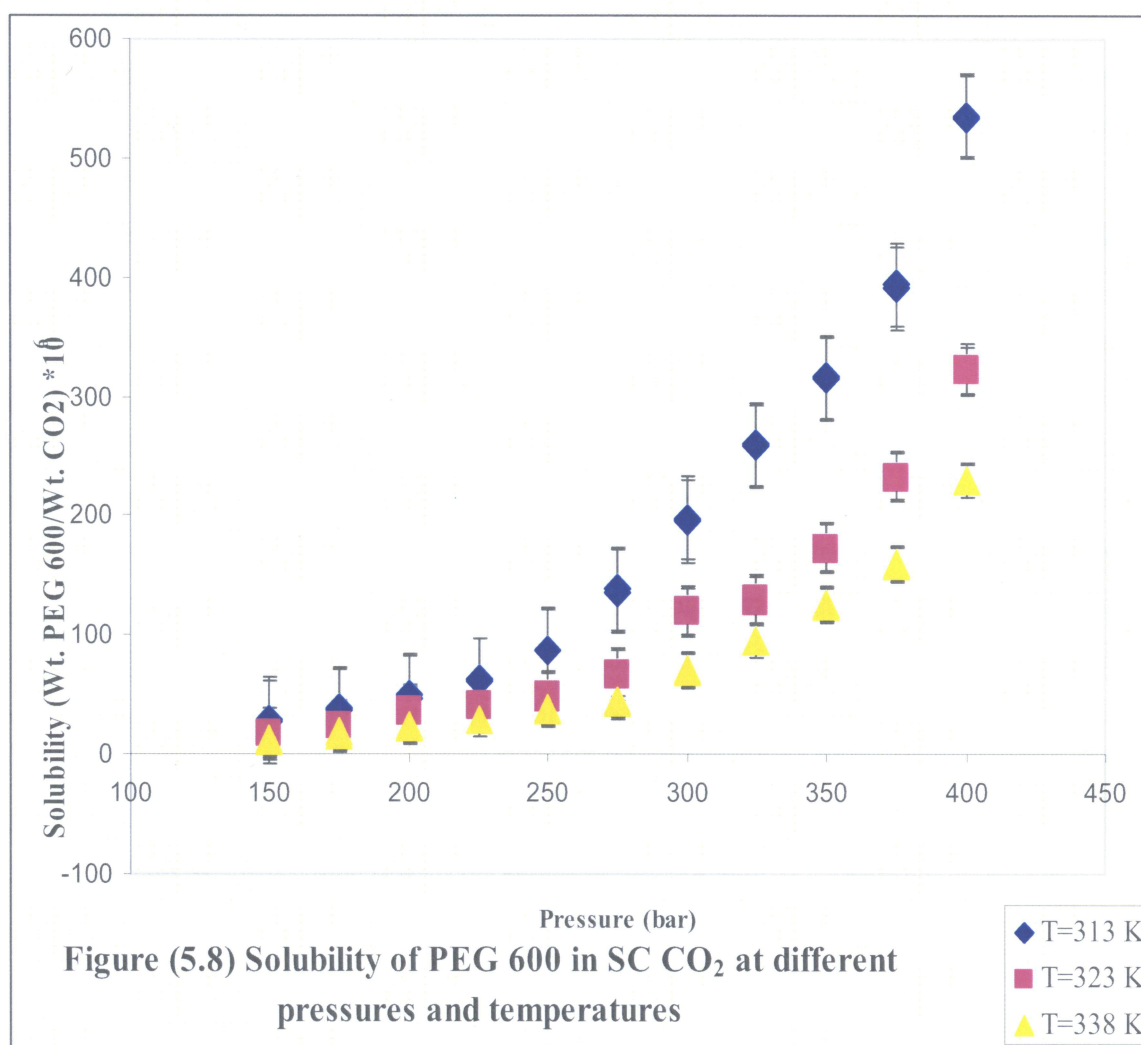
- Pressure value in between 100 and 200 bar
- Temperature value in between 310 and 330 K.

At the above conditions, the solvation power of supercritical carbon dioxide as a solvent will be affected by its density, and at these ranges its density has the predominant effect on the solubility of different kinds of solutes. For high and moderate soluble solid solutes in SC CO₂, there will a jumped solubility values when the density enhanced sharply in these ranges. For polyethylene glycol polymers that have a relatively low solubility in SC CO₂, we noticed a graduate increasing in solubility values during the ranges of modified density. Out of the above ranges, there is another important and significant factor that can affect the solubility of PEG in SC CO₂, this factor is the vapor pressure of the polymer which can be increased with temperature and by this way it will opposite the SC CO₂ density effect and in sometimes will have the predominant effect on the solubility of polymers in SC CO₂.



(5.4) Solubility Measurement of PEG 600 in SC CO₂

Solubility of PEG 600 in SC CO₂ is measured experimentally at different pressures and at three different temperatures as shown in Figure 5.8. PEG 600 has higher solubility in SC CO₂ at low temperatures and at high pressures due to the SC CO₂ density effect on the solvation power. SC CO₂ density increases with pressure and decreases with temperature as noticed from Figures 5.6 and 5.7. Increasing SC CO₂ density will increase its power as a solvent and then a higher polymer solubility values will be achieved. PEG 600 solubility measurements are repeated two times (see Appendix C) as shown from the error bars of figure 5.8.



(5.5) Solubility Measurement of PEG 1500 in SC CO₂

Solubility of polyethylene glycol 1500 in supercritical carbon dioxide is measured at different pressures and at three different temperatures as show in Figure 5.9.

At temperature 338 K (relatively high temperature compare to PEG 1500 melting point), the solubility has less response to the pressure change (it takes longer time to rise up due to increasing in pressure) than the solubility at moderate temperatures (not too far higher than polymer melting point). The only logic and reasonable explanation for this phenomenon is the supercritical carbon dioxide density when it behaves due to the changes in pressures and temperatures.

At moderate pressures (up to 300 bar), the solubility values are close to each other at different temperatures and this is due to the polymer vapor pressure effect which is usually start to present in these ranges.

The PEG 1500 melting point has an average between 44-48 °C (317-321 K), so measuring solubility should be started at temperature just above the polymer melting point in order to keep this polymer in liquid phase during the run. It is difficult if it is not impossible to measure the polymer solubility when it is in solid state.

Due to the effect of carbon dioxide density which is affected by supercritical conditions, PEG 1500 is found to be more soluble at high pressures and at low temperatures. Table C.2 in Appendix C contains the experimental results of PEG 1500 solubility; we repeated the solubility measurement two times.

(5.6) Solubility Measurement of PEG 6000 in SC CO₂

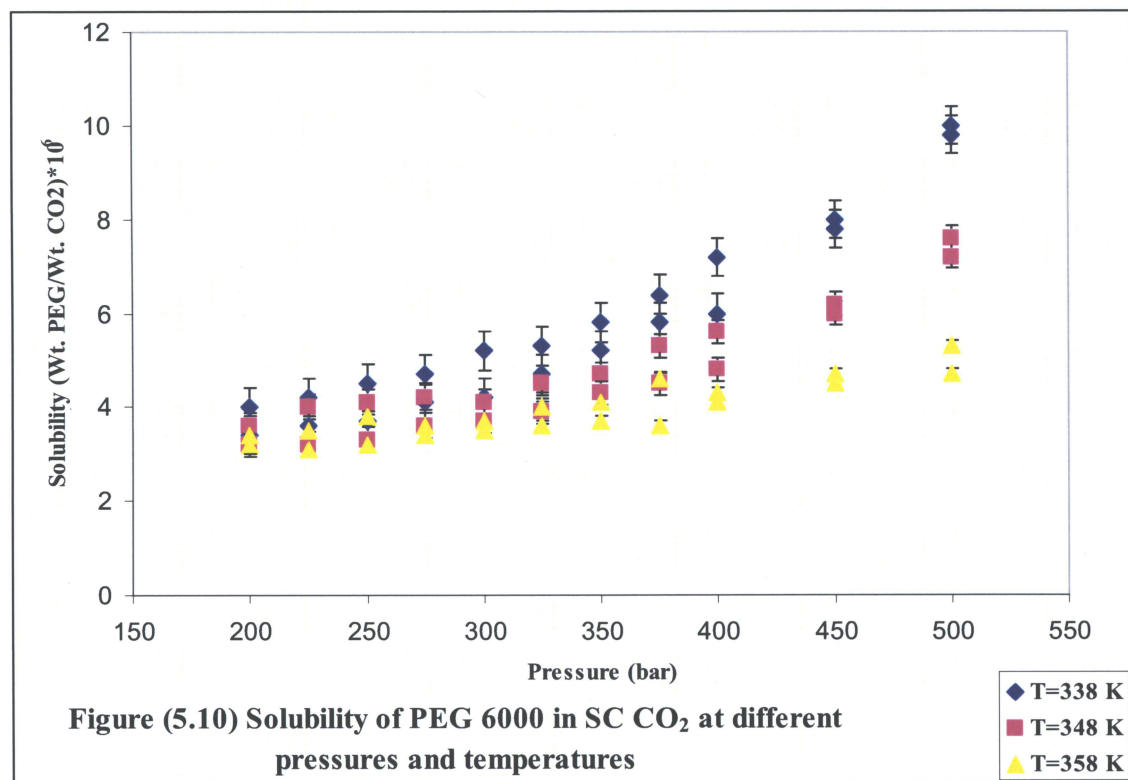
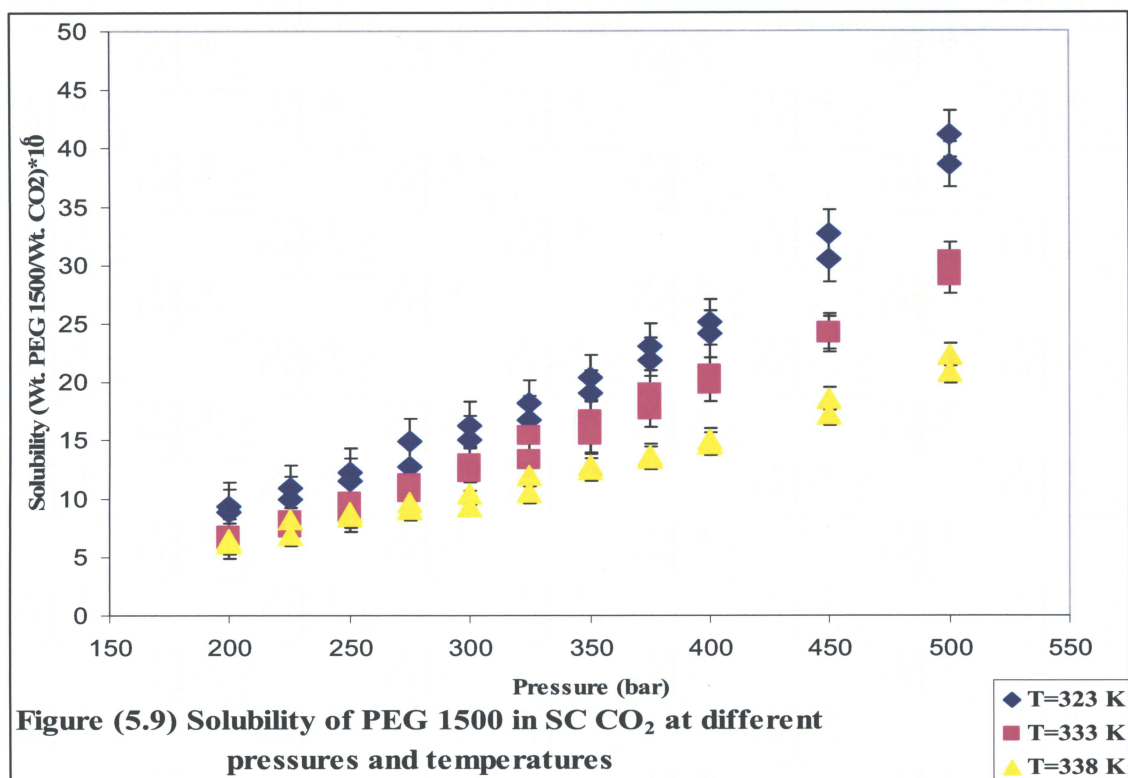
PEG 6000 solubility in supercritical carbon dioxide is measured at different pressures and at three different temperatures as shown in Figure 5.10.

The melting point of PEG 6000 polymer is in between of 60 and 63 °C (333-336 K), so measuring the solubility of this polymer started at temperatures from 338 K and up to 358 K which just above the polymer melting point.

PEG 6000 Solubility at 338 K is behaved almost similarly of what the solubility at 348 K is behaved, but both of them are behaved in different way from what the solubility at 358 K is behaved. Solubility at 358 K increased slowly and less in response due to the pressure build up when it is compared with solubility at low temperature and this is again due to the supercritical carbon dioxide density effect. Up to 300 bar, the solubility values are close to each other at different temperatures, meaning there is another factor (other than supercritical carbon dioxide density) that opposes the density effect by increasing the solubility in spite of increasing system temperature; it is the effect of PEG vapor pressure at high temperatures.

Table C.3 in Appendix C contains the experimental results of PEG 6000 solubility; we repeated the solubility measurement two times.

Due to PEG degree of crystallinity (when it is in solid state), supercritical carbon dioxide has an appreciable effect in dropping the polymers melting point to lower temperatures, and that what is noticed during melting polyethylene glycol during employing CO₂ gas (at the beginning and before pressurizing the cell). As a result, it has been realized that passing CO₂ gas at high pressure in addition to the heating effect will reduce the required energy and the required time to melt the polymer.



(5.7) Solubility Measurement of PEG 12000 in SC CO₂

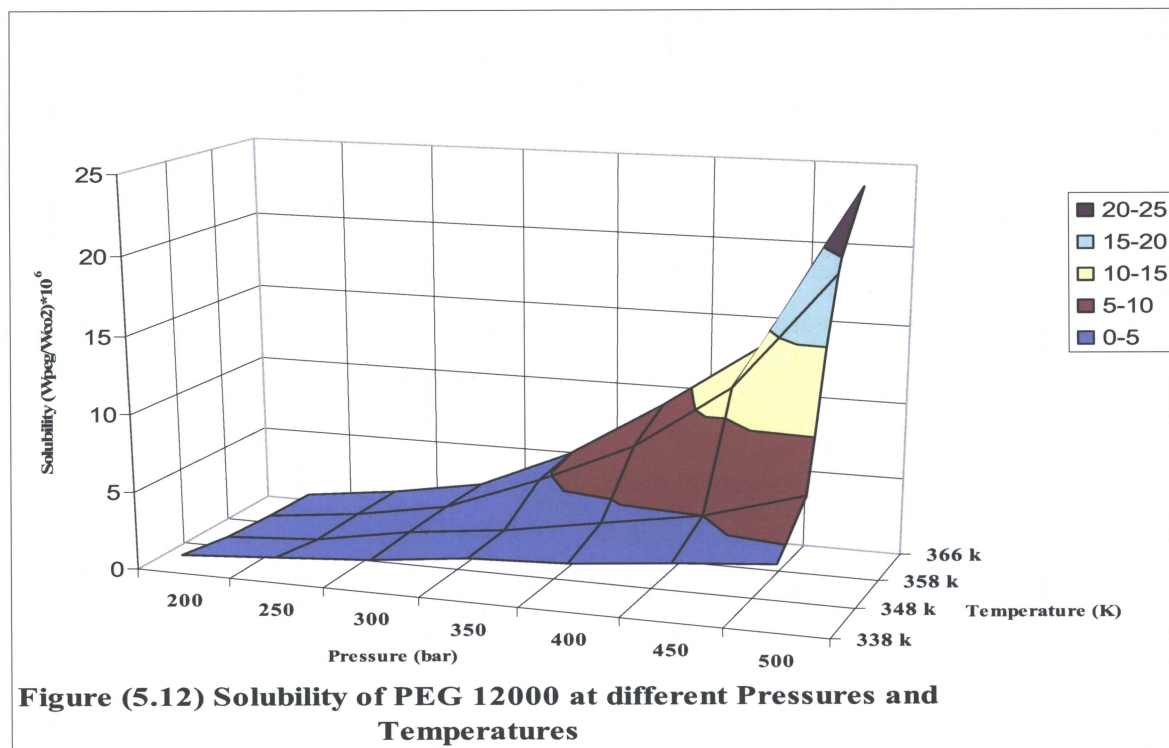
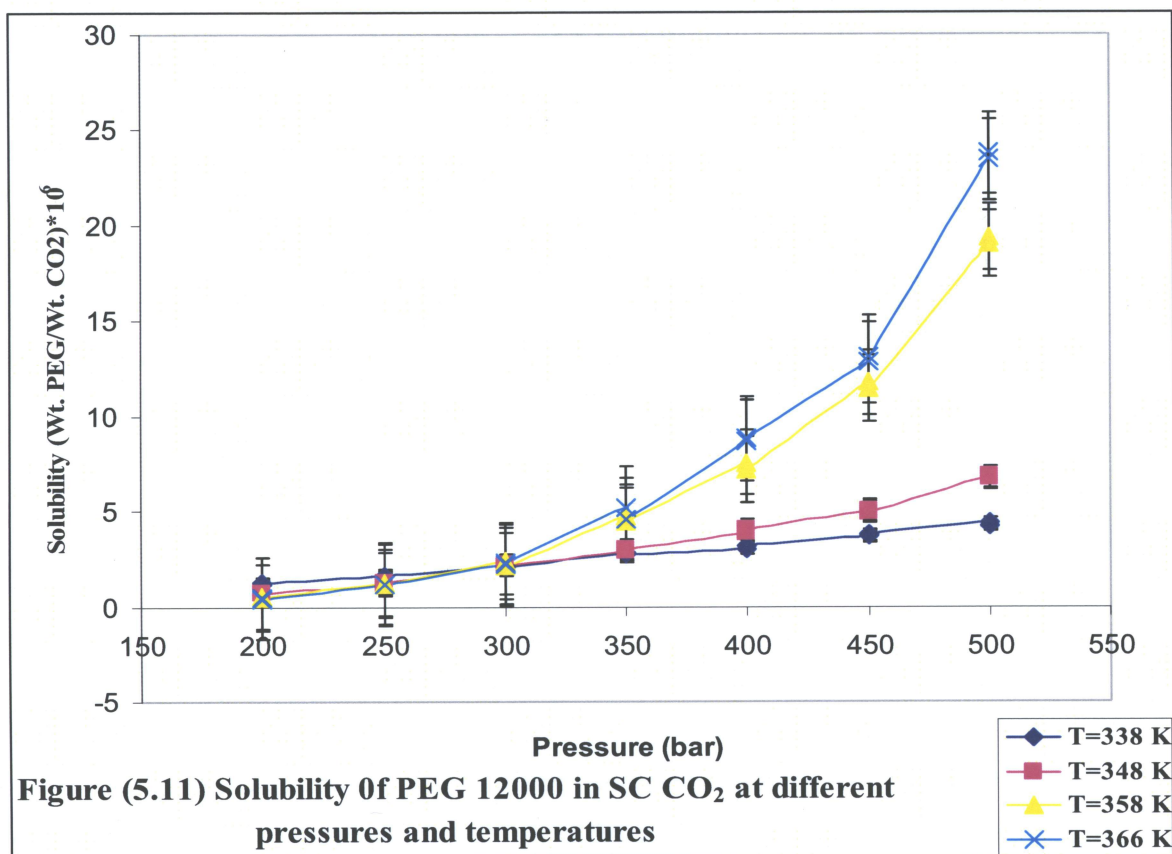
Solubility of PEG 12000 in SC CO₂ at different pressures and at four different temperatures is measured as shown in Figure 5.11.

The solubility of this high molecular weight polyethylene glycol polymer behaved differently compared to what observed earlier for other PEG molecular weights. Here the relationship between the polymer solubility and the system temperature changed from direct to indirect during pressurizing the cell, and this happened at a specific pressure value. First, the solubility increased with increasing pressure and decreased with increasing temperature as usual, and this was true up to pressure of 300 bar then, solubility opposed its behavior after this pressure value when it is increasing with increasing temperature as shown in Figure 5.11.

This common existence pressure is what has been termed “crossover pressure” [41]. This is a pressure around which isotherms at various above critical temperatures tend to converge. Below the crossover pressure (300 bar) the isobaric increase in the system temperature causes a decrease in the solubility of PEG 12000 in SC CO₂.

There are two opposite effects to explain and to understand this unique behavior due to the effects of temperature on solubility. These effects include; the vapor pressure of the polymer which increases by increasing temperature and the density (solvent power) of supercritical carbon dioxide which decreases by increasing temperature. Below the crossover pressure where the compressibility is larger, the density effect will dominate so the solubility will decrease with increasing temperature. At pressures above the crossover pressure, the vapor pressure effect will dominate and then solubility will increase with increasing temperature. Table C.4 in Appendix C contains the experimental results of PEG 12000 solubility; we repeated the solubility measurement two times.

Figure 5.12 gives us a better view to see how the solubility behaves due to the changes of both temperature and pressure at the same time. Solubility here increases with pressure and with temperature as well after it passes the crossover pressure of 300 bar value.



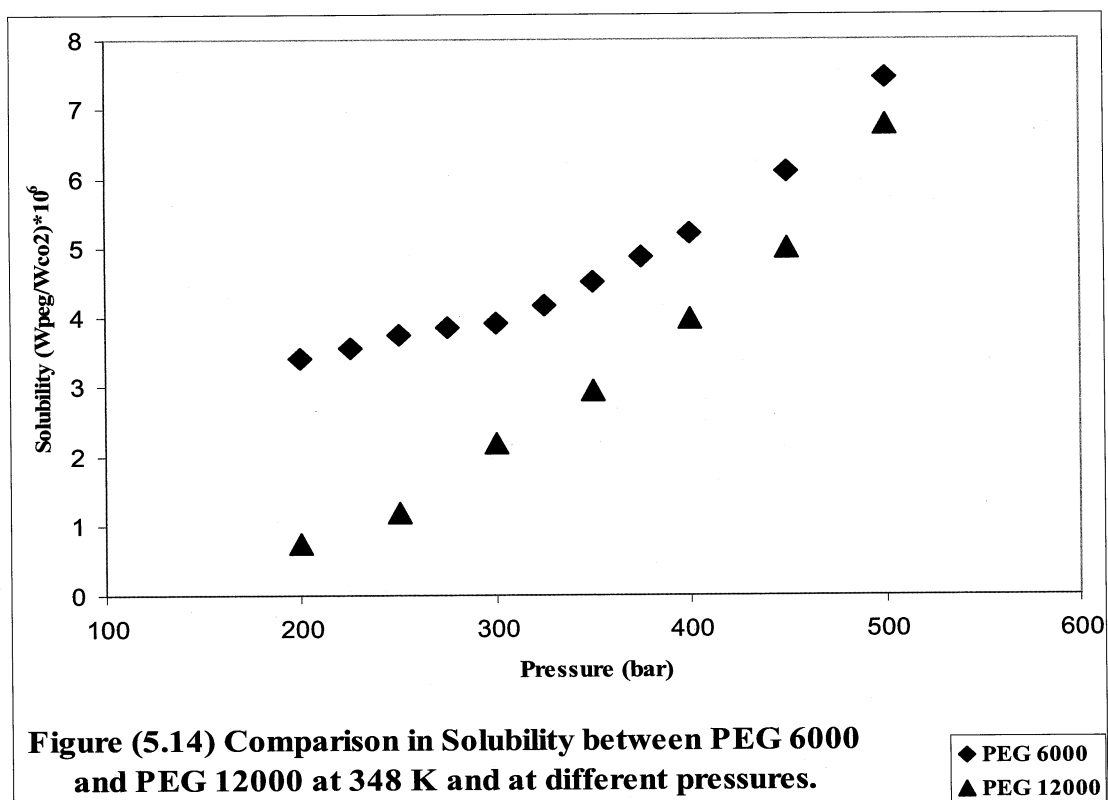
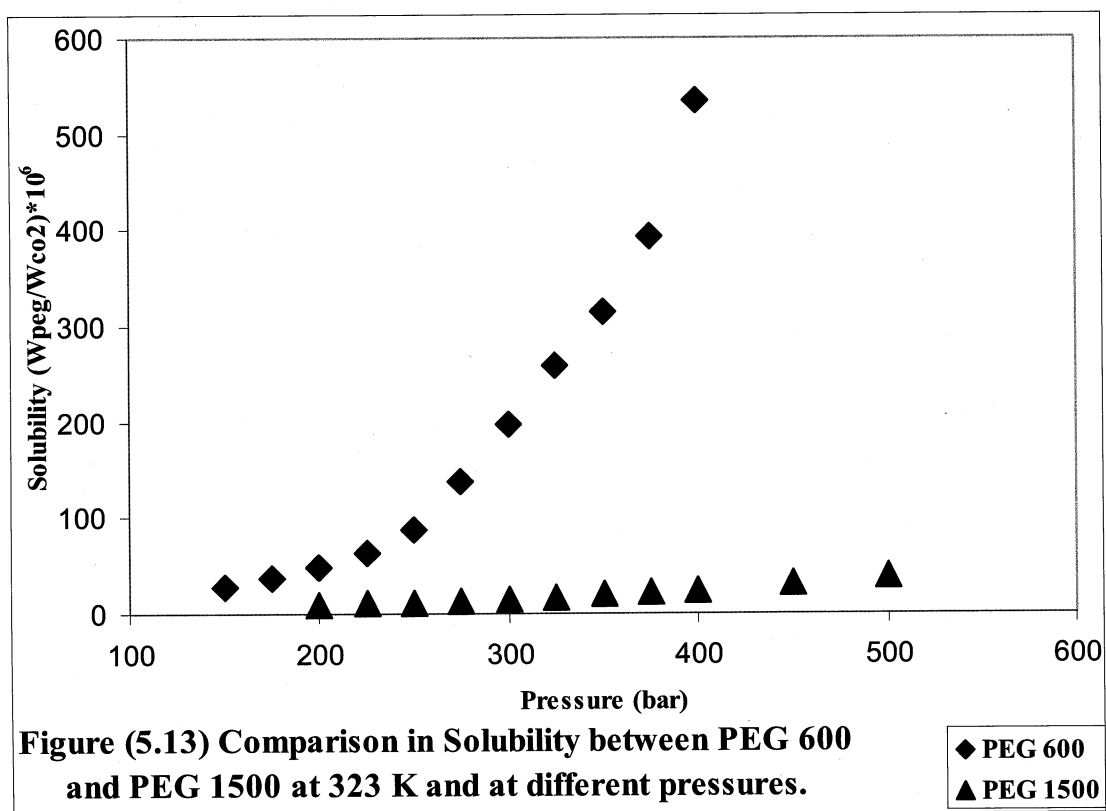
(5.8) Molecular Weight Impact on PEG Solubility

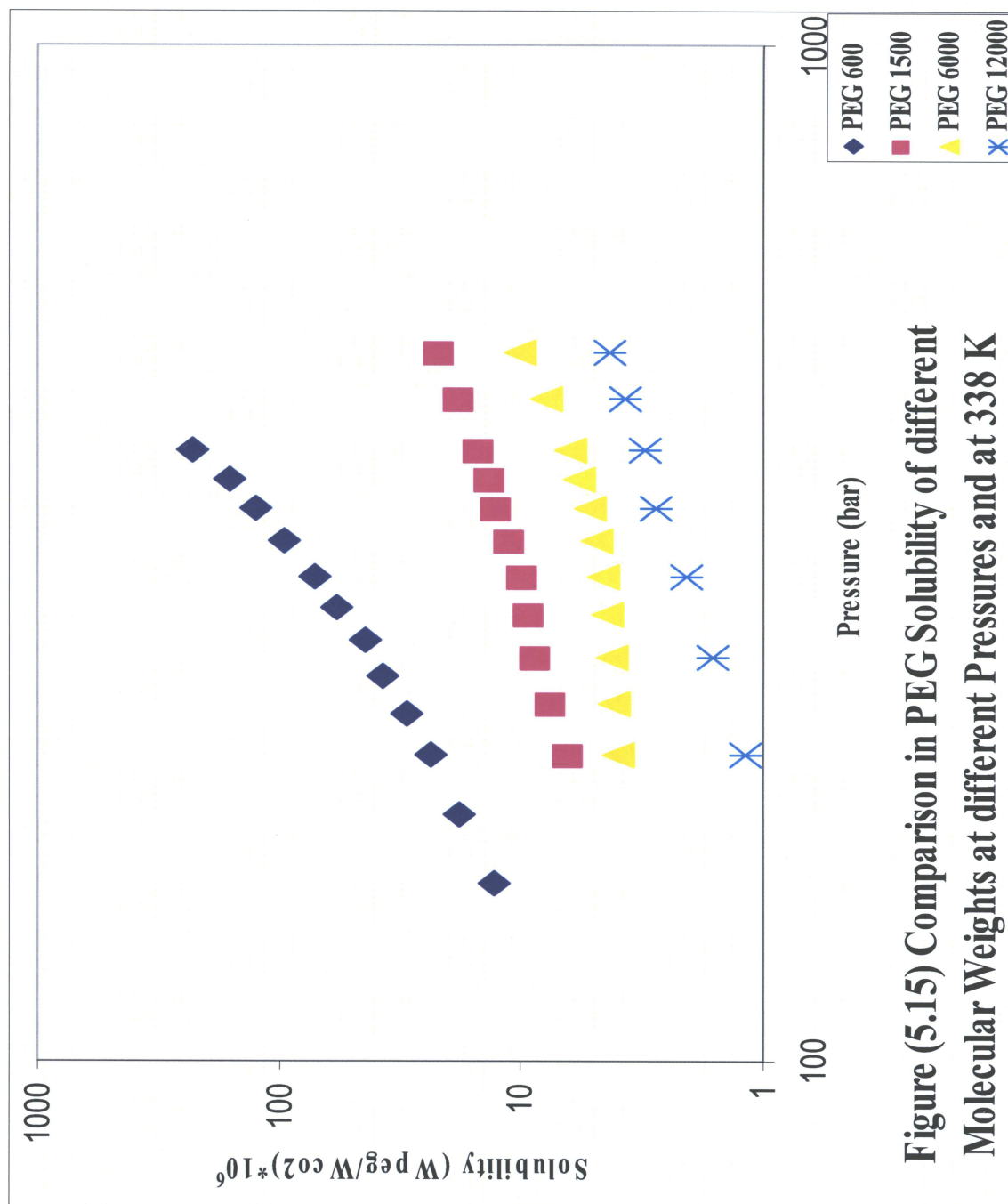
In order to investigate the effect of polymers molecular weights on the solubility of these polymers in supercritical fluids, PEG solubility is compared at different molecular weights in supercritical carbon dioxide at wide ranges of pressures and temperatures. First the comparison in solubility between PEG 600 and PEG 1500 at constant temperature of 323 K as shown in Figure 5.13 showed that low molecular weight polyethylene glycol has more solubility than that of high molecular weight at the same supercritical conditions. The solubility pattern of PEG 600 differs from the solubility pattern of PEG 1500 at the same supercritical conditions; solubility pattern of PEG 600 is affected strongly by pressure increasing and more than what solubility pattern of PEG 1500 does.

Figure 5.14 shows a comparison between the solubility of PEG 6000 and the solubility of PEG 12000 at temperature of 348 K and during the pressurizing process. High molecular weight polyethylene glycol polymer has less solubility than that of low molecular weight. Figure 5.15 shows another comparison in PEG solubility of four different molecular weights in SC CO₂ at 338 K and over a wide range of pressure.

Low molecular weights polyethylene glycol polymers have higher solubility in supercritical carbon dioxide than what high molecular weights PEG have at the same conditions of pressures and temperatures. Solubility of PEG 1500, PEG 6000 and PEG 12000 are close to each other in values and follow almost the same pattern, and they are far behind the solubility of PEG 600 at the same conditions.

Generally at ambient temperatures, liquid state polyethylene glycol polymers (i.e. Mw 600) have much higher solubility in supercritical carbon dioxide than that of solid polyethylene glycol polymers (i.e. Mw 6000 and 12000) at the same conditions. By this way, fractionation process of polyethylene glycol polymers will be a successful process when it carries out at these conditions of pressures and temperatures.



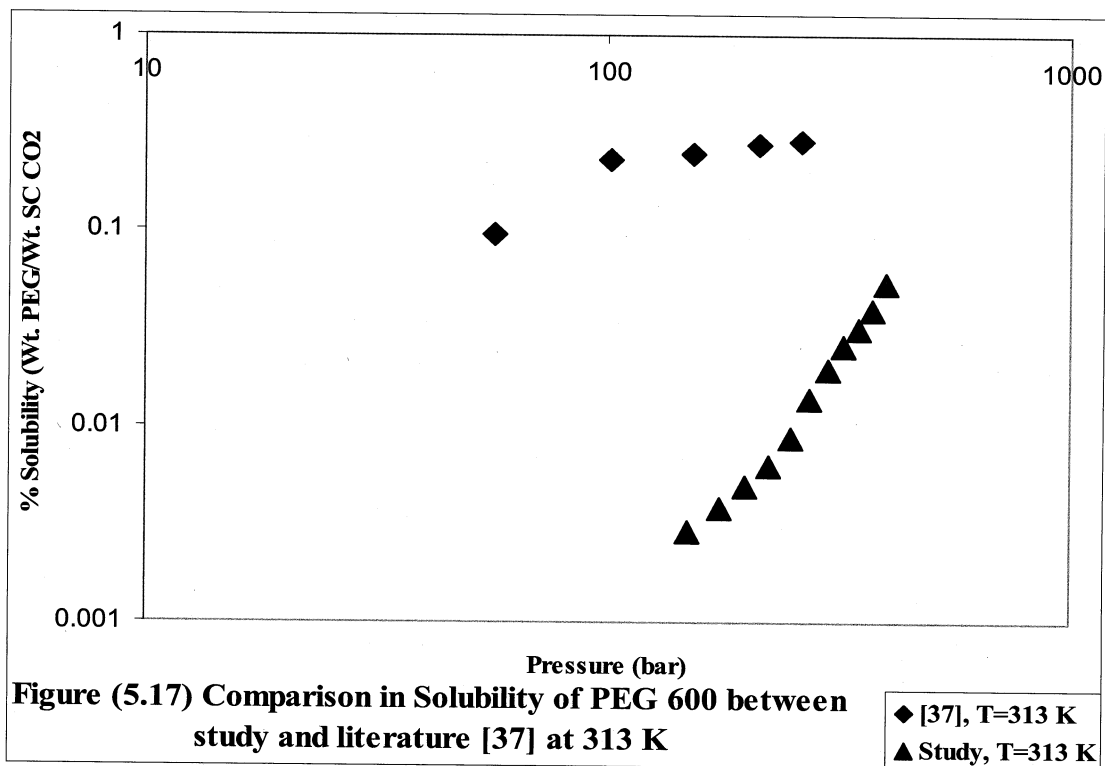
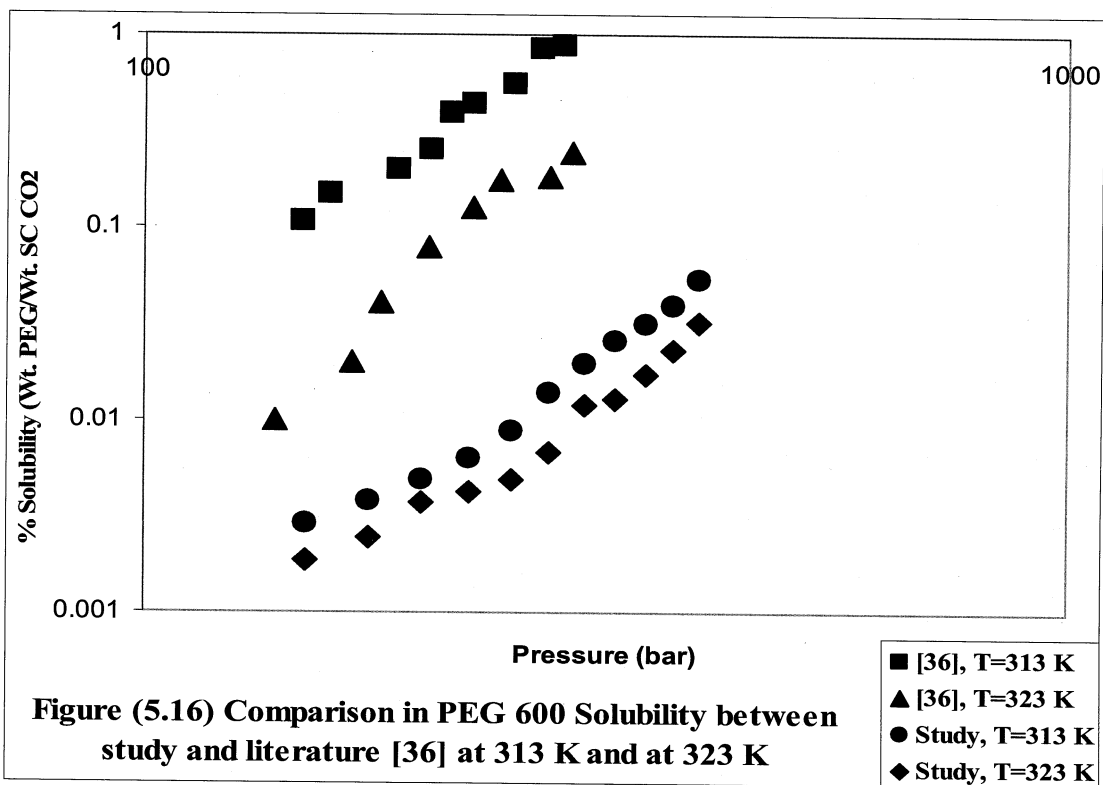


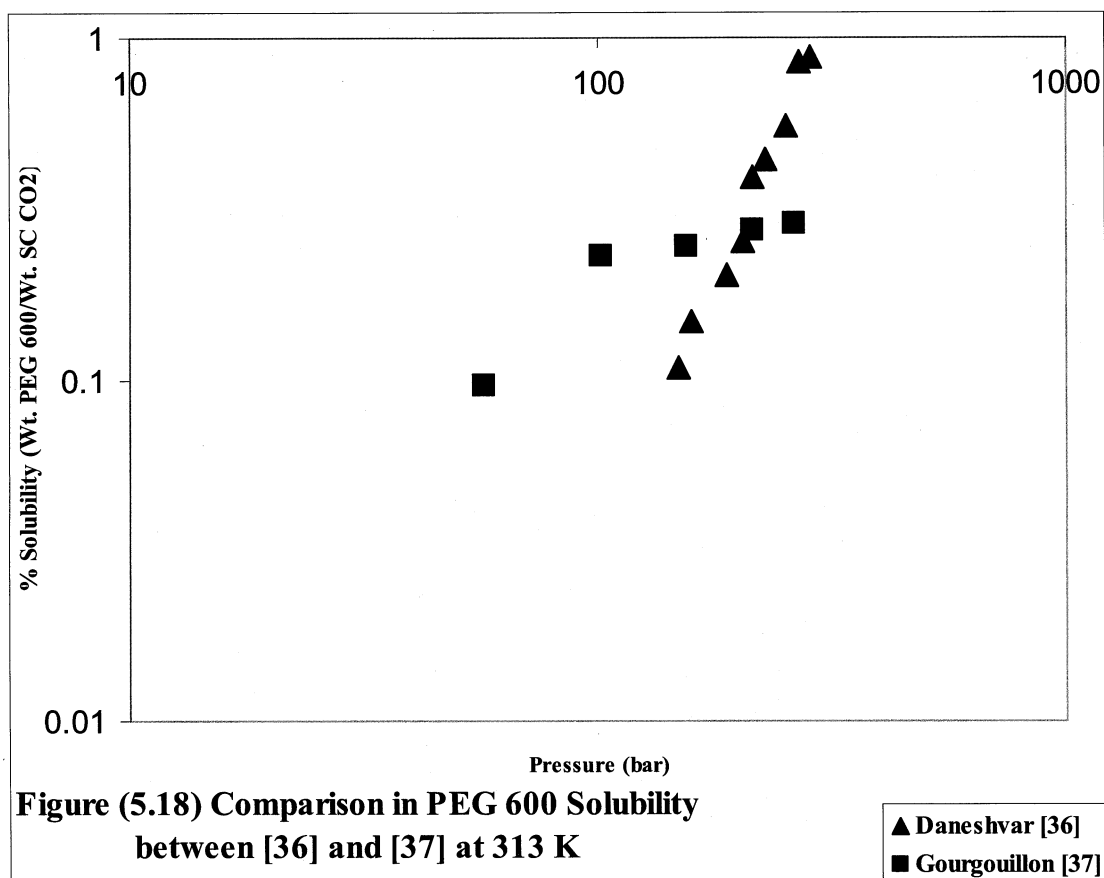
(5.9) Comparing the Study with the Literature

Two comparisons between study results and literature are made and represented in the following two figures, in Figure 5.16; solubility measurement of PEG 600 is compared with the solubility measurement of Daneshvar et. al.[36] at two different temperatures and at wide range of pressure.

There is a difference between the study results and theirs, higher solubility appeared in their experiments than present work which is due to the effect of using different methods (they used recirculation method) in measuring the PEG 600 solubility. Recirculation method is more complex and more expensive than static method. In this method, the large contact surface area between the polymer phase and supercritical phase gives this method its characteristics in reaching short saturation time. This method needs two or more syringe pumps for circulating the phases (polymer and supercritical fluid) in countercurrent flow, beside need for special valves to get samples during the experiment as we mentioned in chapter three.

Figure 5.17 shows another difference in solubility measurement of PEG 600 between study and Gourgouillon et. al [37] readings in spite of both studies have used the same method in measuring the solubility (static method). The difference in solubility measurements may come from the difference in analytical method that has been used in both set up. We analyze our readings by employing a gravimetric method using 10^{-6} gm (micro gram) accuracy scale whereas Gourgouillon et. al. used a differential refractometer coupled to a GPC apparatus [37] which needs the polymer sample to be very pure before analyzing (a complex analyzing method). The differences in solubility measurement results that found between the study and literature [36], [37] are acceptable, especially when we know that there is an appreciable difference between the two literature results themselves as shown in Figure 5.18.





(5.10) Finding the best fitting and Empirical Equations

Many researchers tried to predict the solubility behavior of polymers in supercritical fluids without using equations of state, most of them started from the chemical equilibrium between the polymer phase and the supercritical fluid phase when they reach (or very close to) the equilibrium state. It has been found that it is very hard to model or predict the solubility behavior of different polymers in supercritical carbon dioxide due to the existence of many variables that affecting this behavior starting from polymers characteristics and ending with supercritical conditions. The main disadvantages in using equations of state to describe any solubility behavior are:

- They are specified for a particular case, and it can not generalize them for more cases without modifications.
- It is very hard and sometimes impossible to estimate the constants of these equations.
- The complexity of these equations increases substantially with demanding more accuracy.

For all of the above reasons, many trials were made to find out easy ways to correlate the solubility behavior related directly to pressure and temperature in a relatively wide range using only experimental data that we can get directly from experiments.

In order to find the best fitting correlation that can describe our experimental solubility measurement with pressure and temperature, **TableCurve 2D** [42] is used. In table 5.1, we summarized the empirical equations that give best fitting with a minimum regression value (r^2) for every PEG molecular weight and at wide ranges of pressure and temperature. Y-axes represent the solubility measured, and x-axes represent the pressure at which the solubility is measured (i.e. $y=f(x)$).

Table (5.1) Best fitting and empirical equations of solubility prediction.

PEG Mwt.	Press. & Temp. Ranges	Empirical Equation	r ² Value	Constants a and b
600	150-400 bar, 313-338 K	$Lny = a + bxLnx$	0.9934	a=1.739175, b=0.00168
600	150-400 bar, 313-338 K	$Lny = a + bx$	0.9932	a=1.1991, b=0.01140
600	150-400 bar, 313-338 K	$Lny = a + bx / Lnx$	0.993	a=0.434080, b=0.079721
600	150-400 bar, 313-338 K	$Lny = a + bx^{1.5}$	0.993	a=2.4268866, b=0.0004184
600	150-400 bar, 313-338 K	$1/y = a + bLnx / x^2$	0.992	a=0.0062532, b=249.9088
1500	200-500 bar, 323-338 K	$Lny = a + bx / Lnx$	0.999	a=0.9407774, b=0.034116
1500	200-500 bar, 323-338 K	$Lny = a + bx^{0.5} Lnx$	0.999	a=0.4324072, b=0.0233435
1500	200-500 bar, 323-338 K	$y^{0.5} = a + bx^{1.5}$	0.999	a=1.886211, b=0.0003929
1500	200-500 bar, 323-338 K	$Lny = a + bx^{0.5}$	0.998	a=-0.453776, b=0.1844667
1500	200-500 bar, 323-338 K	$Lny = a + bxLnx$	0.998	a=1.5527358, b=0.0006896
6000	200-500 bar, 338-358 K	$Lny = a + bx^2$	0.996	a=1.1236727, b=0.0000047
6000	200-500 bar, 338-358 K	$1/y = a + bx / Lnx$	0.998	a=0.42074788, b=-0.003994
6000	200-500 bar, 338-358 K	$1/y = a + bx$	0.998	a=0.377921, b=-0.0005576
6000	200-500 bar, 338-358 K	$y^{0.5} = a + bx^2 Lnx$	0.997	a=1.6963844, b=9.26 e -7
6000	200-500 bar, 338-358 K	$Lny = a + bx \ln x$	0.990	a=0.688143, b=0.0005102
12000	200-500 bar, 338-366 K	$1/y = a + b / x^{1.5}$	0.987	a=-0.1572142, b=2230.5966
12000	200-500 bar, 338-366 K	$Lny = a + bLnx$	0.994	a=-25.269138, b=4.5718662
12000	200-500 bar, 338-366 K	$Lny = a + b / Lnx$	0.992	a=29.879896, b=-166.19314
12000	200-500 bar, 338-366 K	$1/y = a + bLnx / x^2$	0.990	a=-0.1149296, b=6326.1718
12000	200-500 bar, 338-366 K	$Lny = a + bxLnx$	0.990	a=-1.556192, b=0.00151705

The most useful equation that existing in all PEG molecular weights solubility measurement is (# 23 of the TableCurve 2D software order):

$$Lny = a + bxLnx$$

Where: y represents the solubility, and x represents the pressure (this equation based on constant temperature). Table 5.2 represents the application of the above equation on each PEG solubility measured curve and at each selected temperature.

Table (5.2) #23 Empirical equation application
on different polymer molecular weights and at different temperatures.

PEG Mwt.	Temperature K	r ² Value	a value constant	b value constant
600	313	0.989	2.48610	0.001586
600	323	0.992	1.73920	0.00168
600	338	0.998	1.35560	0.001696
1500	323	0.998	1.55274	0.0006896
1500	333	0.981	1.41470	0.0006460
1500	338	0.994	1.38460	0.0005460
6000	338	0.989	0.688143	0.0005102
6000	348	0.980	0.7252630	0.0003995
6000	358	0.994	0.940250	0.0002114
12000	338	0.975	-0.187484	0.000541
12000	348	0.980	-0.713033	0.0008492
12000	358	0.995	-1.401277	0.0014023
12000	366	0.993	-1.556192	0.0015171
Standard Deviation		0.0073	1.2000	0.000523

(5.11) Error Analysis

The following points are mention to the major cases where the errors come from:

- The major difficulty in using static method is residing with the withdrawal of the samples of equilibrium phases from the cell without disturbing the system equilibrium and with their transport to analytical device (the micro gram scale) which is usually accompanied by depressurization while avoiding any changes in their homogeneity and composition.
- It is very difficult (if it is not impossible) to fix the amount of polymer powder which is fed to the cell. The difficulty comes from adjusting micro grams of polymer powder that should be inserted inside Pyrex tube manually using scale.
- The presence of a little amount of polymer dissolved in SC CO₂ that may precipitate on the Pyrex tube inside the cell and during the depressurization process, this amount may cause a small error in weighing Pyrex tube containing polymer sample. This amount is very small if it is compared with the total polymer amount that precipitates outside the cell. The ratio of Pyrex tube cross section area to that of cell is around 1:10.
- Pumping SC CO₂ to the cell (in order to keep constant pressure inside the cell) using syringe pump may affect the fix system temperature especially when SC CO₂ flow rate is high.
- The pressure transducer has an accuracy of 0.01% at full scale of 680 bar, whereas the RTD provides +/- 0.5 °C temperature sensing accuracy.
- Weighing polymer sample inside Pyrex tube is repeated 2-3 times (before pressurizing process and after depressurizing process) to be sure the accurate reading is reached. Each solubility measurement of different molecular weights PEG is repeated two times. See Appendix C

(6) Conclusions

Static method with a gravimetric analysis is used in measuring the polyethylene glycol solubility in supercritical carbon dioxide. This method has advantages which include: It is an easy method without any complex preparations for either the sample or the apparatus; just small amount of polymers has been used and also small amount of the CO₂ gas. The equilibrium state between the two phases can be reached simply by an efficient mixing process. PEG solubility in SC CO₂ is measured at pressure range of 15 to 50 MPa, and at temperature range of 310 to 366 K. Different PEG molecular weights are used to compare experimentally the effect of polymers molecular weights on their solubility in supercritical carbon dioxide, low molecular weight polyethylene glycol has higher solubility than that of high molecular weight.

There are two main factors that affect the solubility of polymers in supercritical fluids, the density of supercritical fluid and the polymer vapor pressure. Solubility increased with pressure and decreased with temperature due to SC CO₂ density effect. In some cases, polymers vapor pressure effect may oppose the density effect, and then the solubility will increase with increasing temperature as well as pressure.

Saturation time in reaching equilibrium state of the two phases is estimated for different polyethylene glycol molecular weights at different conditions, and we found that it can reduce this time period by using an efficient mixing process.

At certain pressures (between 100 and 200 bar) and at certain temperatures (between 310 and 330 K), supercritical carbon dioxide density is found to be a very sensitive to any changes in pressure and temperature. These specific conditions represent the most tunable and affective conditions for using SC CO₂ as solvent.

In general, polyethylene glycol polymer has a low solubility in supercritical carbon dioxide at moderate supercritical conditions. This solubility can be enhanced by increasing pressure and decreasing temperature at certain limits above the supercritical conditions. Since different molecular weights of polyethylene glycol polymer have different solubilities in supercritical carbon dioxide, it can use this method to separate (or fractionate) the lower molecular weights from the higher ones by changing the supercritical conditions to introduce different levels of solvent power.

(7) Recommendations for future work

1. We recommend using bigger volumes of high pressure cell with modifying its ability to work at higher pressures to examine the solubility at wider range conditions.
2. We recommend using other methods in measuring the solubility like dynamic methods or chromatographic methods to compare the solubility results of different methods.
3. We recommend using other supercritical fluids and/or using other polymers (or same polymers of different molecular weights) to give better chances to realize the solubility behavior from different ways.
4. We recommend finding a new device or method to measure the changes in liquid polymer level during the pressurizing and depressurizing processes. This measurement will help us to figure out the polymer swelling as a function of time which is an indicator to the solubility of SC CO₂ in the polymer.
5. We recommend using an effective method to enlarge the contact surface area between the polymer phase and supercritical fluid phase inside the cell to modify the system in getting the solubility measurements efficiently and quickly.

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Appendix A

Carbon Dioxide Properties

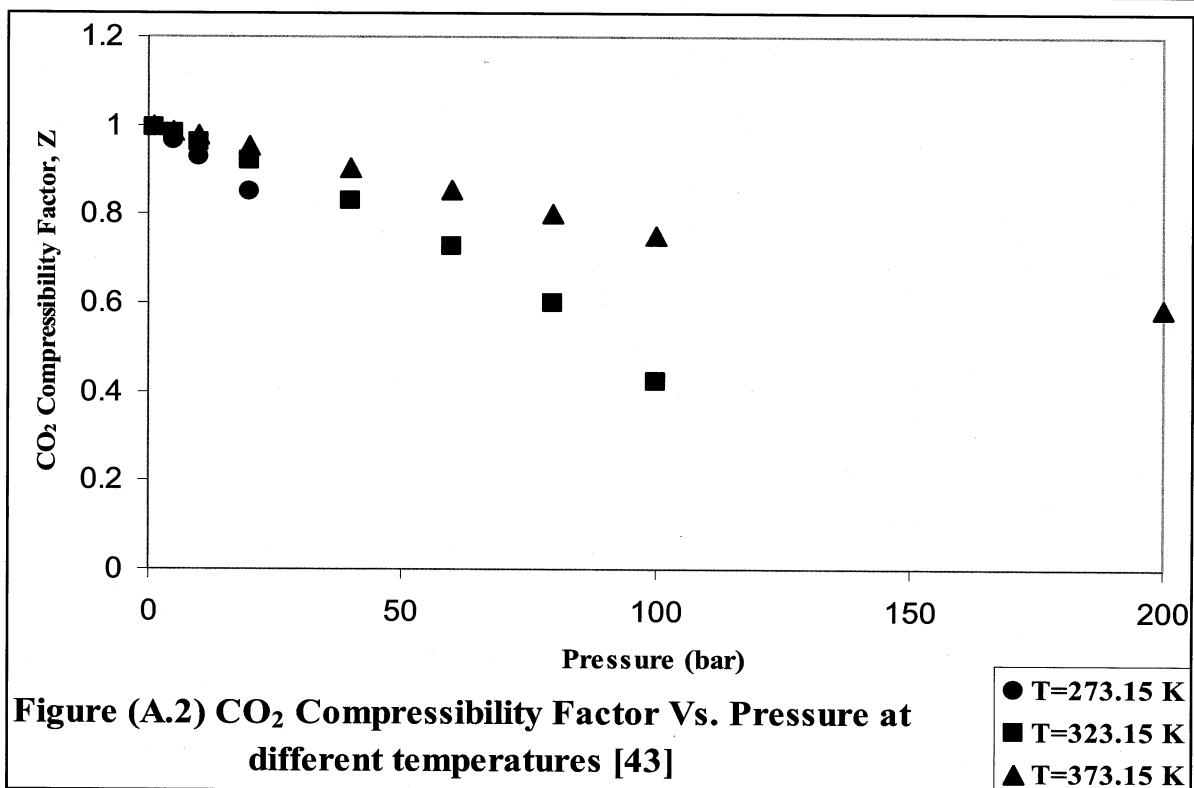
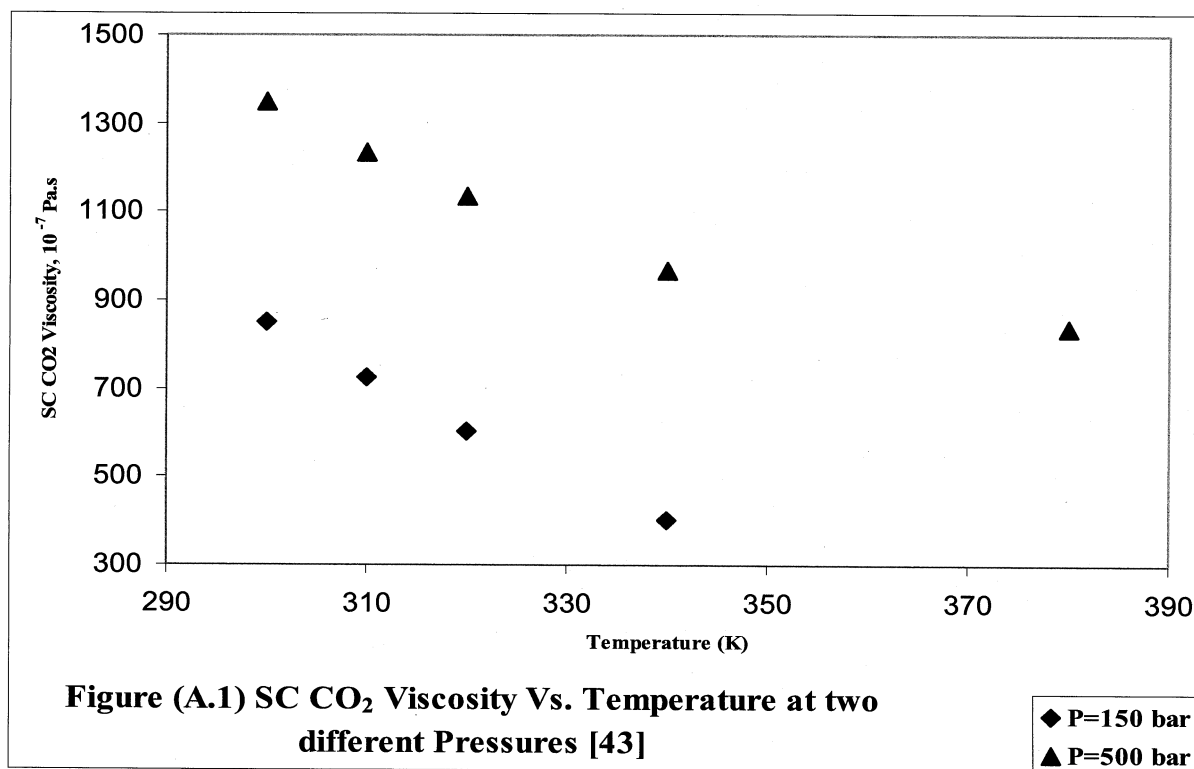
Table (A.1) Supercritical Carbon Dioxide Density. [40]

Pressure (bar)	SC Carbon Dioxide Density (mg/ml)						
	Temperature K						
	313	323	333	338	348	358	366
150	780.92	700.59	605.44	555.49	465.29	411.93	360.89
175	810.69	742.80	664.97	624.04	546.28	488.00	439.59
200	840.46	785.01	724.49	692.59	627.27	564.07	518.30
225	860.27	809.91	755.86	727.62	669.82	612.95	570.43
250	880.07	834.82	787.22	762.64	712.36	661.82	622.55
275	895.25	852.91	808.76	786.09	739.91	693.43	657.01
300	910.43	870.99	830.3	809.55	767.46	725.04	691.47
325	921.96	884.19	845.38	825.65	785.70	745.51	713.68
350	933.49	897.39	860.47	841.74	803.94	765.98	735.89
375	945.02	910.59	875.55	857.84	822.19	786.46	758.10
400	956.55	923.80	890.63	873.94	840.43	806.93	780.31
425	965.35	933.57	901.46	885.32	852.96	820.64	794.98
450	974.14	943.34	912.29	896.69	865.48	834.35	809.64
475	982.93	953.11	923.12	908.07	878.01	848.07	824.31
500	991.72	962.88	933.94	919.45	890.53	861.78	838.98

Appendices

Table (A.2) Critical Properties of common Solvents. [6]

Solvent	Molecular Weight (g/mol)	Critical Temperature (k)	Critical Pressure (MPa)	Critical Density (g/cm³)
Carbon Dioxide	44.01	304.1	7.38	0.469
Water	18.02	647.3	22.12	0.348
Methane	16.04	190.4	4.6	0.162
Ethane	30.07	305.3	4.87	0.203
Propane	44.09	369.8	4.25	0.217
Ethylene	28.05	282.4	5.04	0.215
Propylene	42.08	364.9	4.6	0.232
Methanol	32.04	512.6	8.09	0.272
Ethanol	46.07	513.9	6.14	0.276
Acetone	58.08	508.1	4.7	0.278



Appendix B

(B.1) Sample of Solubility Calculations

$$\text{Solubility (Wt. fraction)} = \frac{\text{Wt.ofPEGdissolved(mg)}}{[\text{Wt.ofPEGdissolved} + \text{Wt.ofSCCO}_2\text{insideCell}]_{p,T} \text{ (mg)}}$$

$$\text{Wt. of PEG dissolved (mg)} = W_2 - W_1$$

Where: W_2 is the weight of Pyrex tube + polymer weight (mg)

(After pressurize them inside the cell for 24-25 hr at the desired pressure and temperature)

W_1 is the weight of Pyrex tube + polymer weight (mg)
(Before the pressurization process)

$$\text{Wt. of SC CO}_2 \text{ inside the cell} = \rho_{CO_2} * \text{Vol. of the cell (mg)}$$

ρ_{CO_2} At desired pressure and temperature has been estimated from the literature [40] as we saw in appendix A. Volume of the cell has been fixed at 3 ml.

Appendices

(B.2) Pressure Cell Volume Calculation

The following calculations are done when the manual displacement pump of the SFT monitor II is all the way in, meaning there will be no carbon dioxide inside the piston/cylinder system.

1. Fill the syringe pump with liquid CO₂, the pump controller monitor shows the following conditions:

P₁ = 63.3 bar, V₁ (pump storage) = 266.36 cm³ and T₁ (room temperature) = 298.15 K, at these conditions we can find compressibility factor Z from Figure A.2, Z₁ = 0.598.

Using the real gas equation, $P * V = Z * n * R * T$

Where R = 83.1447 cm³ bar mol.⁻¹ K⁻¹

$$n_1 = 63.3 \text{ bar} * 266.36 \text{ cm}^3 / \{0.598 * 83.1447 \text{ cm}^3 \text{ bar mol.}^{-1} \text{ K}^{-1} * 298.15 \text{ K}\}$$

$$n_1 = 1.138 \text{ mol.}$$

2. The cell is vacuumed from air, and then the outlet valve of syringe pump is opened to let the carbon dioxide expands to occupy the new volume V₂. Pressure is dropped from 63.3 bar to 61.9 bar, whereas the temperature is still constant at 298.15 K.

The compressibility factor Z is estimated from Figure A.2, Z₂ = 0.6074. Since the number of moles is constant (closed system), n₂ = n₁ = 1.138 mol.

Using the real gas equation, $P * V = Z * n * R * T$ to calculate V₂

$$V_2 = \{0.6074 * 1.138 \text{ mol.} * 83.1447 \text{ cm}^3 \text{ bar mol.}^{-1} \text{ K}^{-1} * 298.15 \text{ K}\} / 61.9 \text{ bar}$$

$$V_2 = 276.82 \text{ cm}^3$$

Appendices

Since $V_2 = \text{Volume of syringe pump} + \text{Volume of cell} + \text{Volume of stainless steel connecting syringe pump and cell}$.

$$\text{Volume of the tube} = \pi/4 * D^2 * L = \pi/4 * (0.22 \text{ cm})^2 * 198 \text{ cm} = 7.527 \text{ cm}^3.$$

$$\text{Volume of the cell} = V_2 (276.82 \text{ cm}^3) - \text{syringe pump volume} (266.36 \text{ cm}^3) - \text{tube volume} (7.527 \text{ cm}^3)$$

$$\text{Volume of the cell} = 2.934 \text{ cm}^3$$

SFT phase monitor II manual mentioned that the cell volume is 3 cm^3 (when the manual displacement pump is all the way in), so the error of our cell volume calculation is 2.2%. This error may come from that we did not consider the valves volume which they placed between the syringe pump and the cell.

Appendix C

Tabulated Results

Table (C.1) Inlet sample weight and Solubility of PEG 600 at different pressures and at different temperatures.

Pressure (bar)	T= 313 K				T= 323 K				T= 338 K			
	PEG Wt. Inlet (mg)	Solubility E 6			PEG Wt. Inlet (mg)	Solubility E 6			PEG Wt. Inlet (mg)	Solubility E 6		
		1 st Trial	2 nd Trial	\bar{X}		1 st Trial	2 nd Trial	\bar{X}		1 st Trial	2 nd Trial	\bar{X}
150	1.742	27.3	29.9	28.6	1.472	18.1	18.7	18.4	1.482	12.3	13.3	12.8
175	1.653	37.1	38.5	37.8	1.837	24.9	23.9	24.4	1.735	19.4	16.8	18.1
200	1.583	49.7	47.1	48.4	1.648	37.6	36.4	37.0	1.372	23.1	24.3	23.7
225	1.783	62.3	62.9	62.6	1.528	42.7	41.3	42.0	1.628	29.9	29.7	29.8
250	1.639	88.2	86.8	87.5	1.482	47.5	49.9	48.7	1.482	36.8	38.4	37.6
275	1.629	136.3	138.9	137.6	1.571	68.8	66.4	67.6	1.547	44.7	44.3	44.5
300	1.428	197.8	195.6	196.7	1.517	119.3	120.7	120.0	1.428	69.6	71.4	70.5
325	1.407	260.1	258.7	259.4	1.639	130.9	128.7	129.8	1.538	96.2	95.6	95.9
350	1.630	314.7	316.5	315.6	1.426	172.4	173.6	173.0	1.385	125.3	126.7	126.0
375	1.728	394.2	391.2	392.7	1.538	231.8	233.6	232.7	1.462	160.7	159.1	159.9
400	1.528	533.8	535.6	534.7	1.634	323.5	321.3	322.4	1.624	230.4	229.0	229.7

Appendices

Table (C.2) Inlet sample weight and Solubility of PEG 1500 at different pressures and at different temperatures.

Pressure (bar)	T= 323 K				T= 333 K				T= 338 K			
	PEG Wt. Inlet (mg)	Solubility E 6			PEG Wt. Inlet (mg)	Solubility E 6			PEG Wt. Inlet (mg)	Solubility E 6		
		1 st Trial	2 nd Trial	\bar{X}		1 st Trial	2 nd Trial	\bar{X}		1 st Trial	2 nd Trial	\bar{X}
200	1.547	8.8	9.4	9.1	1.453	6.4	6.8	6.6	1.664	6.2	6.6	6.4
225	1.472	10.9	9.9	10.4	1.546	8.1	7.5	7.8	1.647	8.3	6.9	7.6
250	1.642	12.3	11.5	11.9	1.554	9.7	8.7	9.2	1.568	8.5	8.9	8.7
275	1.463	12.7	14.9	13.8	1.443	11.3	10.5	10.9	1.495	9.1	9.7	9.4
300	1.637	16.3	15.1	15.7	1.738	12.2	13	12.6	1.638	10.4	9.4	9.9
325	1.552	16.8	18.2	17.5	1.485	15.4	13.4	14.4	1.574	12.0	10.6	11.3
350	1.643	20.4	19.0	19.7	1.562	16.8	15.4	16.1	1.558	12.9	12.5	12.7
375	1.446	21.8	23.0	22.4	1.672	17.6	19	18.3	1.495	13.5	13.7	13.6
400	1.364	25.1	24.1	24.6	1.385	20.6	19.8	20.2	1.617	14.7	15.1	14.9
450	1.456	30.5	32.7	31.6	1.474	24.1	24.3	24.2	1.421	18.6	17.2	17.9
500	1.645	38.6	41.2	39.9	1.582	30.4	29	29.7	1.544	22.3	20.9	21.6

Appendices

Table (C.3) Inlet sample weight and Solubility of PEG 6000 at different pressures and at different temperatures.

Pressure (bar)	T= 338 K				T= 348 K				T= 358 K			
	PEG Wt. Inlet (mg)	Solubility E 6			PEG Wt. Inlet (mg)	Solubility E 6			PEG Wt. Inlet (mg)	Solubility E 6		
		1 st Trial	2 nd Trial	\bar{X}		1 st Trial	2 nd Trial	\bar{X}		1 st Trial	2 nd Trial	\bar{X}
200	1.536	3.4	4.0	3.7	1.637	3.6	3.2	3.4	1.361	3.4	3.2	3.3
225	1.438	4.2	3.6	3.9	1.519	3.2	4.0	3.6	1.449	3.5	3.1	3.3
250	1.621	4.5	3.7	4.1	1.440	3.3	4.1	3.7	1.596	3.2	3.8	3.5
275	1.552	4.1	4.7	4.4	1.381	3.6	4.2	3.9	1.482	3.6	3.4	3.5
300	1.497	5.2	4.2	4.7	1.492	4.1	3.7	3.9	1.440	3.7	3.5	3.6
325	1.511	4.7	5.3	5.0	1.553	4.5	3.9	4.2	1.603	4.0	3.6	3.8
350	1.447	5.2	5.8	5.5	1.408	4.7	4.3	4.5	1.550	3.7	4.1	3.9
375	1.623	6.4	5.8	6.1	1.339	5.3	4.5	4.9	1.492	4.6	3.6	4.1
400	1.611	6.0	7.2	6.6	1.406	5.6	4.8	5.2	1.396	4.1	4.3	4.2
450	1.704	8.0	7.8	7.9	1.550	6.0	6.2	6.1	1.552	4.5	4.7	4.6
500	1.807	10.0	9.8	9.9	1.562	7.2	7.6	7.4	1.660	5.3	4.7	5.0

Appendices

Table (C.4) Inlet sample weight and Solubility of PEG 12000 at different pressures and at different temperatures.

			Pressure (bar)						
			200	250	300	350	400	450	500
T=338 K	PEG Wt. Inlet (mg)		1.554	1.546	1.528	1.637	1.448	1.512	1.620
	Solubility E 6	1st Trial	1.15	1.66	2.10	2.82	3.03	3.68	4.37
		2nd Trial	1.23	1.60	2.02	2.72	3.17	3.76	4.23
		\bar{X}	1.19	1.63	2.06	2.77	3.10	3.72	4.30
T=348 K	PEG Wt. Inlet (mg)		1.475	1.548	1.448	1.562	1.621	1.508	1.571
	Solubility E 6	1st Trial	0.71	1.15	2.20	2.90	3.88	5.04	6.82
		2nd Trial	0.77	1.23	2.14	3.0	4.06	4.96	6.74
		\bar{X}	0.74	1.19	2.17	2.95	3.97	5.0	6.78
T=358 K	PEG Wt. Inlet (mg)		1.482	1.491	1.503	1.507	1.513	1.541	1.520
	Solubility E 6	1st Trial	0.53	1.26	2.43	4.71	7.58	11.76	19.0
		2nd Trial	0.47	1.14	2.17	4.49	7.22	11.44	19.4
		\bar{X}	0.5	1.20	2.30	4.60	7.40	11.6	19.2
T=366 K	PEG Wt. Inlet (mg)		1.449	1.482	1.492	1.502	1.518	1.542	1.533
	Solubility E 6	1st Trial	0.48	1.20	2.22	5.21	8.69	12.84	23.45
		2nd Trial	0.44	1.16	2.28	4.59	8.85	13.14	23.79
		\bar{X}	0.46	1.18	2.25	4.9	8.77	12.99	23.62

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