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INFLUENCE OF COSOLVENTS ON THE SOLUBILITY OF CHOLESTEROL IN SUPERCRITICAL CARBON DIOXIDE

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ABSTRACT

The solubility of cholesterol in supercritical carbon dioxide with and without cosolvents was calculated using the Peng-Robinson equation of state. Calculations were carried out at 318.15 and 328.15 K under pressure range 100-240 bar. All results are correlated with previous measurements by minimizing the objective function Average Absolute Relative Deviation (AARD). Acetone and methanol were used as polar cosolvents with 3 mol% (solute-free basis), while Ethane with 50 mol% (solute-free basis) and hexane with 3.5 mol% (solute-free basis) were used as non-polar cosolvents. It has been observed that the addition of small amounts of cosolvents in general enhances the solubility of cholesterol in supercritical CO_2. The solubility enhancements for the four ternary systems investigated were pronounced at lower pressures. The highest solubility is observed in the hexane system while acetone and methanol behave with no valuable difference in enhancement. The addition of 50 mol% ethane to CO_2 results in a smallest solubility enhancement. An alternative method of presenting cosolvents solubility data is the cosolvent effect, which is defined as the ratio of the ternary solubility to the binary solubility. The expected minimum cosolvents effect value is 1 (at cosolvent concentration = 0). All the ternary systems exhibit a decreasing cosolvent effect with increasing pressure until a minimum point then it increases slightly with pressure. The largest cosolvent effect is caused by the addition of hexane while the smallest is caused by addition of ethane through the pressure rang

1. INTRODUCTION

Supercritical fluid extraction SCFE is considered fairly new and practical separation technology, in which a solute can be extracted at supercritical conditions of the solvent, and separated by reducing pressure or temperature below the critical conditions of the solvent. SCFE has great applications in many separation and purification processes, such as in food, pharmaceutical, polymer processing and biochemical industries, etc. Thermally labile compounds can be extracted from pharmaceutical and food products using supercritical solvents (Hartono, et al., 2001). Any gas above its critical temperature retains the free mobility of the gaseous state but with increasing pressure its density will increase towards that of a liquid. Supercritical fluids are as dense as highly compressed gases and as such they combine valuable properties of both liquid and gas (Hartono, et al., 2001).

Because carbon dioxide CO_2 is environmentally benign, nonflammable, nontoxic, and inexpensive and has relatively low critical pressure and critical temperature, it is one of the most commonly used solvents for supercritical fluid extraction. Carbon dioxide, however, has the limitation that it is not particularly good solvent for polar organic compounds, owing to its low polarity and lack of capacity for specific solvent-solute interactions. Therefore, there is a great incentive to improve its polarity.

The most common method that treats the SCF phase as a dense gas and uses an equation of state to calculate the solubility (mole fraction) of the solute in the fluid phase (Huang, et al., 2007). The Peng-Robinson equation of state (PR EOS) is commonly used to model the solubility of polar and non-polar solutes in supercritical fluids. . PR EOS is given by (Peng and Robinson, 1976):

$$P = \frac{RT}{v-b} - \frac{a(T)}{v(v+b)+b(v-b)} \qquad (1.1)$$

Although the concept of adding cosolvents to supercritical fluids has received attention for years, there are very few studies concerning the influence of cosolvents on solubility of solid solutes in SC-CO_2. Most of researchers measured the solubility in SC-CO_2 with and without cosolvents, but few of them tried to model the solubility using easily measurable properties.

Singh, et al. (1993) presented measurement for the solubility of cholesterol in supercritical ethane as well as the solubility in ethane with propane and ethane with supercritical carbon dioxide of different concentration at temperatures from 308.1 to 338.1 K and pressures from 85 to 220 bar. Foster, et al. (1993) studied the solubility of cholesterol in SC-CO_2 and in C_2H_6 both containing small amounts (1.75-6.0 mol%) of acetone and hexane cosolvents. The experimental results were correlated with modified PR EOS. The feature of this study is the reversal of cosolvent effects for acetone and hexane in the two SCFs. Acetone gives larger cosolvent effect in ethane than that in SC-CO_2 while hexane gives larger cosolvent effect in SC-CO_2 than that in ethane. The highest absolute solubility was observed in the ethane-acetone system.

Hartono, et al. (2001) used six different cubic equations of state to predict the solubility of cholesterol and β-carotene, as two representative biomolecules, in supercritical fluids. The EOSs are: van der Waals, Redlich–Kwong, Mohsen-Nia–Moddaress–Mansoori (MMM), Peng–Robinson (PR) and Patel–Teja and modified PR equations.

Huang, et al. (2004) measured solubilities of cholesterol and its three esters: cholesterol acetate, cholesterol butyrate and cholesterol benzoate in SC-CO_2. Also, they examined the effect of a polar cosolvent, namely methanol or acetone on the solubility. They found that the solubilities of these compounds were enhanced several folds depending on the pressure. They correlated their solubility data using PR EOS and the empirical density-base models of Chrastil and Kumar and Johnston.

A review of solubility data for solid compounds in sub- and supercritical fluids published in the literature between 2005 and 2010 was done by Škerget, et al. (2011). All data obtained in this period were tabulated along with temperature and pressure ranges as well as correlation methods employed for modeling the experimentally measured data. This review found for over 380 different pure solid compounds, for which solubilities were measured in different sub- and supercritical fluids without or with cosolvents. Most of experimental solubility data were for binary systems and the solid solutes considered in this research do not exist between these compounds. In addition, SC-CO_2 was the preferred solvent for most of the publication, although there is an observed interest in other solvents such as water, fluorinated hydrocarbons, ethane, and propane.

Most of the investigations on solubility are concerned with binary systems consisting of a single solute in contact with a single supercritical fluid. The importance of studying ternary systems comes from the potential applications of SCF just like removal of valuable components from a matrix of compounds. In addition, how such components act through their intermolecular interactions can greatly affect the selectivity of the SCF. Similarly, in the extraction of solid mixtures with pure SCF, the solubilities of the individual solutes using cosolvents can be significantly greater than their respective binary solubilities

What distinguishes this research is the study of the effect of different cosolvents on the solubility of various solutes in SC-CO_2 using models based on PR EOS. Experimental measurements were used to obtain binary interaction parameters where necessary. Modeling is important to correlate existing solubility data and to predict it in the regions where data are not experimentally available or attainable.

The purpose of this study is to investigate fundamental aspects of the influence of addition of cosolvents on the solubility of cholesterol in SC-CO_2 using PR EOS. Both polar substances (acetone and methanol) and nonpolar substances (ethane and hexane), were adopted as cosolvents to examine their effects on the solubility of cholesterol in SC-CO_2 over different temperature and pressure ranges. Another goal of this study is to correlate available equilibrium data using PR EOS in order to predict phase behavior in regions where data are not experimentally available.

3. THEORY

3.1 Supercritical Phase Equilibrium Involving a Condensed Phase

In predicting the phase equilibrium between a supercritical phase and a condensed (solid) phase, the equality of fugacity of each component in each phase is required. The solubility profile of a solute in a supercritical fluid significantly changes with pressure and temperature. It can be directly related to the pressure and temperature, based on fugacities, solubility parameters, and fluid density (Cansell and Rey, 1998).

At equilibrium of phases in a multi component system (n components), intensive variables to describe the state are: the pressure P, the temperature T, and different mole fractions of each component (y_i = 1,...(n-1)). Phase equilibrium occurs when chemical potentials (μ_i) for each component in all phases are equal:

$$\mu_i^{\alpha} = \mu_i^{\beta} = \ldots = \mu_i^{\gamma} \tag{3.1}$$

$(\alpha, \beta, \ldots, \gamma)$ denote the various phases and i indicates the component (i=1,2,…,n). Moreover, the chemical potential equality is translated into fugacity equality, f, which can be deduced directly by using a suitable equation of state. For supercritical phase in equilibrium with solid phase (Ksibi, 2004):

$$f_i^{s} = f_i^{SC} \tag{3.2}$$

where superscripts s and SC denote solid and supercritical phases, respectively.

Because the solid phase is pure, the fugacity of component i is given by (Prausnitz et al., 1999):

$$f_i^{s} = P_i^{sat} \varphi_i^{s} \exp\left(\int_{P_i^{sat}}^{P} \frac{v_i^{s}}{RT} dP \right) \tag{3.3}$$

$$f_i^{SC} = \varphi_i^{SC} y_i P \tag{3.4}$$

where P_i^{sat} is the saturation pressure of solid solute, φ_i^{s} is the fugacity coefficient of the solid phase at P_i^{sat}, v_i^{S} the molar volume of solute, P the operating pressure, T the operating temperature, R the gas constant, y_{i} the solubility in SC phase, and φ_i^{SC} is the fugacity coefficient of solute in supercritical phase.

The general solubility equation based on equality of fugacities which characterizes the solubility of a solid solute in a supercritical fluid is expressed as follows (Prausnitz, et al., 1999):

$$y_i = \left(\frac{P_i^{sat}}{P} \right) \left(\frac{\varphi_i^{s}}{\varphi_i^{SC}} \right) \exp\left\{ \int_{P_i^{sat}}^{P} \frac{v_i^{s}}{RT} dP \right\} \tag{3.5}$$

The saturation pressure of the solid phase, P_i^{sat}, is usually very small, so that the fugacity coefficient of the solid phase at saturation can be assumed to be $\varphi_i^{s} \to 1$. If the molar volume of the solid phase is independent of pressure, the solubility equation can be reduced to its final form:

$$y_i = \frac{P_i^{sat} \exp\left[v_i^{s} \left(P - P_i^{sat} \right) / RT \right]}{\varphi_i^{SC} P} \tag{3.6}$$

The solute solubility in a supercritical fluid can be directly calculated from the previous equation once the fugacity coefficient of the supercritical phase is known. An equation of state (EOS) is used to determine the values of the solute fugacity coefficient at different temperatures and pressures.

3.2 Peng-Robinson Equation of State (PR EOS)

The prediction of solubility using the chosen EOS model assumes that the solute phase remains pure. This assumption is thought to be quite reasonable for solid solutes. However, in the case of liquid solutes, it is likely that carbon dioxide will dissolve into the liquid solute at the same time as the liquid is dissolving in the supercritical carbon dioxide. McHugh and Krukonis (1994) provided the necessary equations to handle the phase equilibrium of the liquid solute within the supercritical fluid (Ksibi, 2004).

Cubic equations of state are valuable engineering tool for process design of any complex system and probably the most widely used to evaluate the solute fugacity in the SC phase. Moreover, cubic equations of state are mathematically simple in analyzing experimental data and remarkably successful in modeling supercritical fluid phase behavior. The Peng–Robinson equation of state (PR EOS) gives a good qualitative picture of all types of SC phase behavior and reasonably good quantitative fits for a wide variety of systems (Huang, et al., 2007). The PR EOS is given by (Peng and Robinson, 1976):

$$P = \frac{RT}{v - b} - \frac{a(T)}{v(v + b) + b(v - b)} \tag{1.1}$$

where v the molar volume, a energy interaction parameter and b the covolume parameters. The parameters a and b for pure components are defined in terms of the critical properties and acentric factor of the substance. These properties are independently determined and used as input parameters to the model. The PR EOS parameters are given by (Sandler, 1999):

$$a(T) = 0.45724 \frac{(RT_c)^2}{P_c} \alpha(T) \tag{3.7}$$

$$\alpha(T) = \left[1 + \kappa\left(1 - \sqrt{\frac{T}{T_c}}\right)\right]^2 \qquad (3.8)$$

$$\kappa = 0.37464 + 1.5422\omega - 0.26992\omega^2 \qquad (3.9)$$

$$b = 0.07779\frac{RT_c}{P_c} \qquad (3.10)$$

where T_c is the critical temperature, P_c is the critical pressure, and ω is the Pitzer's acentric factor.

3.3 Mixing and Combining Rules

The mixing rule is a relation which states how the parameters *a* and *b* for the mixture depend on the composition. The conventional mixing rules can be taken as quadratic function of composition, in this research, the van der Waal mixing rules are used:

$$a = \sum_{i=1}^{N}\sum_{j=1}^{N} y_i y_j a_{ij} \qquad (3.11)$$

$$b = \sum_{i=1}^{N}\sum_{j=1}^{N} y_i y_j b_{ij} \qquad (3.12)$$

where a_{ii} and b_{ii} are pure component parameters as defined by Peng and Robinson, and y_i is the mole fraction of component *i*, a_{ij} and b_{ij} are the cross parameters which can be obtained from the combining rules. Classical combining rules – van der Waal's one fluid vdW1 (Lorentz-Berthelot) for the energy and the covolume parameters as given by Prausnitz, et al. (1999) are used:

$$a_{ij} = (a_{ii}a_{jj})^{1/2}(1 - k_{ij}) \qquad (3.13)$$

$$b_{ij} = \frac{1}{2}(b_{ii} + b_{jj}) \qquad (3.14)$$

the k_{ij} ($k_{ij} = 0$ for like terms) is the binary interaction parameter which is adjusted to improve correlation of experimental data by the selected EOS.

3.4 Fugacity Coefficient According to PR EOS

The fugacity coefficient of the solid solute in the supercritical phase, φ_i^{SC}, can be derived from the EOS through the following expression (Hartono, et al., 2001):

$$RT\ln\varphi_i^{SC} = \int_{SC}^{\infty}\left[\left(\frac{\partial P}{\partial n_i}\right)_{T,V,n_{j\neq i}} - \frac{RT}{V}\right]dV - RT\ln Z \qquad (3.15)$$

where Z is the compressibility factor, $Z = Pv/RT$. Based on PR EOS, the fugacity coefficient of component *i* is given by:

$$\ln\varphi_i^{SC} = -\ln(Z - B) + \frac{B_i}{B}(Z - 1) - \frac{A}{\sqrt{8}B}\ln\left[\frac{Z + (1+\sqrt{2})B}{Z + (1-\sqrt{2})B}\right]\left[\frac{2A_i}{A} - \frac{B_i}{B}\right] \qquad (3.16)$$

and other parameters are defined as the following:

$$A = \frac{aP}{(RT)^2} \qquad (3.17)$$

$$B = \frac{bP}{RT} \qquad (3.18)$$

$$A_i = \left(\sum_{k=1}^{N} y_k a_{ik}\right)\frac{P}{(RT)^2} \qquad (3.19)$$

$$B_i = \left(2\sum_{k=1}^{N} y_k b_{ik} - b\right)\frac{P}{RT} \qquad (3.20)$$

3.5 Critical Properties

In applying equations of state for calculation of solubility of solutes in supercritical solvents, data for the critical properties, i.e. the critical temperature and pressure, of the compounds, saturated pressure and density (molar volume) and acentric factor data of solute involved are needed. The experimental critical properties, acentric factor of some solid solutes are not available in the literature. Cholesterol compound decomposes at high temperatures, making it impossible to measure its critical properties and saturation pressures at high temperature, which are needed to calculate the acentric factor. In these cases, methods for estimation of critical properties are available in the literature.

3.6 Binary Interaction Parameter k_{ij} Optimization

The binary interaction parameter k_{ij} is adjusted to maximize agreement between the EOS calculations and experimental data. To model the solubility for binary system (1: carbon dioxide and 2: solute) using the Peng–Robinson equation of state, the binary interaction parameter k_{12} at a given temperature is obtained by regressing the model against experimental solubility data. The optimization technique of the solubility is quantified by the objective function at each temperature, which is the percentage average absolute relative deviation (%AARD) between the calculated and experimental solubility, AARD approach is the most widely used assessment for evaluating the success of the model (Huang, et al., 2004):

$$\%\mathrm{AARD} = \frac{100}{N} \sum_{i=1}^{N} \frac{\left| y_{i,\exp} - y_{i,cal} \right|}{y_{i,\exp}} \qquad (3.21)$$

where N is the number of experimental data points. The $y_{i,\mathrm{exp}}$ and $y_{i,\mathrm{cal}}$ are experimental and calculated solubility values, respectively.

To model the solubility of ternary systems (1: carbon dioxide, 2: solute, 3: cosolvent) using the Peng–Robinson equation of state, three interaction parameters: k_{12}, k_{13} and k_{23} are used. The carbon dioxide–solute interaction parameter k_{12} is already available from binary mixture calculations described earlier. The carbon dioxide–cosolvent interaction parameter k_{13} is obtained independently by applying the PR EOS to fit carbon dioxide–cosolvent or carbon dioxide–cosolvent vapor–liquid equilibrium (VLE) data. When no VLE data exists at the temperature of interest, the value of k_{13} was set to zero. To model the solubility of solid in the ternary mixture, the parameter k_{23} that accounts for solute–cosolvent interactions was adjusted by regressing the PR EOS predictions against experimental data.

3.7 Cosolvent Effect

Supercritical carbon dioxide has limited solvent power for most polar and nonvolatile organic compounds with higher molecular weights due to its nonpolarity and incapability of specific interactions with solutes (Huang, et al., 2004). Usually, addition of a small amount of cosolvent cannot only increase the solubility of solutes but also improves the selectivity. The cosolvent effect, R_{CE}, defined as the ratio of solubility with and without cosolvent is introduced to quantify the effect in solubility due to a cosolvent more clearly, and to quantitatively compare the strength of different types of interaction between solute and cosolvent, especially hydrogen bonding (Huang, et al., 2004):

$$\mathrm{R}_{\mathrm{CE}} = \frac{y_{ternary}}{y_{binary}} \qquad (3.22)$$

where $y_{ternary}$ and y_{binary} are the solubilities of solid solute in supercritical solvent with and without cosolvent respectively. At the same conditions, cosolvent effect is expected to take values more than unity (cosolvent effect =1 at zero concentration of cosolvent). While some cosolvents act as anti-solvents where the cosolvent effect is less than unity (negative cosolvent effect).

4. SOLUTION METHODOLOGY

The solubility of solids in supercritical fluids can be correlated with the equation of state approach. Although Peng-Robinson equation of state has the advantage that it is mathematically simple (cubic polynomial in v) to use, the solubility calculations is iterative and needs optimization which requires computional work.

In this Research, Matlab® in parallel with Microsoft Excel® were used to predict the solubility (mole fraction) of cholesterol in SC-CO_2 and to model the results against experimental data. The AARD minimizing approach was accomplished using Solver Add-in in Microsoft Excel®.

4.1 Estimation of Physical Properties

The PR EOS uses the critical point as a corresponding state, and as a result, the critical properties of all components must be known in order to do phase equilibrium calculations. The physical and critical properties rquired to evaluate the pure component parameters in the PR EOS are listed in Table 4.1.1. The critical properties of the solvent CO_2 and all cosolvents are obtained from Prausnitz et al. (1999), but the properties of cholesterol was not experimentally available and needed to be estimated. The properties of cholesterol are obtained from Huang et al. (2004) and Ksibi and Moussa. (2007).

Table 4.1.1 Required physical and critical properties of all compounds used

Compound	T_c (K)	P_c (bar)	ω	P^{sat} (Pa)	
				318.15 K	328.15 K
Solvent					
CO_2	304.1^a	73.8^a	0.225^a		
Cosolvents					
Acetone	508.1^a	47.01^a	0.309^a		
Methanol	512.6^a	80.96^a	0.559^a		
Ethane	305.4^a	48.8^a	0.099^a		
Hexane	507.4^a	30.1^a	0.299^a		

Solutes					
Cholesterol	1168.23[b]	41.55[b]	0.950[b]	0.0573[b]	0.179[b]

[a] Prausnitz, et al. (1999)
[b] Huang, et al. (2004)

4.2 Solubility Prediction and Optimization

The PR EOS was used to predict the solubility of cholesterol in SC-CO_2 with and without polar or nonpolar cosolvents. Modeling of binary and ternary systems are listed below.

4.2.1 Modeling of binary solubilities

The solubility of choelesterol in pure SC-CO_2 is predicted using Lorentz-Berthelot combining rule. The calculated values were correlated using experimental data listed in literature by minimizing the objective function AARD and the binary interaction parameter k_{12} (1: solvent, 2:solute) which accounts for solvent-solute interactions is obtained.

4.2.2 Modeling of ternary solubilities

The solubility of cholesterol in SC-CO_2 with polar and nonpolar cosolvents is predicted and correlated using experimental data listed in the literature.

5. RESULTS AND DISCUSSION

The solubility of cholesterol in SC-CO_2 with and without polar and nonpolar cosolvents were predicted using PR EOS and correlated against experimental data when available. The following sections present and discuss the results for both binary and ternary systems studied in this research.

5.1 Solubility of cholesterol in pure SC-CO_2

The solubilities of cholesterol at 318.15 and 328.15 K in pure CO_2 were predicted. The effect of pressure on the solute solubility in SC-CO_2 takes expected trends, the solubility of cholesterol in pure CO_2 increases with increasing operational pressure at same temperature. This is expected since as the pressure increases the density of the supercritical phase increases, as a result the solubility will increase. Also, the operational temperature play a role on the solubility. As temperature increases, the density of the supercritical phase decreases resulting in the decreasing in solubility. On the other hand, the saturation pressure of the solid solute increases with temperature, the increase in the saturation pressure makes the solute more soluble in the supercritical phase. The opposite effects of these two factors are obviously shown in Figure 5.1.1. The solubility isotherms cross each other in the low pressure region, so the density effect is dominant at low pressures while the saturation pressure effect is clearly the dominant at higher pressure values.

To correlate the solubility data, the one-parameter mixing rules which involve the temperature-dependent binary interaction parameter k_{12} (1: CO_2, 2: solute) between CO_2 and solute was determined. For each binary system and at each isotherm, the best value of the binary interaction parameter was found by fitting the calculated solubilities using previous experimental data (Huang, et al., 2004), (Kosal, et al., 1992) by minimizing the absolute average relative deviation (AARD) in Excel Worksheet. Optimum values of k_{12} for different binary systems are shown in Table 5.1.1. The overall performance of the PR EOS was satisfactory with an AARD less than 24%. The equation produced a good qualitative agreement with the experimental data as can be seen in Figures 5.1.1.

Table 5.1.1 Regressed interaction parameters k_{12} between SC-CO_2 and the cholesterol

T **(K)**	***P*** **(bar)**	***N***	**AARD (%)** k_{12}**=0**	k_{12}	**AARD (%)**
318.15	100-240	7	3858.9	0.4898	14.73
328.15	120-240	6	3037.9	0.4858	18.99

N: Number of data points

Table 5.1.1 also compares the solubilities of the five solid solutes in SC-CO_2 correlated by the PR EOS having the optimum values of the binary interaction parameters k_{12} with those by the PR EOS having zero k_{12}. The Large values of AARD indicate poor estimation of the EOS model when using zero value of binary interaction parameter. In general, k_{12} values obtained from regression of experimental data are function of temperature but there is no obvious trend of this dependence. Development of a generalized correlation can be considered in further studies.

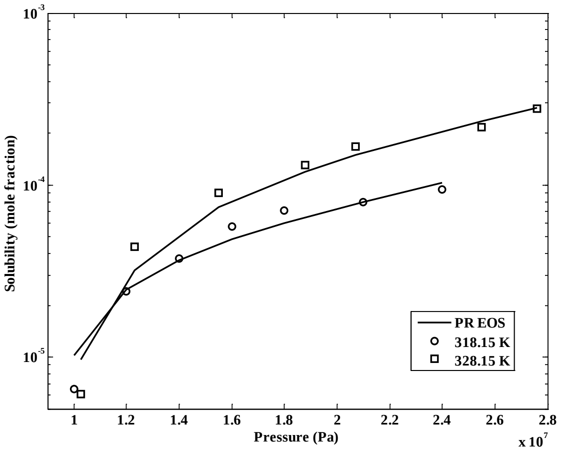

Figure 5.1.1 Isothermal equilibrium solubility of cholesterol in SC-CO_2 as a function of pressure as compared to those predicted by PR EOS at 318.15 K (Huang, et al., 2004) and 328.15 K(Kosal, et al., 1992)

5.2 Solubility of cholesterol in SC-CO_2 with cosolvents

The solubility of cholesterol in SC-CO_2 with polar cosolvents: acetone and methanol, and nonpolar cosolvents: ethane and hexane were predicted and correlated using PR EOS at 318.15 and 328.15 K and pressure ranging from 100 to 240 bar. As such cosolvents were chosen because they provided a contrast of molecular properties, polarity, and polarizability. The cosolvents concentrations (solute-free basis) along with fitting results are shown in Table 5.2.1.

The cosolvent concentrations are chosen as experimentally published in the literature and listed in Table 5.2.1. The ternary system experimental solubility data were at pressures different from those for binary, the required binary data were obtained by third order spline interpolation using Matlab® function: spline(x,y).

The solubility of cholesterol in both binary and ternary systems are relatively low, ranging from 10^{-5} to 10^{-4} mole fraction. Except for CO_2-methanol ternary system, the solubility isotherms have crossover point at low pressure.

To model the solubility in ternary systems using PR EOS, the binary interaction parameters k_{12}, k_{13}, and k_{23} were used (1: CO_2, 2: cholesterol, 3: cosolvent). The binary interaction parameter k_{12} used are those listed in Table 5.1.1, while k_{13} parameter was obtained at the temperature of interest from the literature (Huang, et al., 2004), (Huang, et al., 2007), and (Foster et al., 1993). The last binary interaction parameter k_{23} is adjusted via experimental data for ternary system by minimizing the objective function AARD. Table 5.2.1 presents the adjusted k_{23} along with AARD values less than 25%. The results show that PR EOS was able to represents the solubility of cholesterol with cosolvents using the three binary interaction parameters.

Table 5.2.1 Binary interaction parameters k_{13} and k_{23} for ternary cholesterol system

Cosolvent	*T* (K)	Mole (%)[a]	*N*	AARD (%) $k_{12}=k_{13}=k_{23}=0$	k_{13}	k_{23}[d]	AARD (%)
Acetone	318.15	3.0	7	1149.6	0.0037[b]	0.2729	8.46
	328.15	3.0	6	991.0	0.0037[b]	0.4780	5.97
Methanol	318.15	3.0	7	1346.0	0.066[c]	0.2558	12.38
	328.15	3.0	6	1379.7	0.067[c]	0.6132	15.66
Ethane	318.15	50.0	7	2569.5	0.08[d]	0.4550	24.08
	328.15	50.0	5	1246.2	0.08[d]	0.4835	19.49
Hexane	318.15	3.5	7	942.3	0.0[e]	0.2526	7.84
	328.15	3.5	6	742.8	0.0[e]	0.4170	4.99

[a] Solute-free basis
[b] Huang, et al. (2004)
[c] Huang, et al. (2007)
[d] This work
[e] Foster, et al. (1993)

The effect of adding of cosolvents on the solubility of cholesterol in SC-CO_2 was also examined and investigated in this study. Figure 5.2.5 through Figure 5.2.8 show a significant enhancement in the solubilities for ternary systems compared to those for binary systems. Solubility enhancement was observed with all the cosolvents. The solubility enhancements were more pronounced in the low pressure range. Solubility enhancement resulted from adding cosolvents may be attributed to increase in solvent density and/or intermolecular interactions between the solute and the cosolvent. The addition of cosolvent increased the bulk density of the supercritical phase due to higher density of the cosolvent and clustering of supercritical fluid molecules around the cosolvent (Lemert and Johnston, 1990).

Cosolvent addition may also affect the crossover of solubility isotherms in SC-CO_2, which arises from the competing effects of temperature on solvent density and solute saturation pressure. The cosolvent addition generally increases the crossover isotherms to higher pressure.

The addition of acetone or methanol to SC-CO_2 resulted in smaller solubility enhancement compared with the addition of hexane. Although the concentration of ethane was 50 mol%, it had the lowest solubility enhancement among the three other cosolvents. This could be easily investigated using Figure 5.2.9 which introduces the cosolvent effect, defined as the ratio of solubility with cosolvent to solubility without cosolvent both at the same pressure and temperature. Results depicted on showed variations of cosolvent effect for the four polar or nonpolar ternary systems with pressure. The cosolvent effect is always greater than unity at all pressures. The order of increase of cosolvents effect is hexane > acetone > methanol > ethane. However, acetone and methanol both had almost the same solubility enhancement on cholesterol-CO_2 system.

It was also observed that polar cosolvent systems (acetone and methanol) exhibited a decreasing cosolvent effect with increasing pressure up to 180 bar, after which the decreasing became negligible. On the other hand, nonpolar cosolvent systems (ethane and hexane) exhibited a decreasing cosolvent effect with increasing pressure up to about 160 bar. Beyond 160 bar, the cosolvent effect increased with the increase in pressure, resulting in a minimum cosolvent effect which can be considered as the worst operating condition where the solubility enhancement is minimum.

Solubility enhancement by polar cosolvents results mainly from the interaction of the cosolvent (acetone or methanol) with the solute (cholesterol) due to their polarity. But the large cosolvent effect caused by 3.5 mol% hexane gives an idea about the molecular behavior of cholesterol. Despite the fact that cholesterol is a large hydrocarbon and has a single polar functional group which contributes to the measured dipole moment of 1.9 D (McClellan, 1963), the dispersion interactions with nonpolar hexane is larger than the dipole-dipole interaction between cholesterol with acetone or methanol. The solubility of cholesterol in CO_2 with ethane is quite low with respect to cholesterol in CO_2 with hexane. This is can be explained by the long chain in the molecular structure of cholesterol which is closer in size to hexane chain. As a result, the dispersion forces are dominant.

Indeed, the magnitude of the cosolvent effect is dependent on the cosolvent concentration as well the type of cosolvent used. The effect of different concentrations of hexane was examined and the behavior of cholesterol solubility is also investigated. Figure 5.2.10 and Figure 5.2.11 show the solubility of cholesterol in CO_2 with 3.5, 5, 10 mol% hexane at 318.15 and 328.15 K, respectively. In general, there is a significant enhancement in the solubility due to adding hexane cosolvent and it increases with cosolvent concentration. The enhancement of the solubility with respect to concentration increasing has an upper limit (up to 10 mol%) for the two isotherms. Cosolvent effect due to adding different concentrations of hexane is also calculated and presented in Figure 5.2.12 and 5.2.13.

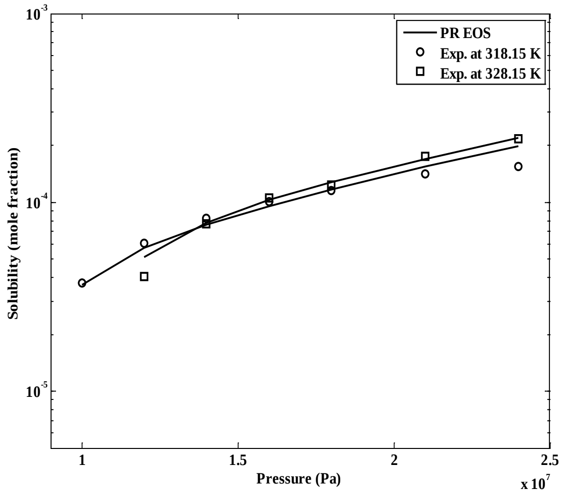

Figure 5.2.1 Experimental and predicted solubility of cholesterol in SC-CO_2 with 3.0 mol% acetone (Huang, et al., 2004)

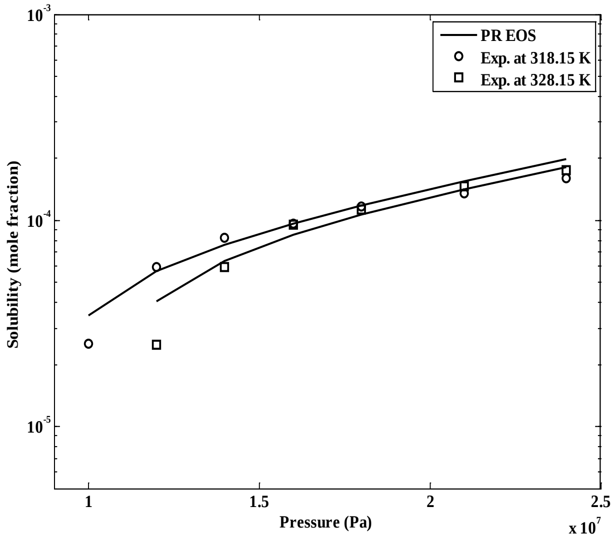

Figure 5.2.2 Experimental and predicted solubility of cholesterol in SC-CO_2 with 3.0 mol% methanol (Huang, et al., 2004)

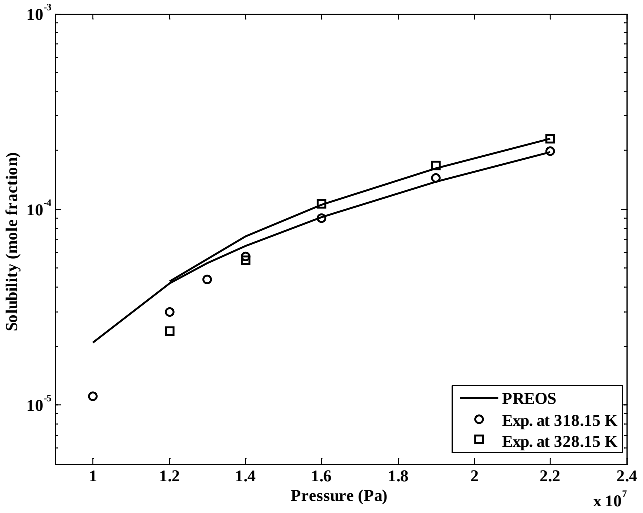

Figure 5.2.3 Experimental and predicted solubility of cholesterol in SC-CO_2 with 50.0 mol% ethane (Singh, et al., 1993)

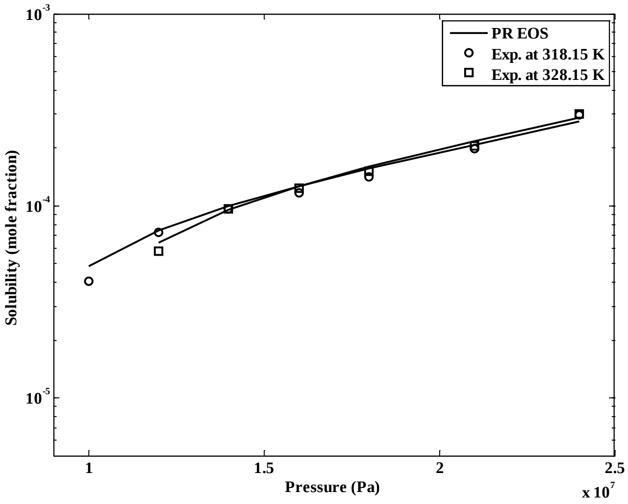

Figure 5.2.4 Experimental and predicted solubility of cholesterol in SC-CO_2 with 3.5 mol% hexane (Foster, et al., 1993)

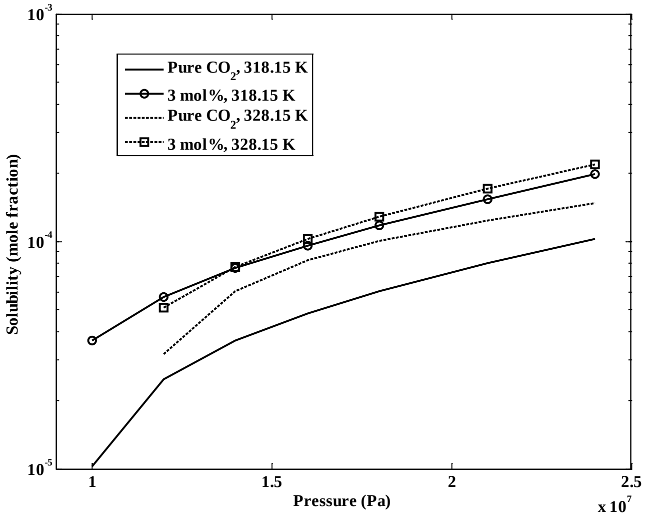

Figure 5.2.5 Solubility of cholesterol in SC-CO_2 with 3.0 mol% acetone

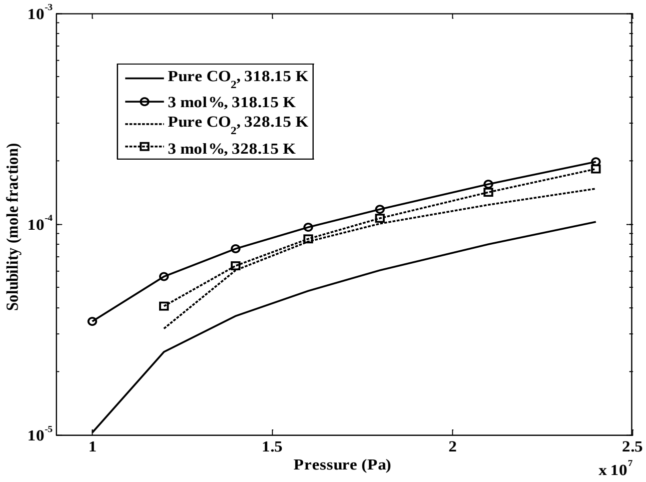

Figure 5.2.6 Solubility of cholesterol in SC-CO_2 with 3.0 mol% methanol

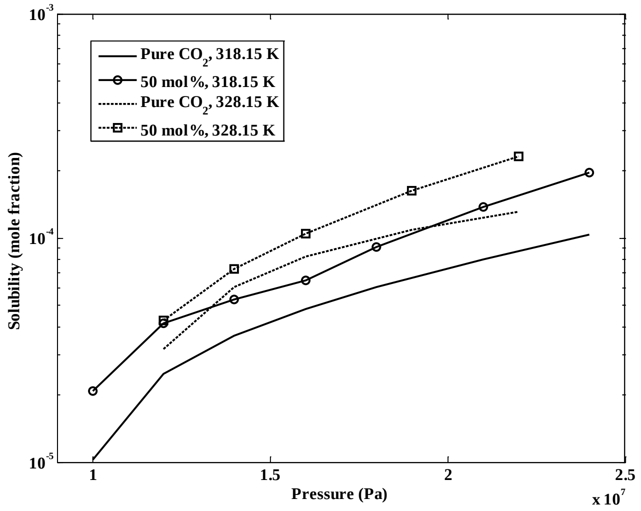

Figure 5.2.7 Solubility of cholesterol in SC-CO_2 with 50.0 mol% ethane

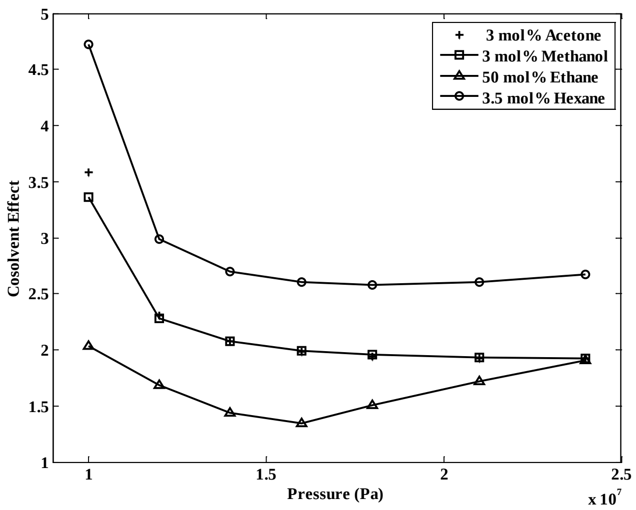

Figure 5.2.9 Cosolvent Effect on supercritical CO_2-cholesterol system as a function of pressure at 318.15 K

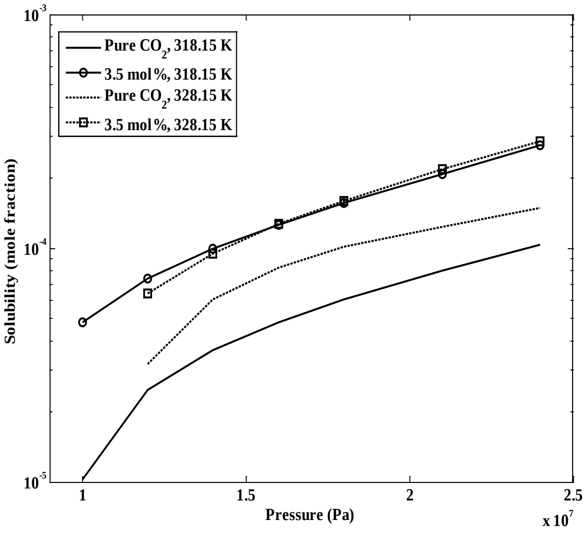

Figure 5.2.8 Solubility of cholesterol in SC-CO_2 with 3.5 mol% hexane

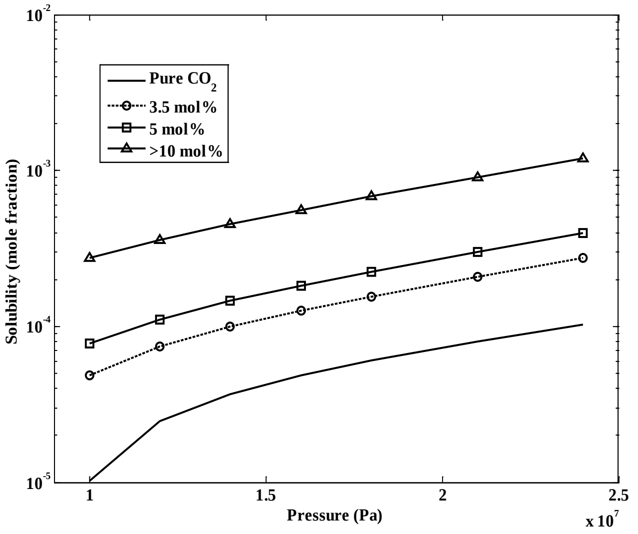

Figure 5.2.10 Solubility of cholesterol in SC-CO_2 with different concentrations of hexane at 318.15 K

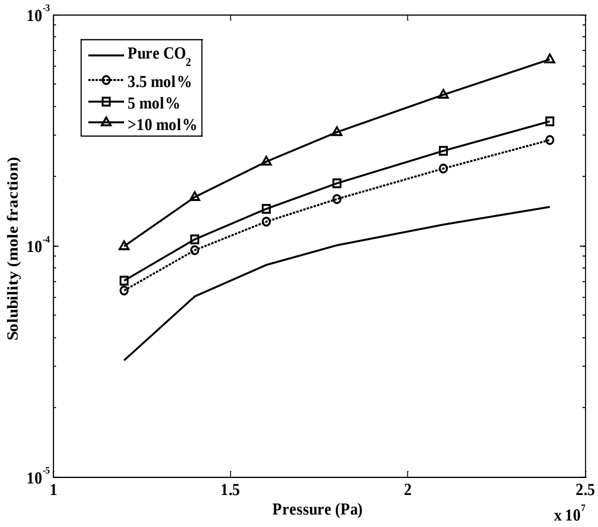

Figure 5.2.11 Solubility of cholesterol in SC-CO_2 with different concentrations of hexane at 328.15 K

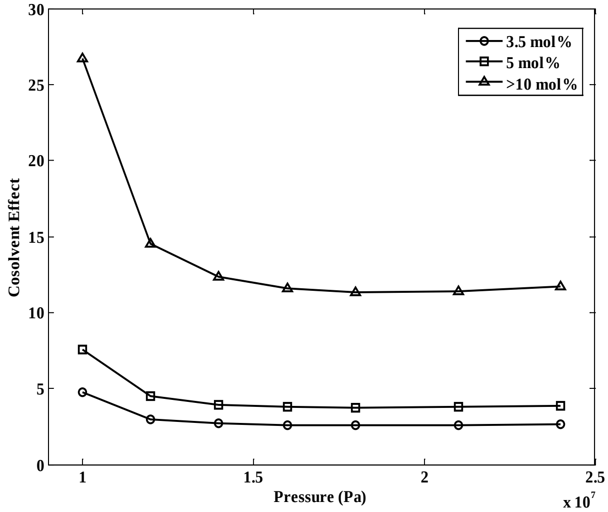

Figure 5.2.12 Cosolvent effect on CO_2-cholesterol-hexane system as a function of pressure at 318.15 K

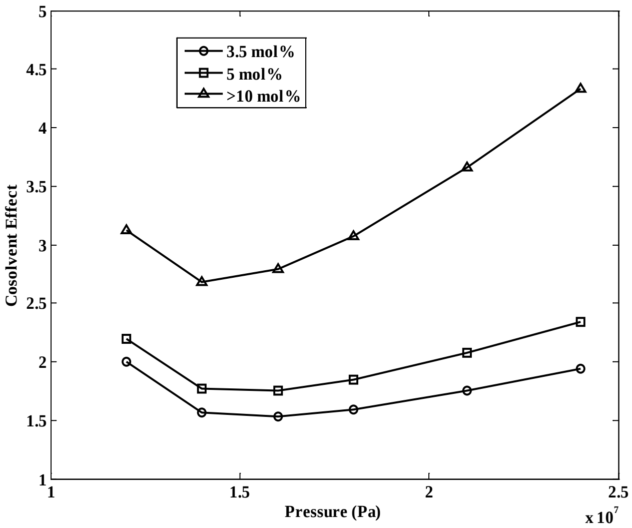

Figure 5.2.13 Cosolvent effect on CO_2-cholesterol-hexane system as a function of pressure at 328.15 K

6. CONCLUSIONS

The solubility of cholesterol in SC-CO_2 was predicted using PR EOS and Lorentz-Berthelot combining rules and correlated against experimental data by minimizing the objective function AARD. A good agreement between experimental and predicted data was observed. Both polar and nonpolar solvents were adopted as cosolvents, and the cosolvent effects were investigated in all ternary systems. Solubility enhancement caused by the addition of a cosolvent to SC-CO_2 results from intermolecular interactions between the cosolvent and the solute and by increasing the solvent density. Selectivety of a separation can be improved by cosolvent addtion if there are some intermolecular interactions between the cosolvent and one or more of the solutes in the supercritical phase. The solubility of cholesterol increases by adding cosolvents. Cholesterol behaves as a hydrocarbon where the dispersion interactions with hexane dominate the solubility. While dipole-dipole interactions with acetone and methanol are less than dispersion interaction with hexane. Cosolvent effect is dependent on the cosolvent and its concentration, solute, and the operating conditions. The cosolvent effect increases with cosolvent concentration (up to specific value). The cosolvent addition also affects the crossover of solubility isotherms in SC-CO_2 that arises from the effect of temperature on the saturation pressure of solute and on the solvent density with opposite effects.

7. NOMENCLATURE

AARD	Average Absolute Relative Deviations
CO_2	Carbon Dioxide
CP	Critical Point
EOS	Equations of State
MW	Molecular Weight
PR EOS	Peng-Robinson Equation of State
R_{CE}	Cosolvent Effect
SC	Supercritical
SC-CO_2	Supercritical Carbon Dioxide
SCF	Supercritical Fluid
SCFE	Supercritical Fluid Extraction
vdW	Van der Waals
VLE	Vapor Liquid Equilibrium

SYMBOLS

a	Attraction Energy Parameter
A	Individual Species Attraction Energy Parameter
B	Individual Species Reduced Size Parameter
b	Covolume Parameter
c	Concentration
f_i^s	Fugacity of Pure Solid at Temperature T
f_i^{SC}	Fugacity of the Solid in the SCF at the System Temperature and Pressure
k_{ij}	Attraction Energy Binary Interaction Parameter
N	Number of Species
P	Pressure
P_c	Critical Pressure
P_i^{sat}	Saturation Pressure of the Pure Solid at the System Temperature
R	Ideal Gas Constant
T	Temperature
T_c	Critical Temperature
V	Molar Volume
v_i^s	Molar Volume of Solid Solute
V	Volume
y_i	Mole Fraction (Solubility) of Component i
Z	Compressibility Factor for the SCF Phase

GREEK SYMBOLS

φ_i^s	Fugacity Coefficient of the Solute in the Solid Phase
φ_i^{SC}	Fugacity Coefficient of the Solid in the SCF
μ_i	Chemical Potential of component i
ω	Pitzer's Acentric Factor

SUBSCRIPTS AND SUPERSCRIPTS

cal	Calculated Solubility
exp	Experimental Solubility
s	Solid Phase
1	Solvent
2	Solute
3	Cosolvent

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