Regular Article

Determining the Optimal Thermodynamic Conditions of Ternary Systems Containing (CO₂, Solvent, 5-Fluorouracil) in the GAS Process

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ABSTRACT

One of the methods to reduce the particle size is the GAS method. In this method, the solute and antisolvent should be dissolved well in a solvent. But the solute is not dissolved in a solvent. The aim of studying this model is to determine the phase equilibrium and thermodynamic conditions of (CO₂, solvent, 5-Fluorouracil) in the GAS process. The solvents include methanol, ethanol, acetone, 1-propanol, and 1-butanol. The Peng-Robinson equation of state with a linear combination of Vidal and Michelsen mixing rules (PR-LCVM) was used for the thermodynamic modeling. The volume expansion of the binary system (CO₂, solvent) and ternary system (CO₂, solvent, 5-Fluorouracil) at the temperature range of 313.15-319.15 K was investigated. The P_{min} values for the binary system were 66.7, 69.6, 60, 73.7, and 76.8 bar respectively for methanol, ethanol, acetone, 1-propanol, and 1-butanol at 313.15 K,. The P_{min} for the ternary system was also calculated. The comparison between the P_{min} values of binary and ternary systems showed that for a constant temperature and a certain solvent, the calculated minimum pressure in the ternary system was greater than the same in the binary system.

1. Introduction

Most pharmaceutical compounds have poor water solubility. Therefore, the bioavailability is limited and the dosage used is high. The dissolution rate is increased via the reduction of the particle size. The solubility of micronized particles increases because they have a higher surface area that is in contact with water. Therefore, the dosage used is decreases.

In recent years, supercritical fluids (SCFs) have been used in many fields such as the chemical, biological, petrochemical, and pharmaceutical industries [1-6]. Because in

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this method, very small particles of the product without impurities are produced from organic solvents. The operating temperature of the process is low. Product particle size distribution can be controlled through operational variables. In most pharmaceutical micronization operations performed with supercritical fluids, the rates of dissolution and decomposition are very high [6].

In the GAS process, the solute is dissolved in a suitable solvent and loaded into the cell. Then, Supercritical carbon dioxide is injected into the cell. When carbon dioxide dissolves in a solvent, volume expansion occurs. The solubility power of the solute in the solvent is reduced. As a result, the solute appears as particles in the solid phase. The precipitation of solid particles occurs under special operating conditions. Therefore, the accurate knowledge of thermodynamic conditions is important in the GAS process. One way to obtain this thermodynamic condition is to use a phase equilibrium model based on the equations of state [7-10].

Najafi et al. [11] studied the phase behavior of a ternary system comprising carbon dioxide, dimethyl sulfoxide, finasteride (FNS), where the lowest pressures at 308.15, 318.15, 328.15 and 338.15 K were 7.49, 8.13, 8.51 and 9.03 MPa respectively. Sajadian et al. [12] studied the solubility of favipiravir (as an anti-COVID-19) in supercritical carbon dioxide. Esfandiari and Sajadian [13] studied the solubility of glibenclamide in the supercritical carbon dioxide for the first time at the temperature range of 308-338 K and pressure range of 12-30 MPa. Esfandiari and Ghoreishi [14] determined the optimal thermodynamic conditions of a ternary mixture made up of carbon dioxide, DMSO, and ampicillin, in which CO_2 was used as an antisolvent, and found out the minimum

pressures of a the ternary mixture at different temperatures. Liu et al. [15] studied the phase behavior of a ternary mixture system (cholesterol, acetone, carbon dioxide) in which carbon dioxide had an antisolvent role in the recrystallization of cholesterol at 308.15 and 318.15 K and the pressures in the range of 0.1 to 7.5 MPa. Tombokan et al. [16] conducted an investigation of modeling about the phase equilibrium of a ternary system (sclareol, ethyl lactate, carbon dioxide), where they successfully used Peng-Robinson EOS and LCVM mixing rule to determine the thermodynamic conditions of this process. Paviani et al. [17] investigated the phase equilibrium behavior of a ternary system (ethanol, CO_2, curcumin).

In some previous researches, the phase behavior of the solvent and carbon dioxide at high temperatures and pressures has been studied. However, a comparison between data obtained from different solvents has rarely been done. There was no studies on the behavior of solvents and their structure and molecular weight. The modeling of the ternary system (CO_2, solvent, 5-Fluorouracil) with different solvents has been investigated for the first time .This investigation has been dedicated to modeling the thermodynamic conditions of (CO_2, solvent, 5-Fluorouracil). The solvents contain methanol, ethanol, acetone, 1-propanol, and 1-butanol. The Peng-Robinson EOS has been combined with Vidaland Michelsen mixing rule (LCVM) to determine the optimum thermodynamic condition of the GAS process.

2. Thermodynamic models
The volume expansion of the liquid phase has been chosen as a criterion to determine the optimum conditions of the GAS process. This parameter is expressed as follows [14, 18]:

$$\frac{\Delta v}{v} = \frac{v(T,P) - v_0(T,P_0)}{v_0(T,P_0)} \qquad (1)$$

In Eq. (1), v is a molar volume, T shows the operating temperature, P is the pressure, and the subscript 0 indicates the initial condition. The equilibrium criteria are the equality of temperature, pressure, and fugacity of three components (CO_2, solvent, 5-Fluorouracil) in all equilibrium phases.

This equality can be stated as follows [14]:

$$\frac{\hat{\varphi}_1^l}{\hat{\varphi}_1^v} x_1 - y_1 = 0 \qquad (2)$$

$$\frac{\hat{\varphi}_2^l}{\hat{\varphi}_2^v} x_2 - y_2 = 0 \qquad (3)$$

$$\frac{\hat{\varphi}_3^l}{\hat{\varphi}_3^v} x_3 - y_3 = 0 \qquad (4)$$

If the solid phase is considered as a pure solid in a solid-liquid equilibrium, the following expression can be written [14]:

$$\frac{\varphi_3^s}{\hat{\varphi}_3^l} x_3 - y_3 = 0 \qquad (5)$$

$$\alpha = \left(\frac{\lambda}{A_V} + \frac{1-\lambda}{A_M}\right)\frac{G^E}{RT} + \frac{1-\lambda}{A_M}\sum x_i \ln\frac{b}{b_i} + \sum x_i \bar{\alpha}_i \qquad (9)$$

$$\alpha = \frac{a}{bRT} \qquad (10)$$

$$\bar{\alpha}_i = [\frac{\partial n\alpha}{\partial n_i}]_{T,P,n_{j\neq 0}} = \left(\frac{\lambda}{A_V} + \frac{1-\lambda}{A_M}\right)\ln\gamma_i + \frac{1-\lambda}{A_M}\left(\ln\frac{b}{b_i} + \frac{b_i}{b} - 1\right) + \alpha_i \qquad (11)$$

$$\bar{\alpha}_i = \frac{\alpha_i}{b_i RT} \qquad (12)$$

In Eq. (9), $A_M=-0.52$, $A_V=-0.623$, $\lambda=0.36$, G^E is the excess Gibbs energy and γ_i is the activity coefficient of the component i computed based on the UNIFAC model [14].

The fugacity coefficient of each component in the liquid and vapor mixture has been computed as follows [14]:

$$\hat{\varphi}_i = \exp\left[\frac{b_i}{b}(Z-1) - \ln(Z-1) - \frac{\bar{\alpha}_i}{2\sqrt{2}}\ln\left(\frac{Z+2.414b}{Z+0.414b}\right)\right] \qquad (13)$$

In Eq. (5), φ_3^s is the fugacity of the solute in the solid phase. Moreover, the sum of mole fractions in liquid and vapor phases is equal to one.

In this study, the Peng-Robinson (PR), combined with the Vidal and Michelsen mixing rules (LCVM), was used to model the liquid and vapor phases. The PR EOS is stated as follows [19]:

$$P = \frac{RT}{v-b} - \frac{a(T)}{v(v+b)+b(v-b)} \qquad (6)$$

$$a_i(T) = 0.45724\left(\frac{(RT_{ci})^2}{P_{ci}}\right)\left[1 + \left(0.37464 + 1.54226\omega_i - 0.26992\omega_i^2\right)(1 - \sqrt{\frac{T}{T_{ci}}})\right]^2 \qquad (7)$$

$$b_i = 0.0778\frac{RT_{ci}}{P_{ci}} \qquad (8)$$

Furthermore, the LCVM mixing rule is stated as follows:

The fugacity of the solid phase is shown in the following equation [18].

$$\ln\varphi_3^s = \ln\varphi_3^l + \frac{\Delta H_{tp}}{R}\left(\frac{1}{T_{tp}} - \frac{1}{T}\right) + \frac{v_{tp}}{RT}\left(P - P_{tp}\right) \qquad (14)$$

In Eq. (14), the subscript tp belongs to the triple point.

3. Results and discussion
3.1. Binary mixtures

In this work, first the binary mixtures of (CO_2, solvent) were considered. Methanol, ethanol, acetone, 1-propanol, and 1-butanol were selected as solvents. The phase equilibrium calculations were done based on the Peng-Robinson equation of state and the LCVM mixing rule. The volume expansion of the liquid phase was determined. The temperature is in the range of 313.15-319.15 K. At each operating temperature, the operation pressure was determined by plotting the relative change of the molar volume in terms of pressure. In each figure, a minimum point was observed. After this point, a sharp increase in the relative change of the molar volume was also seen.

Figure 1 shows the relative change of the molar volume in terms of pressure for the binary system (CO_2, methanol) at the temperature of 315.15 K, where the minimum pressure (P_{min}) was 66.7 bar.
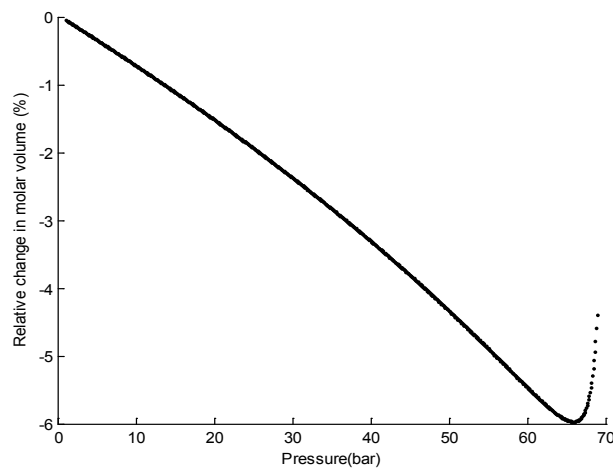
Figure 1. Relative expansion of the liquid phase as a function of pressure, for (CO_2, methanol) at 315.15 K.

Figure 2 shows the relative change of the molar volume in terms of pressure for the binary system (CO_2, methanol). The calculated P_{min} values were 66.7, 68.8, and 75 bar at 313.15, 315.15, and 319.15 K respectively. The operating pressure must be above the P_{min}. According to Figure 2, it can be concluded that by increasing the temperature, the operating pressure increases.
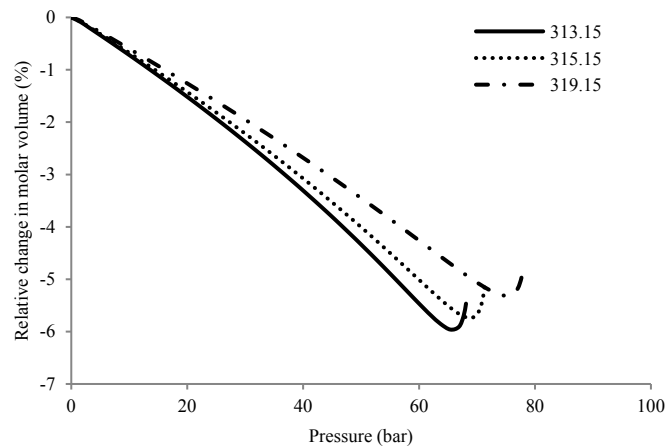
Figure 2. Relative expansion of the liquid phase as a function of pressure, for (CO_2, methanol) at different temperatures.

In this study, the relative expansion of the liquid phase versus pressure for different solvents (methanol, ethanol, acetone, 1-propanol, and 1-butanol) were studied. The results of that modeling at the temperatures of 313.15, 315.15, and 319.15 K were collected in Table 1.

As indicated in Table 1, the value of the minimum pressure (P_{min}) depended on temperature. P_{min} increased with temperature, and as the molecular weight of the hydrocarbon solvent increased, the P_{min} increased, this result is not true for acetone, meaning that although the molecular weight of acetone is greater than that of methanol and ethanol, its P_{min} is lower than theirs.

Figure 3 shows the relative molar volume change in terms of the mole fraction of carbon dioxide in the liquid phase for the binary system (CO_2, methanol) at 315.15 K. This figure has a trend very similar to that of Figure 1. The minimum mole fraction of carbon dioxide to achieve the volume expansion of the liquid phase in the binary system (CO_2, methanol) at 315.15 K was to be 0.48, this value was 0.67 for the binary system (CO_2, ethanol) by Rahmanzadeh Derisi and Esfandiari [20]. Therefore, in a binary system containing methanol compared to ethanol in a smaller amount of carbon dioxide in the liquid phase, the volume expansion is observed.

Table 1

Results of the modeling the binary system of CO_2, solvent via different solvents.

Solvent	Mw(g/mol)	P_{min} (bar) at 313.15 K	P_{min} (bar) at 315.15 K	P_{min} (bar) at 319.15 K
Methanol	32.04	66.7	68.8	75
Ethanol	46.069	69.6	72	78.2
Acetone	58.09	60	63	65
1-Propanol	60	73.7	76.7	82.8
1-Butanol	74	76.8	80	87
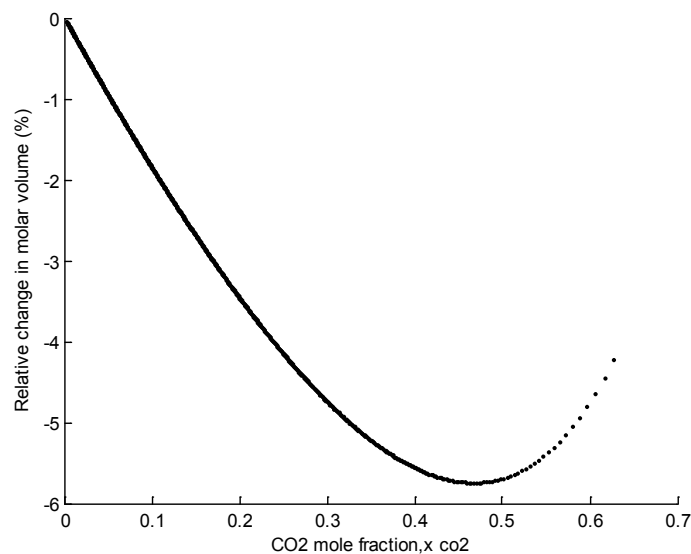
Figure 3. Relative expansion of the liquid phase as a function of the mole fraction of CO_2 in the liquid phase for the binary system (methanol, CO_2) at 315.15 K.

The trend of changes in Figure 3 can be explained based on the concept of the liquid molar volume of a solution which can be defined as follows [21]:

$$v = x_1\overline{v_1} + x_2\overline{v_2} \qquad (15)$$

Based on Eq. (15):

$$\left(\frac{\partial v}{\partial x_1}\right)_{P,T} = (\overline{v_1} - \overline{v_2}) \qquad (16)$$

Until $\overline{v_1} > \overline{v_2}$, the molar volume of the liquid phase decreased when the dissolution of carbon dioxide increased. If $\overline{v_1} = \overline{v_2}$, a minimum of relative change in molar volume is observed and there was no change in the molar volume of the liquid phase. After this point (x_{1min}), the molar volume of the liquid phase increases. Also, at a constant temperature, the following equation can be written [21]:

$$\frac{dv}{dx_1} = \left(\frac{\partial v}{\partial P}\right)_{T,x_1}\frac{dP}{dx_1} + \left(\frac{\partial v}{\partial x_1}\right)_{P,T} \qquad (17)$$

The first term of Eq. (17), $\left(\frac{\partial v}{\partial P}\right)_{T,x_1}\frac{dP}{dx_1}$ was negative and small, so it can be neglected. The second term $\left(\frac{\partial v}{\partial x_1}\right)_{P,T}$ was initially negative and later positive. Due to this, the trends in Figures 1 and 2 are the same [20].

Figure 4 shows the vapor-liquid equilibrium of the binary system (CO_2, methanol) at 315.15 K. The miscibility of methanol and carbon dioxide was studied via this figure. A similar trend was observed in the results of CO_2-ethanol by Rahmanzadeh Derisi and Esfandiari [20]. The mole fraction of carbon dioxide in the liquid phase increases by increasing pressure. A trend very similar to that of the phase equilibrium behavior of CO_2-DMSO at high pressures and temperatures via the Peng-Robinson equation of state was indicated by Esfandiari and Ghoreishi [14].
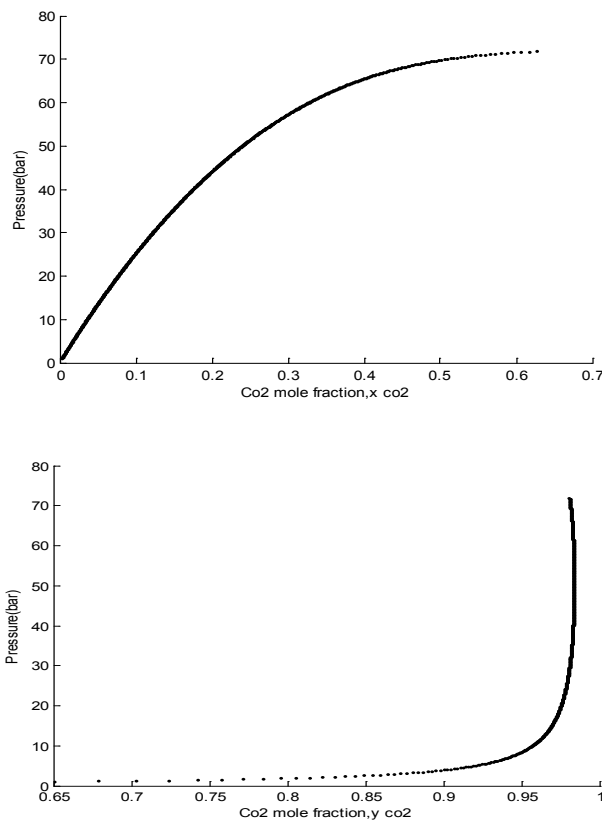

Figure 4. Vapor-liquid equilibrium of the binary system (CO_2, methanol) at 315.15 K.

3.2. Ternary mixtures

In this section, the phase equilibrium of (CO_2, solvent, 5-Fluorouracil) the ternary mixture was studied. Figure 5 shows the relative change of the molar volume in terms of pressure for the ternary system (CO_2, methanol, 5-Fluorouracil) at the temperature

of 315.15 K, and the minimum pressure (P_{min}) of 87.4 bar. The P_{min} values for the ternary system (CO_2, 1-propanol, ampicillin) calculated by Rahmanzadeh Derisi and Esfandiari were 70.8, 80, and 87.4 bar at 308.15, 313.15, and 316.15 K respectively [20].
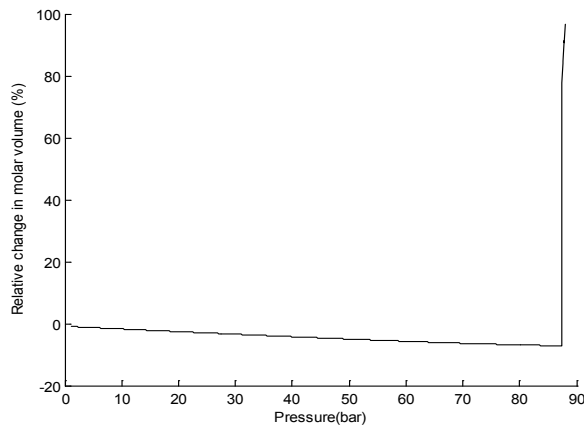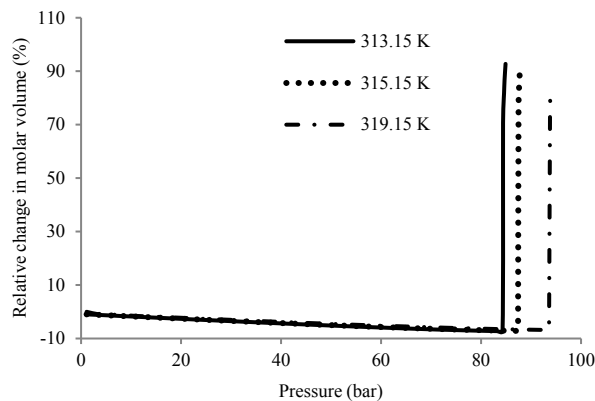

Figure 5. Relative expansion of the liquid phase as a function of pressure, for (CO_2, methanol, 5-Fluorouracil) at 315.15 K.

Figure 6 shows a relative change of the molar volume in terms of pressure for the ternary system (CO_2, methanol, 5-Fluorouracil) at the temperatures of 313.15, 315.15, and 319.15 K, where the minimum pressures were 84.3, 87.4, and 93.5 bar respectively. According to the results obtained in the ternary system, like in the binary system, the operating pressure

increased by increasing temperature and at a certain temperature, the minimum pressure in a ternary system (CO_2, solvent, 5-Fluorouracil) was greater than its value in a binary system (CO_2, solvent).

Table 2 shows the modeling of the ternary system (CO_2, solvent, 5-Fluorouracil) at 313.15, 315.15 and 319.15 K for different solvents.

Figure 6. Relative expansion of the liquid phase as a function of pressure for the ternary system of CO_2, methanol, 5-Fluorouracil at different temperatures.

Table 2

Results of the modeling of the ternary system of CO_2, solvent, 5-Fluorouracil via different solvents.

Solvent	Mw(g/mol)	P_{min} (bar) at 313.15 K	P_{min} (bar) at 315.15 K	P_{min} (bar) at 319.15 K
Methanol	32.04	84.3	87.4	93.5
Ethanol	46.069	85.1	88.1	94.6
Acetone	58.09	82.4	85.2	91.2
1-Propanol	60	85.6	89.1	95.6
1-Butanol	74	86.6	90.1	97.6

Figure 7 shows the solubility of 5-Fluorouracil in a ternary system (methanol, carbon dioxide, 5-Fluorouracil) at 315.15 K. This figure shows a slight increase in the solubility of 5-Fluorouracil in the liquid phase at low pressures. When the pressure increases to up to 87.4 bar, a sudden decrease in the solubility of 5-Fluorouracil occurs in the liquid phase, and at a pressure of above 87.4 bar almost all 5-Fluorouracil precipitates. Esfandiari and Ghoreishi [14] studied the solubility of ampicillin in the liquid phase in a ternary system (DMSO, CO_2, ampicillin) at 308 K. Almost all of the ampicillin was precipitated at 73 bar.

Figure 8 shows the changes of the molar volume with the pressure for the (CO_2, solvent, 5- Fluorouracil) ternary system at 315.15 K. The calculated P_{min} values were 87.4, 88.1, 85.2, 89.1, and 90.1 bar for methanol, ethanol, acetone, 1-propanol, and 1-butanol respectively. According to these results, when the molecular weight of the hydrocarbon solvent was increased, the value of P_{min} was increased, but acetone does not follow this result. A similar trend was observed in the results of the solubility of morin hydrate and deferasirox in different solvents (methanol, ethanol, 1-propanol, and 1-buthanol). Solubility increased with the increase in the molecular weight of solvent [22, 23].
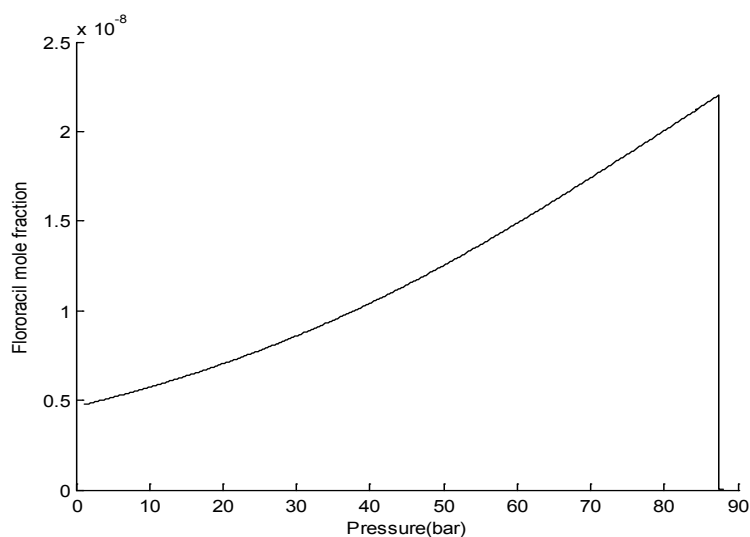
Figure 7. Calculated solubility of 5-Fluorouracil in the liquid phase in the ternary system of CO_2, methanol, 5-Fluorouracil at 315.15 K.
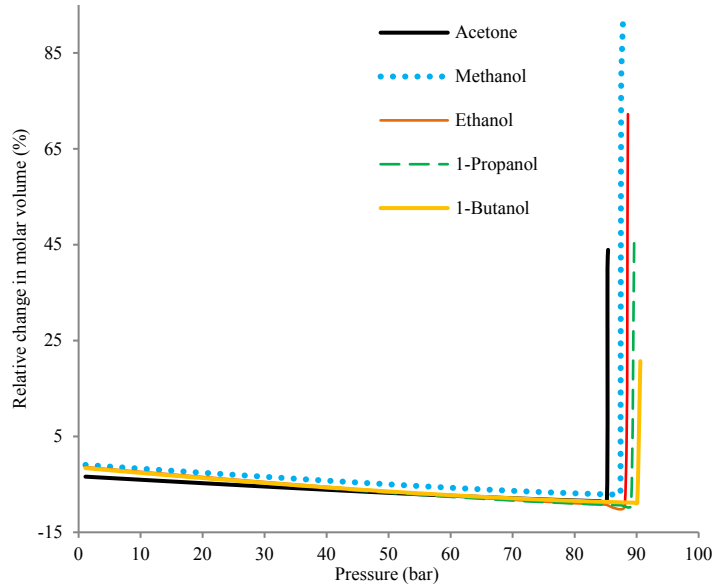
Figure 8. Relative expansion of the liquid phase as a function of pressure for the ternary system (CO_2, solvent, 5- Fluorouracil) at 315.15 K.

3.3. Model validity

Figure 9 shows the calculated equilibrium mole fraction of CO_2 in the binary system of CO_2-ethanol which was compared with the experimental data reported by Mehl et al. [24] at 314, 325, 313.2, 318.2 K. the model prediction for the binary system of CO_2-ethanol was in good agreement with experimental data. A comparison of the model prediction for the binary system of CO_2-methanol with experimental data reported by Joung et al. [25] and Kariznovi et al. [26] at the temperatures of 313 and 323 K showed the accuracy of the model (Figure 10).
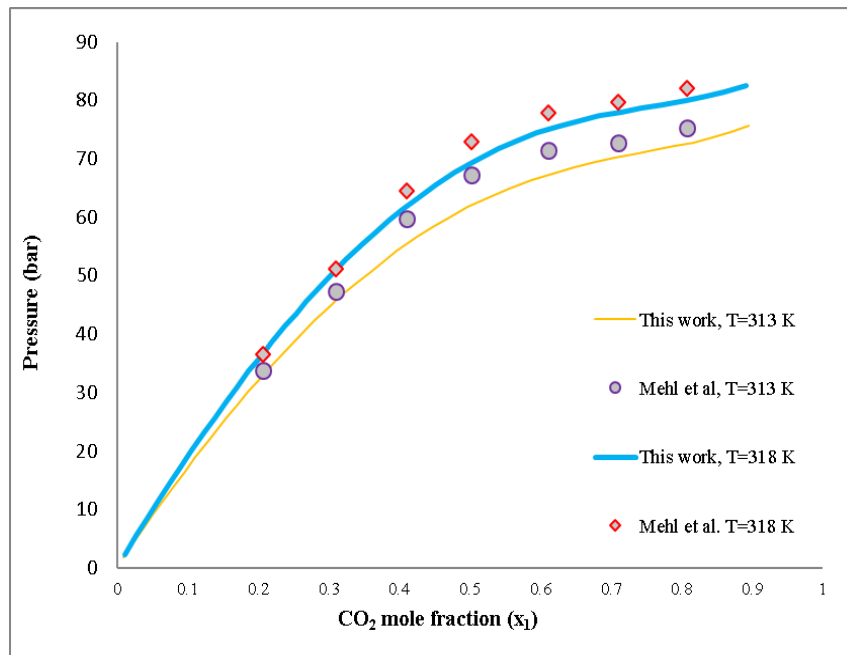
Figure 9. Comparison of the binary system (CO_2-ethanol) calculated according to PR-EoS with experimental data by Mehl et al. [24] at different temperatures.
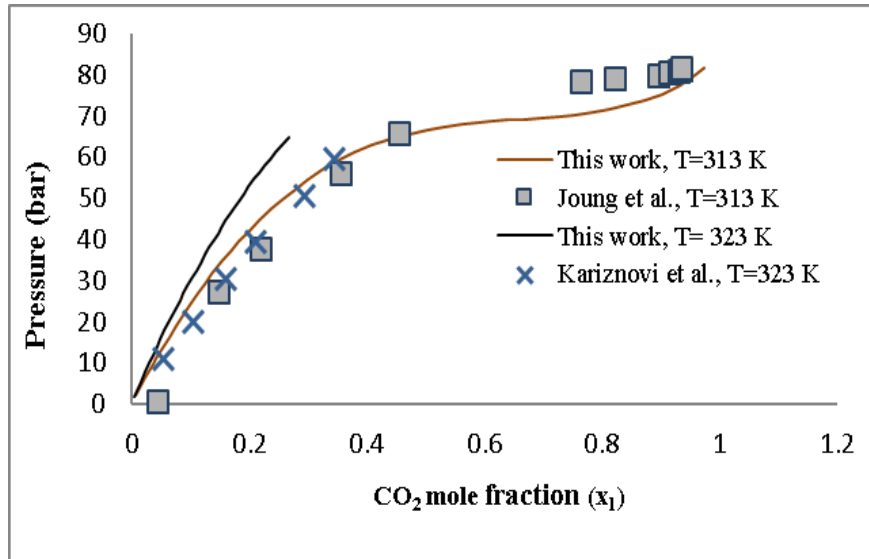
Figure 10. Comparison of the binary system (CO_2-methanol) calculated according to PR-EoS with experimental data by Joung et al. [25], Kariznovi et al. [26] at the temperatures of 313 and 323 K.

4. Conclusions

In this study, the phase equilibrium of binary systems (CO_2, solvent) and ternary sytems (CO_2, solvent, 5-Fluorouracil) was determined. Methanol, ethanol, acetone, 1-propanol, and 1-butanol were selected as solvents. The combination of Peng-Robinson EOS and the Vidaland Michelsen mixing rule (LCVM) was used to determine the optimum operating condition of the GAS process. The optimal operational condition of each mixture was determined by the relative volume expansion of the liquid phase. The results showed that in the same chemical structure, the minimum pressure increased by increasing the molecular weight of the solvent, but this result is not true for acetone. Also, by increasing temperature, the minimum pressure increases and the minimum pressure in the ternary system (CO_2, solvent, 5-Fluorouracil) is greater than that in a binary system (CO_2, solvent). The model prediction for binary systems was in good agreement with experimental data.

Acknowledgement

Nomenclature

a	parameter in the PR-EOS [J m^3/mol^2].
b	parameter in the PR-EOS [m^3/mol].
G^E	excess Gibbs energy [J/mol].
H	heat of fusion [J/mol].
P	pressure [Pa].
R	universal gas constant, R= 8.34 [J/mol K].
T	temperature [K].
v_α	molar volume of the α phase [m^3/mol].
x_i	mole fraction of component i in liquid phase.
y_i	mole fraction of component i in vapor phase.
z	compressibility factor.

Greek letters

Δ	property change.
φ	fugacity coefficient.
ω	acentric factor.
α	correction factor of attractive parameter.
γ_i	activity coefficient.

Superscripts and subscripts

0	reference condition.
i	species i.
1	Antisolvent.
2	solvent.
3	solute.
c	critical.
t_p	triple point.
L	liquid.
V	vapor.

S   solid.

α   phase.

References

[1] Yoon, T. J., Son, W. S., Park, H. J., Seo, B., Kim, T. and Lee, Y. W., "Tetracycline nanoparticles precipitation using supercritical and liquid CO_2 as anti-solvent", *J. Supercrit. Fluids*, **107**, 51 (2016).

[2] Tsai, C. C., Lin, H. M. and Lee, M. J., "Phase equilibrium and micronization for flufenamic acid with supercritical carbon dioxide", *J. Taiwan Inst. Chem. Eng.*, **000**, 1 (2017).

[3] Fattahi, A., Karimi-Sabet, J., Keshavarz, A., Golzary, A. A., Rafiee-Tehrani, M. and Dorkoosh, F. A., "Preparation and characterization of simvastatin nanoparticles using rapid expansion of supercritical solution (RESS) with trifluoromethane", *J. Supercrit. Fluid*, **170**, 469 (2016).

[4] Esfandiari, N. and Sajadian, S. A., "CO_2 utilization as gas antisolvent for the pharmaceutical micro and nanoparticle production: A review", *Arabian J. Chem.*, **15**, 104164 (2022).

[5] Ghoreishi, S. M., Hedayat, A. and Kordnejad, M., "Micronization of chitosan via rapid expansion of supercritical solution", *J. Supercrit. Fluid*, **111**, 162 (2016).

[6] Esfandiari, N., "Production of micro and nanoparticles of pharmaceutical by supercritical carbon dioxide", *J. Supercrit. Fluid*, **100**, 129 (2015).

[7] Mendes, M. F., Uller, A. M. C. and Pessoa, F. L. P., "Simulation and thermodynamic modeling of the extraction of tocopherol from a synthetic mixture of tocopherol, squalene, and CO_2", *J. Chem. Eng.*, **17**, 761 (2000).

[8] Spiliotis, N., Magoulas, K. and Tassios, D., "Prediction of the solubility of aromatic hydrocarbons in supercritical CO_2 with EOS/GE models", *Fluid Phase Equilib.*, **102**, 121 (1999).

[9] Zhang, Q., Yan, X., Zheng, P. and Wang, Z., "Influence factors on activity of Ru–Zn catalysts in selective hydrogenation of benzene", *Chinese J. Chem. Eng.*, **25**, 294 (2017).

[10] Gerszt, R., Pessoa, F. L. P. and Mendes, M. F., "Phase behavior of sterols and vitamins in supercritical CO_2", *Braz. J. Chem. Eng.*, **17**, 261 (2000).

[11] Najafi, M., Esfandiari, N., Honarvar, B. and Arab Aboosadi, Z., "Thermodynamic modeling of the gas-anti solvent (GAS) process for precipitation of finasteride", *J. Chem. Petrol. Eng.*, **54**, 297 (2020).

[12] Sajadian, S. A., Ardestani, N. S., Esfandiari, N. and Jouyban, A., "Solubility of favipiravir (as an anti-COVID-19) in supercritical carbon dioxide: An experimental analysis and thermodynamic modeling", *J. Supercrit. Fluid.*, **183**, 105539 (2022).

[13] Esfandiari, N. and Sajadian, S. A., "Experimental and modeling investigation of glibenclamide solubility in supercritical carbon dioxide", *Fluid Phase Equilib.*, **556**, 113408 (2022).

[14] Esfandiari, N. and Ghoreishi, S. M., "Optimal thermodynamic conditions for ternary system (CO_2, DMSO, ampicillin) in supercritical CO_2 anti solvent process", *J. Chem. Eng.,*. **502**, 31 (2015).

[15] Liu, Z., Wang, J., Song, L., Yang, G. and Han, B., "Study on the phase behavior of cholesterol–acetone–CO_2 system and crystallization of cholesterol by anti-solvent CO_2", *J. Supercrit. Fluid.*, **24**, 1

(2002).

[16] Tombokan, X. C., Aguda, R. M., Danehower, D. A., Kilpatrick, P. K. and Carbonell, R. G., "Three-component phase behavior of the sclareol-ethyl lactate-carbon dioxide system for GAS applications", *J. Supercrit. Fluid.*, **45**, 146 (2008).

[17] Paviani, L. C., Chiari, M. R. S., Crespo, T. R. and Cabral, F. A., "Thermodynamic modeling of phase equilibrium behavior of curcumin-CO_2-ethanol", Proceedings of *III Iberoamerican Conference on Supercritical Fluids*, Cartagena de Indias, Colombia, (2013).

[18] de la Fuente, J. C., Shariati, A. and Peters, C. J., "On the selection of optimum thermodynamic conditions for the GAS process", *J. Supercrit. Fluid.*, **32**, 55 (2004).

[19] Walas, S. M., Phase equilibria in chemical engineering, 1st ed., Butterworth-Heinemann, Boston, (1985).

[20] Rahmanzadeh Derisi, M. and Esfandiari, N., "Effect of solvents on the optimal thermodynamic conditions of ternary system (CO_2, Alcohol, Ampicillin) in GAS Process", *Iranian J. Chem. Eng.*, **17**, 37 (2020).

[21] Mukhopadhyay, M., "Partial molar volume reduction of solvent for solute crystallization using carbon dioxide as anti-solvent", *J. Supercrit. Fluids.*, **25**, 213 (2003).

[22] Yazdanshenas, R. and Gharib, F., "Solubility and thermodynamic functions measurement of morin hydrate in different alcohols", *J. Mol. Liq.*, **233**, 9 (2017).

[23] Boroujeni, H. C. and Gharib, F., "Solubility and thermodynamic functions of deferasirox in different solvents", *J. Mol. Liq.*, **219**, 350 (2016).

[24] Mehl, A., Nascimento, F. P., Falcão, P. W., Pessoa, F. L. P. and Cardozo-Filho, L., "Vapor-liquid equilibrium of carbon dioxide + ethanol: Experimental measurements with acoustic method and thermodynamic modeling", *J. Thermodyn.*, **2011**, 1 (2011).

[25] Joung, S. N., Yoo, C. W., Shin, H. Y., Kim, S. Y., Yoo, K. -P., Lee, C. S. and Huh, W. S., "Measurements and correlation of high-pressure VLE of binary CO_2–alcohol systems (methanol, ethanol, 2-methoxyethanol and 2-ethoxyethanol)", *Fluid Phase Equilib.*, **185**, 219 (2001).

[26] Kariznovi, M., Nourozieh, H. and Abedi, J., "Experimental measurements and predictions of density, viscosity, and carbon dioxide solubility in methanol, ethanol, and 1-propanol", *J. Chem. Thermodynamics*, **57**, 408 (2013).