

High-Pressure Vapor-Liquid Equilibrium Data for Ternary Systems CO₂ + Organic Solvent + Curcumin

Willyan M. Giufrida¹, Rogério Favareto¹, Vladimir F. Cabral¹, M. Angela A. Meireles³, Lucio Cardozo-Filho^{*1} and Marcos L. Corazza²

¹DEQ/UEM, Bloco D-90, Avenida Colombo, 5790, PR 87020-900, Maringá, PR, Brazil

²DEQ/UFPR, Centro Politécnico, Jardim das Américas, 81531-980, Curitiba, PR, Brazil

³LASEFI/DEA/FEA (College of Food Eng)/UNICAMP (University of Campinas), Rua Monteiro Lobato, 80; 13083-862 Campinas, São Paulo, Brazil

Abstract: In the present work phase equilibrium data for the ternary systems CO₂ + ethanol + curcumin and CO₂ + ethyl acetate + curcumin, at different concentrations of curcumin in the organic solvent (0.01 g·cm⁻³, 0.005 g·cm⁻³ for ethanol and 0.01 g·cm⁻³, 0.0025 g·cm⁻³ for ethyl acetate) are reported. The static synthetic method, using a variable-volume view cell was employed for obtaining the experimental data in the temperature range of (303 to 333) K and pressures up to 11 MPa. Vapor-liquid phase transitions were observed as bubble and dew points for the overall compositions investigated. The phase equilibria of the ternary systems were fitted to the Peng-Robinson equation of state (PR-EoS) using only binary system information. Experimental data together with modeling results may constitute relevant information for the precipitation of curcumin using the supercritical antisolvent process.

Keywords: Phase equilibrium, vapor-solid-liquid, CO₂, curcumin, organic solvents.

INTRODUCTION

Curcuma longa L. is a perennial herbaceous plant with medicinal properties that belongs to the family of Zingiberaceae. Such plant is cultivated in Indian, China and other countries with tropical weather, is considered one of the main pigments produced in Brazil. The rhizome is the part of the plant used in medical applications and it has a yellow color and may be used as a food coloring. Curcumin ((E,E)-1,7-bis(4-Hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is the major non-volatile active compound of the rhizome. This curcuminoid has anti-oxidative, anti-carcinogenic, anti-mutagenic, anti-inflammatory and anti-fungicidal effects. The application of supercritical fluids as antisolvents for precipitation of curcumin can be an attractive technique due to the low solubility of this substance in supercritical fluid in comparison with conventional methods that use organic solvents. In order to develop or to optimize these processes for producing micronized particles, the knowledge of the phase behavior of solute + solvent + antisolvent is a crucial aspect.

Since ancient times, curcumin present in turmeric is known by Ayurvedic and Chinese medicines. New researches showed that curcumin has therapeutic effects on various diseases like Alzheimer, AIDS and cancer. The numerous therapeutic activities of curcumin can be found in the works of professor Aggarwal and collaborators [1]. According to Baskaya [2] curcumin (1,7-bis(4-hydroxy-3-methoxy-

fenil)-1,6-heptadiene-3,5-dione) is a highly polar substance, insoluble in water or neutral pH, poorly soluble in hydrocarbon solvents, and soluble in alcohols. However, clinical application of curcumin is limited due to poor aqueous solubility, and consequently, minimal systemic bioavailability. *In vitro* absorption studies showed that nanoparticles of curcumin have the potential to bypass poor solubility and poor systemic bioavailability [3]. A method that is an alternative to conventional precipitation techniques such as organic solvents or spray drying is supercritical fluids technology [4].

The application of supercritical CO₂ as antisolvents for curcumin precipitation can be adequate because it is a strongly polar substance, with a high molecular mass, and two phenyl and two carbonyl groups. The knowledge of phase behavior of the solute + solvent + antisolvent system plays an important role to determine appropriate operating conditions to conduct precipitation and understanding the kinetic nucleation mechanism and growth of the particles. Due to the potential applications of curcumin in the chemical, pharmaceutical and cosmetic industries there are a lot of work available in literature. However, the majority of the studies that use supercritical technology are related to supercritical fluid extraction [5-7] and few works provide phase equilibrium data [2, 8].

In this context, the aims of the present work were: (1) to measure phase equilibrium (transition points) data for the ternary systems CO₂ (1) + ethanol (2) + curcumin (3) and CO₂ (1) + ethyl acetate (2) + curcumin (3), at different concentrations of curcumin in the organic solvent and at different temperatures and (2) to fit the experimental data to the Peng-Robinson equation of state (PR-EoS) using quadratic mixing rule.

*Address correspondence to this author at the DEQ/UEM, Bloco D-90, Avenida Colombo, 5790, PR 87020-900, Maringá, PR, Brazil; Tel: +55 44 32614749; E-mail: cardozo@deq.uem.br

EXPERIMENTAL

Material

Ethyl acetate (99.5%) was purchased from VETEC (Rio de Janeiro, Brazil), and ethanol (99.5%) was obtained from Merck (Darmstadt, Germany). Curcumin with a minimum purity of 95% was purchased from Sigma-Aldrich (USA), and CO₂ (99.9% pure) was supplied by White Martins S.A. All materials were used as received, without any further purification. The organic stock solutions were previously prepared using two concentrations of curcumin in ethyl acetate (0.0025 g·cm⁻³ and 0.010 g·cm⁻³) and in ethanol (0.005 g·cm⁻³ and 0.010 g·cm⁻³).

Apparatus and Experimental Procedure

Phase equilibrium experiments were conducted employing the static synthetic method in a high-pressure variable-volume view cell. The experimental apparatus and procedure have been used in a variety of studies [9-14]. Briefly, the experimental apparatus consists of a variable-volume view cell, with a maximum internal volume of 27 cm³, with two sapphire windows for visual observation, an absolute pressure transducer (Smar LD 301, Sertãozinho, Brazil), with a precision of 0.03 MPa, a portable programmer (Smar, HT 201, Sertãozinho, Brazil) for the pressure data acquisition, and a syringe pump (ISCO 260D, Lincoln, USA). The equilibrium cell contains a movable piston, which permits pressure control inside the cell. Phase transitions were recorded visually through manipulation of the pressure by the syringe pump using the solvent as a pneumatic fluid. Initially, a known mass of the solute (either the organic solvent or a mixture of curcumin + organic solvent) was weighed on a precision scale balance (Marte AM-220, ± 0.0001 g, Santa Rita do Sapucaí, Brazil) and loaded into the equilibrium cell. The cell was then flushed with low-pressure CO₂ to remove any residual air. The charge of a known volume of CO₂ was performed with the help of the syringe pump (resulting in accuracy of ± 0.005 g in CO₂ loadings) until a desired global composition was achieved. On the basis of the uncertainty in CO₂ loading and other compound weight, we estimate that the uncertainty in global mass fraction of the mixtures was lower than 0.005 %. The cell content was kept under continuous agitation with the help of a magnetic stirrer and a Teflon-coated stirring bar. The temperature control was then turned on, and once the desired temperature was reached and controlled within ± 0.5 K, the pressure system was increased until the visualization of a one-phase system in the cell. At this point, the system was kept for at least 30 min to allow stabilization, and then the pressure was slowly decreased, typically at a rate of (0.1 to 0.5) MPa·min⁻¹, until incipient formation of a new phase. In the bubble point transition, a small vapor bubble appears, while in the dew point transition, a small amount of dew, or fog, is formed in the cell. This procedure was repeated at least three times for each temperature and global composition. After completion of the measurement at a given temperature, the cell temperature was stabilized at a new value and the experimental procedure was repeated.

Thermodynamic Modeling

The experimental data of liquid-vapor transition were modeled by the Peng-Robinson equation of state with van

der Waals quadratic mixing rule (vdW2). The isofugacity approach was used in the vapor-liquid equilibrium (VLE) calculations using the EoS-PR. The EoS-PR is given by the following equation:

$$P = \frac{RT}{v-b} - \frac{a}{v(v+b)+b(v-b)} \quad (1)$$

where P is the absolute pressure of the system, T is the absolute temperature, and v is the molar volume. The two-parameter of vdW2 mixing rules are given by:

$$a = \sum_{i=1}^{nc} \sum_{j=1}^{nc} x_i x_j \sqrt{a_i a_j} (1 - k_{ij}) \quad (2)$$

$$b = \sum_{i=1}^{nc} \sum_{j=1}^{nc} x_i x_j \left(\frac{b_i + b_j}{2} \right) (1 - l_{ij}) \quad (3)$$

$$a_i = \left(\frac{0.4572 R^2 T_c^2}{P_{c_i}} \right) \left[1 + (0.37464 + 1.54226 \omega_i - 0.26992 \omega_i^2) \left(1 - \sqrt{\frac{T}{T_{c_i}}} \right) \right] \quad (4)$$

where $k_{i,j}$ and $l_{i,j}$ are the binary interaction parameters of the components in the mixture. The pure component parameters a_i and b_i are given by the equations:

$$b_i = 0.07779 R \frac{T_{c_i}}{P_{c_i}} \quad (5)$$

where T_{c_i} , P_{c_i} , ω_i are the critical temperature, critical pressure, and the acentric factor of the i-component, respectively. Table 1 presents the critical properties, acentric factor of pure compounds used in this work and the melting temperature (T_{fus}) and enthalpy of fusion (Δh_{fus}) of curcumin [2,14-16].

In this approach only binary information (binary interactions parameters, k_{ij} and l_{ij}) were used to model the VLE of the ternary systems. The binary interaction parameters for system CO₂ + ethanol ($k_{12} = 0.0703$ and $l_{12} = -0.0262$) and CO₂ + ethyl acetate ($k_{12} = -0.0373$ and $l_{12} = -0.0639$) were taken from literature [14]. The binary interaction parameters for CO₂ + curcumin, ethanol + curcumin and ethyl acetate + curcumin were set to zero.

RESULTS AND DISCUSSIONS

In order to measure the phase equilibrium data two stock solutions with different concentrations of curcumin in ethanol and ethyl acetate were prepared. For the ternary system CO₂ (1) + ethanol (2) + curcumin (3) the concentrations of curcumin in ethanol were used (0.010 g·cm⁻³ and 0.005 g·cm⁻³), whereas for the ternary system CO₂ (1) + ethyl acetate (2) + curcumin (3) the concentrations of curcumin in ethyl acetate were of 0.010 g·cm⁻³ and 0.0025 g·cm⁻³; the solution concentration uncertainty was lower than 0.0005 g·cm⁻³.

Tables 2 and 3 present the results for the ternary system CO₂ (1) + ethanol (2) + curcumin (3) at the two investigated concentrations of curcumin. In Table 2 the experimental data refer to vapor-liquid coexistence curve at curcumin concentration of 0.010 g·cm⁻³, where one can notice the occurrence of biphasic vapor-liquid transition (bubble or dew point transitions type) in the presence of solid phase was observed at all CO₂ mole fraction investigated in this work. It must be emphasized that the solid was precipitated from the CO₂ fed

Table 1. Critical Properties and Acentric Factor of Pure Compounds

Compound	T _c [K]	P _c [bar]	ω	M _w [g·cm ⁻³]	T _{melting} [K]	Δh_{fus} [J·mol ⁻¹]
CO ₂ ^(a)	304.10	73.80	0.2390	44.01	-	-
Ethanol ^(a)	516.20	63.00	0.6350	46.069	-	-
Ethyl Acetate ^(a)	523.20	38.30	0.3620	88.107	-	-
Curcumin ^(c,b)	1013.60	18.38	1.608	368.40	454.65	44134.32

(a) Reid *et al.* [15]; (b) Kaewnopparat *et al.* [16]; (c) Baskaya [2].**Table 2. Experimental Vapor-Liquid Transition Data for the System CO₂ (1) + ethanol (2) + curcumin “from Curcuma Longa” (3) at a Curcumin Concentration of 0.010 g·cm⁻³ in Ethanol (CO₂-free Basis)**

T	P	σ^a	transition	T	P	σ^a	transition
K	bar	bar	type ^b	K	bar	bar	type ^b
$x_I = 0.3094$				$x_I = 0.7622$			
303	45.2	0.1	BP(S)	303	61.9	0.4	BP(S)
313	52.9	0.2	BP(S)	313	75.8	0.1	BP(S)
323	60.5	0.2	BP(S)	323	89.0	0.1	BP(S)
333	68.2	0.4	BP(S)	333	104.3	0.3	BP(S)
$x_I = 0.4117$				$x_I = 0.8319$			
303	51.3	0.1	BP(S)	303	62.1	0.1	BP(S)
313	62.6	0.3	BP(S)	313	75.8	0.1	BP(S)
323	73.7	0.2	BP(S)	323	90.5	0.1	BP(S)
333	83.6	0.3	BP(S)	333	104.8	0.1	BP(S)
$x_I = 0.5126$				$x_I = 0.9041$			
303	58.3	0.1	BP(S)	303	66.6	0.1	BP(S)
313	69.4	0.2	BP(S)	313	80.1	0.1	BP(S)
323	81.2	0.2	BP(S)	323	93.7	0.2	BP(S)
333	92.5	0.1	BP(S)	333	107.4	0.1	DP(S)
$x_I = 0.6999$				$x_I = 0.9690$			
303	61.1	0.4	BP(S)	303	64.7	0.2	BP(S)
313	75.6	0.2	BP(S)	313	78.7	0.1	BP(S)
323	88.3	0.1	BP(S)	323	91.1	0.2	DP(S)
333	101.0	0.6	BP(S)	333	100.2	0.2	DP(S)

^aExperimental standard deviation in pressure; ^bBP = bubble point; DP = dew point, BP(S) and DP(S) refers to phase transitions in the presence of solid (precipitated).

into the cell. In Table 3, which refers to curcumin concentration of 0.005 g·cm⁻³, the vapor-liquid transitions with precipitated curcumin were observed from CO₂ mole fraction $x_I = 0.6110$ up to $x_I = 0.9522$.

Tables 4 and 5 present the results for the ternary system CO₂ (1) + ethyl acetate (2) + curcumin (3) at the two investigated concentrations of curcumin in organic solutions, 0.010 g·cm⁻³ and 0.0025 g·cm⁻³, respectively. Vapor-liquid transitions were observed at all composition range investigated in

this work at concentration of curcumin (in the original stock solutions) at 0.010 g·cm⁻³, as indicated in Table 4 by symbol BP(S) or DP(S) (bubble point or dew point in the presence of precipitated curcumin). In Table 5, at curcumin concentration 0.0025 g·cm⁻³, it can be noted that vapor-liquid transitions in the presence of solid phase were observed for $x_I \geq 0.6839$. Below this mixture composition vapor-liquid (BP) transitions were observed.

Table 3. Experimental Vapor-Liquid Transition Data for the System CO₂ (1) + Ethanol (2) + Curcumin (3) at a Curcumin Concentration of 0.005 g·cm⁻³ in Ethanol (CO₂-free Basis)

T	P	σ ^a	transition	T	P	σ ^a	transition
K	bar	bar	type ^b	K	bar	bar	type ^b
$x_1 = 0.3099$				$x_1 = 0.7097$			
303	45.4	0.1	BP	303	59.7	0.1	BP(S)
313	53.7	0.1	BP	313	73.4	0.2	BP(S)
323	61.5	0.1	BP	323	88.3	0.2	BP(S)
333	68.3	0.1	BP	333	102.3	0.1	BP(S)
$x_1 = 0.4113$				$x_1 = 0.8075$			
303	53.6	0.1	BP	303	61.1	0.1	BP(S)
313	63.8	0.1	BP	313	75.5	0.2	BP(S)
323	73.8	0.2	BP	323	90.7	0.1	BP(S)
333	83.5	0.1	BP	333	105.1	0.1	BP(S)
$x_1 = 0.5114$				$x_1 = 0.9041$			
303	58.6	0.1	BP	303	63.4	0.1	BP(S)
313	70.3	0.2	BP	313	78.6	0.1	BP(S)
323	82.5	0.1	BP	323	91.2	0.2	BP(S)
333	94.1	0.1	BP	333	104.0	0.1	BP(S)
$x_1 = 0.6110$				$x_1 = 0.9522$			
303	61.4	0.1	BP(S)	303	63.9	0.2	BP(S)
313	74.9	0.1	BP(S)	313	76.8	0.1	BP(S)
323	87.6	0.2	BP(S)	323	88.6	0.2	DP(S)
333	101.1	0.1	BP(S)				

^aExperimental standard deviation in pressure; ^bBP = bubble point; DP = dew point, BP(S) and DP(S) refers to phase transitions in the presence of solid (precipitated).

Table 4. Experimental Vapor-Liquid Transition Data for the System CO₂ (1) + Ethyl Acetate (2) + Curcumin (3) at a Curcumin Concentration of 0.01 g·cm⁻³ in Ethyl Acetate (CO₂-Free Basis)

T	P	σ ^a	transition	T	P	σ ^a	transition
K	bar	bar	type ^b	K	bar	bar	type ^b
$x_1 = 0.4622$				$x_1 = 0.8371$			
303	25.4	0.2	BP(S)	303	52.0	0.2	BP(S)
313	30.1	0.2	BP(S)	313	62.7	0.1	BP(S)
323	34.8	0.2	BP(S)	323	73.8	0.2	BP(S)
333	41.6	0.1	BP(S)	333	84.7	0.1	BP(S)
$x_1 = 0.5718$				$x_1 = 0.9248$			
303	31.3	0.2	BP(S)	303	58.8	0.1	BP(S)
313	38.1	0.1	BP(S)	313	71.9	0.1	BP(S)
323	45.5	0.1	BP(S)	323	85.5	0.3	DP(S)
333	53.4	0.1	BP(S)	333	95.6	0.2	DP(S)
$x_1 = 0.7099$				$x_1 = 0.9584$			
303	41.7	0.1	BP(S)	303	63.2	0.1	BP(S)
313	50.1	0.1	BP(S)	313	74.8	0.1	BP(S)
323	59.7	0.1	BP(S)	323	89.6	0.3	DP(S)
333	69.2	0.1	BP(S)	333	96.5	0.2	DP(S)

^aExperimental standard deviation in pressure; ^bBP = bubble point; DP = dew point, BP(S) and DP(S) refers to phase transitions in the presence of solid (precipitated).

Table 5. Experimental Transition Vapor-Liquid Data for the CO₂ (1) + Ethyl Acetate (2) + Curcumin (3) at a Curcumin Concentration of 0.0025 g·cm⁻³ in Ethyl Acetate (CO₂-Free Basis)

T	P	σ^a	transition	T	P	σ^a	transition
K	bar	bar	type ^b	K	bar	bar	type ^b
$x_1 = 0.4611$				$x_1 = 0.8374$			
303	29.2	0.1	BP	303	54.0	0.1	BP(S)
313	34.7	0.1	BP	313	65.7	0.1	BP(S)
323	40.4	0.1	BP	323	78.5	0.3	BP(S)
333	46.1	0.1	BP	333	90.5	0.1	BP(S)
$x_1 = 0.5711$				$x_1 = 0.9194$			
303	34.9	0.1	BP	303	60.4	0.1	BP(S)
313	42.0	0.1	BP	313	74.2	0.1	BP(S)
323	49.4	0.1	BP	323	87.2	0.1	BP(S)
333	56.3	0.1	BP	333	98.0	0.1	BP(S)
$x_1 = 0.6839$				$x_1 = 0.9475$			
303	42.4	0.1	BP(S)	303	65.3	0.1	BP(S)
313	51.2	0.1	BP(S)	313	78.6	0.2	BP(S)
323	59.6	0.1	BP(S)	323	89.8	0.1	DP(S)
333	69.1	0.1	BP(S)	333	97.8	0.1	DP(S)

^aExperimental standard deviation in pressure; ^bBP = bubble point; DP = dew point, BP(S) and DP(S) refers to phase transitions in the presence of solid (precipitated).

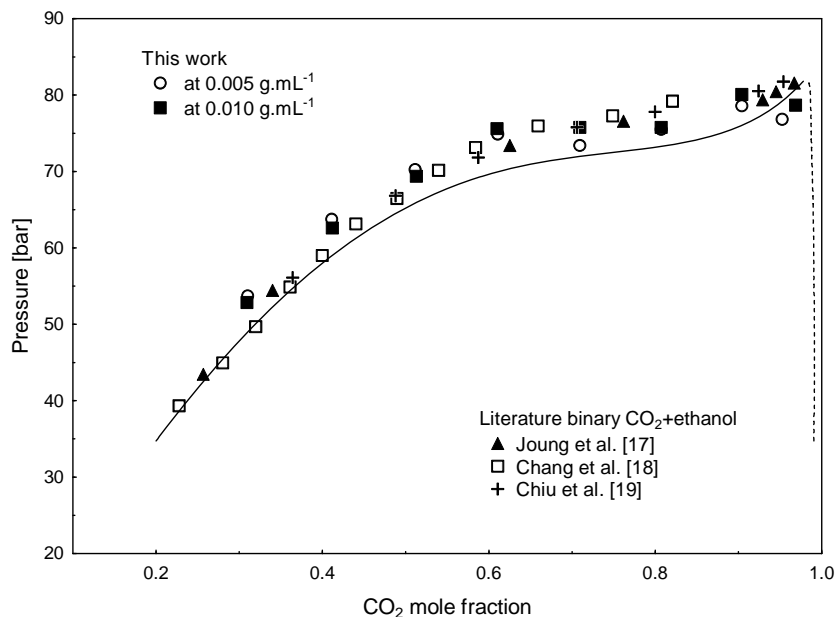


Fig. (1). P-x-y VLE data for ternary system CO₂ (1) + ethanol (2) + curcumin (3) of this work and literature experimental data at 313 K.

Fig. (1) provides a comparison in the pressure-composition diagram between experimental data obtained in this work for the ternary system CO₂ + ethanol + curcumin for the two curcumin concentrations (0.010 g·cm⁻³ and 0.005 g·cm⁻³) and binary data from literature at 313 K [17-19]; Fig. (2) presents the same comparisons for the temperatures of 303 K and 333 K.

Figs. (1 and 2) show that the presence of did not lead to significant changes in the pressure transitions when compared to the corresponding binary systems; the presence of solute did not modify the shape of vapor-liquid region. The thermodynamic model fitted well the experimental data.

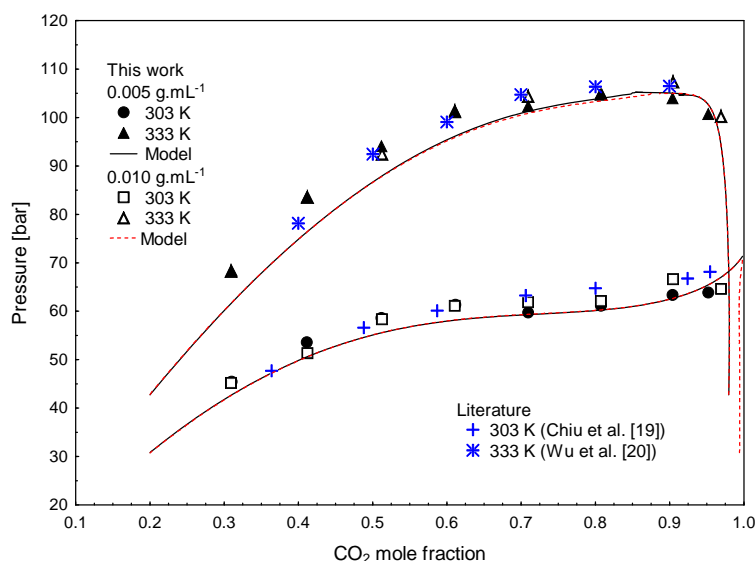


Fig. (2). P-x-y VLE data for ternary system CO₂ (1) + ethanol (2) + curcumin (3) of this work and literature experimental data at 303 K and 333 K.

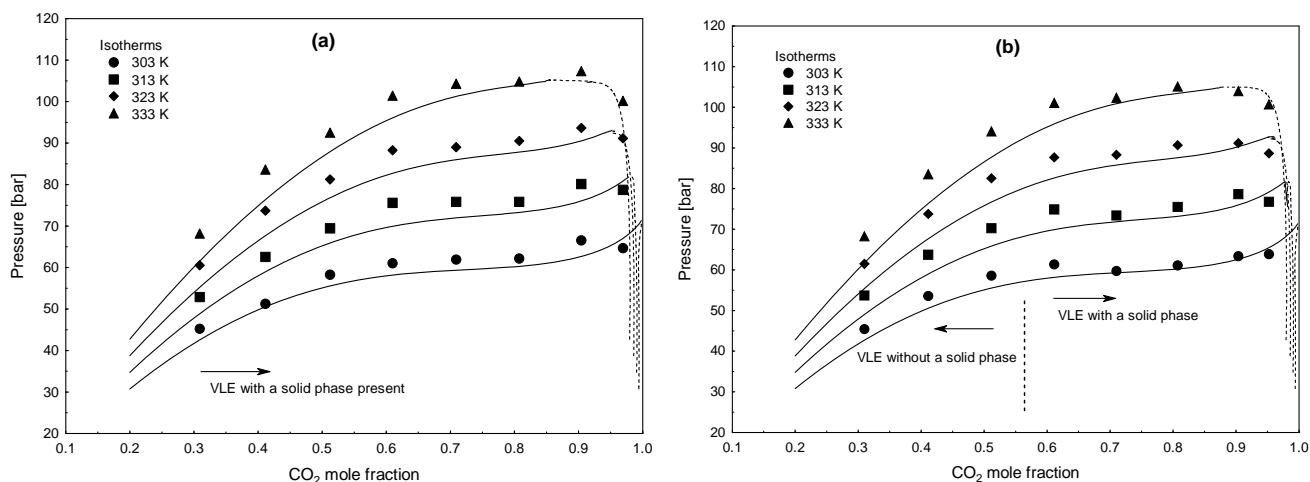


Fig. (3). P-x-y VLE diagram for system CO₂ (1) + ethanol (2) + curcumin (3) at curcumin concentration in ethanol of (a) 0.01 g·cm⁻³ and (b) 0.005 g·cm⁻³.

In Figs. (3(a) and 3(b)) are indicated regions where the vapor-liquid transitions were observed in the presence of solid (curcumin precipitated) (as also indicated in Table 2 and Table 3). Vertical dashed lines are the qualitative indication of these distinct regions. Taking into account this experimental evidence, it can be seen the anti-solvent effect of CO₂ in the organic phase (solvent + curcumin). The CO₂ amount necessary to precipitate the curcumin from organic solution is higher according to decreasing curcumin concentration in ethanol. As it can be observed from Tables 2 and 3 this anti-solvency effect of CO₂ was observed at all temperature range investigated in this work (303 to 333 K).

Fig. (4) provides a comparison between experimental data obtained in this work with experimental data from the literature for the binary system of CO₂ (1) + ethyl acetate (2) at 303 and 333 K [14].

Data on the curcumin saturation pressure are scarce in literature however its saturation pressure is approximately zero. Therefore, systems with higher-pressure transition are generally those with lower concentrations of curcumin.

In Figs. (5(a) and 5(b)) are indicated the regions where the vapor-liquid transition were observed in the presence of solid (curcumin precipitated) (see also Table 4 and Table 5). For curcumin concentration of 0.010 g·cm⁻³ (Fig. 5(a)) vapor-liquid transitions occurred in the presence of solid phase (curcumin). When the concentration of curcumin in ethyl acetate was 0.0025 g·cm⁻³ the solid phase occurrence was observed for $x_1 \geq 0.6839$ as indicated by the vertical dashed line in Fig. 5(b). This behavior is similar to that observed for the system with ethanol (Figs. 3(a) and 3(b)), i.e., smaller CO₂ amounts are necessary to precipitate curcumin from organic phase as the curcumin concentration in organic solvent (ethanol or ethyl acetate) increased. The anti-solvency

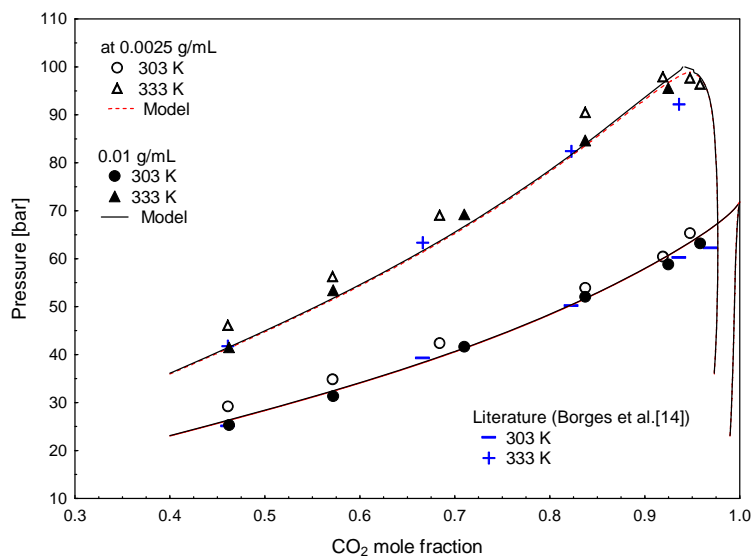


Fig. (4). P-x-y VLE data for ternary system CO₂ (1) + ethyl acetate (2) + curcumin (3) of this work and literature experimental data at 303 K and 333 K.

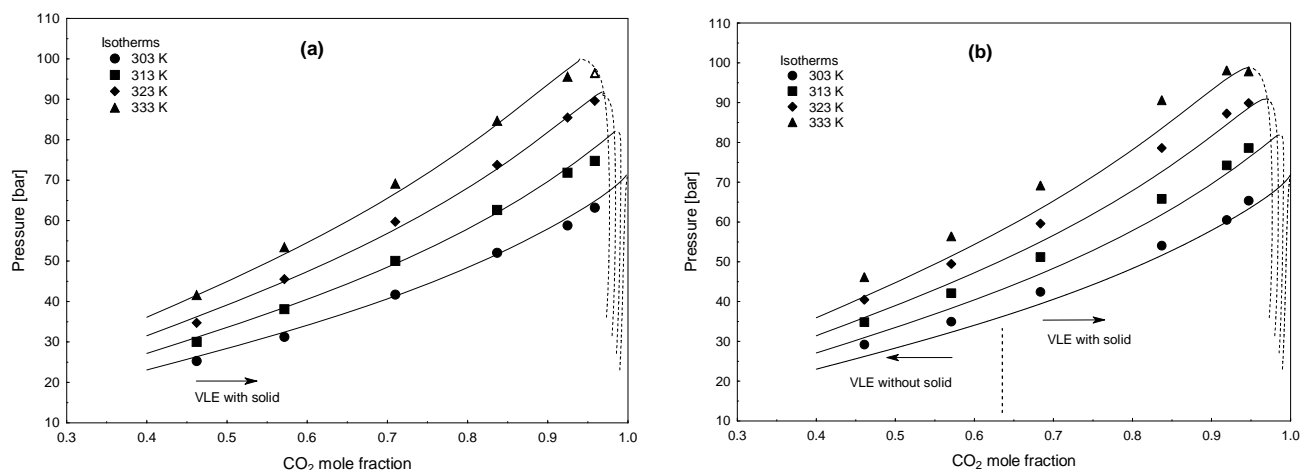


Fig. (5). P-x-y VLE diagram for system CO₂ (1) + ethyl acetate (2) + curcumin (3) at curcumin concentration in ethanol of (a) 0.01 g-cm⁻³ and (b) 0.0025 g-cm⁻³ is presented.

effect of CO₂ was observed for all temperatures in the range investigated in this work (303 to 333 K) (Tables 4 and 5).

CONCLUSIONS

Phase transition measurements for the ternary systems CO₂ (1) + ethanol (2) + curcumin (3) and CO₂ (1) + ethyl acetate (2) + curcumin (3) were reported in this work and modeled with the PR-EoS with quadratic mixing rules. It was experimentally observed that the addition of curcumin to the binary systems of CO₂/organic solvent did not lead to changes in the pressure transitions. The approach employed to predict phase equilibrium data of the ternary systems us-

ing only binary (CO₂ + organic solvents - ethanol or ethyl acetate) information proved to be reliable, affording satisfactory agreement between experiment and theory. Results obtained in this work may be relevant for those interested in processing curcumin using an innovative high-pressure anti-solvent technique.

ACKNOWLEDGEMENTS

The authors thank CNPq, CAPES and FAPESP (process number 06/60909-9) for the financial support and scholarships.

REFERENCES

- [1] B.B. Aggarwal, C. Sundaram, N. Malani, and H. Ichikawa, "Curcumin: the Indian solid gold", *Adv. Exp. Med. Biol.*, vol. 595, pp. 1-75, 2007.
- [2] F.S. Baskaya, "Phase equilibrium at supercritical (sc) conditions: solubility analysis of curcumin in supercritical CO₂ and cosolvent mixtures, and phase equilibrium analysis of cis-1,4-(poly)isoprene in propane and co-solvent mixtures", M.S. thesis, University of Akron, 2005, Akron, USA.
- [3] S. Bisht, G. Feldmann, S. Soni, R. Ravi, C. Karikar, and A. Maitra, "Polymeric nanoparticle-encapsulated curcumin ("nanocurcumin"): a novel strategy for human cancer therapy", *J. Nanobiotechnol.*, vol. 5, pp. 1-18, 2007.
- [4] A. Shariati, and C.J. Peters, "Recent developments in particle design using supercritical fluids", *Curr. Opin. Solid State Mater. Sci.*, vol. 7, pp. 371-383, 2003.
- [5] N.T. Machado, M.A.A. Meireles, A.L. Chassagnez-Mendez, and M.E. Araujo, "Supercritical CO₂ extraction of curcumins and essential oil from the Rhizomes of turmeric (*Curcuma longa* L.)", *Ind. Eng. Chem. Res.*, vol. 39, pp. 4729-4733, 2000.
- [6] B. Gopalan, M. Goto, A. Kodama, and T. Hirose, "Supercritical carbon dioxide extraction of turmeric (*Curcuma longa*)", *J. Agric. Food Chem.*, vol. 48, pp. 2189-2192, 2000.
- [7] M.E.M. Braga, P.F. Leal, J.E. Carvalho, and M.A.A. Meireles, "Comparison of yield, composition, and antioxidant activity of turmeric (*Curcuma longa* L.) extracts obtained using various techniques", *J. Agric. Food Chem.*, vol. 51, pp. 6604-6611, 2003.
- [8] L. Kao, C.-R. Chen, and C.-M.J. Chang, "Supercritical CO₂ extraction of turmerones from turmeric and high-pressure phase equilibrium of CO₂ + turmerones", *J. Supercrit. Fluids*, vol. 43, pp. 276-282, 2007.
- [9] M.L. Corazza, L. Cardozo-Filho, O.A.C. Antunes, and C. Dariva, "Phase behavior of the reaction medium of limonene oxidation in supercritical carbon dioxide", *Ind. Eng. Chem. Res.*, vol. 42, pp. 3150-3155, 2003.
- [10] P.M. Ndiaye, E. Franceschi, D. Oliveira, C. Dariva, F.W. Tavares, and J.V. Oliveira, "Phase behavior of soybean oil, castor oil and their fatty acid ethyl esters in carbon dioxide at high pressures", *J. Supercrit. Fluids*, vol. 37, pp. 29-37, 2006.
- [11] E. Franceschi, M.H. Kunita, A.F. Rubira, E.C. Muniz, M.L. Corazza, J.V. Oliveira, and C. Dariva, "Phase behavior of binary and ternary systems involving carbon dioxide, propane, and glycidyl methacrylate at high pressure", *J. Chem. Eng. Data*, vol. 51, pp. 686-690, 2006.
- [12] T. Benazzi, E. Franceschi, M.L. Corazza, J.V. Oliveira, and C. Dariva, "High-pressure multiphase equilibria in the system glycerol + olive oil + propane + AOT", *Fluid Phase Equilib.*, vol. 244, pp. 128-136, 2006.
- [13] R. Favareto, V.F. Cabral, M.L. Corazza, and L. Cardozo-Filho, "Vapor-liquid and solid-fluid equilibrium for progesterone + CO₂, progesterone + propane, and progesterone + n-butane systems at elevated pressures", *J. Supercrit. Fluids*, vol. 45, pp. 161-170, 2008.
- [14] G.R. Borges, A. Junges, E. Franceschi, F.C. Corazza, M.L. Corazza, J.V. Oliveira, and C. Dariva, "High-pressure vapor-liquid equilibrium data for system involving carbon dioxide + organic solvent + β -carotene", *J. Chem. Eng. Data*, vol. 52, pp. 1437-1441, 2007.
- [15] R.C. Reid, J.M. Prausnitz, B.E. Poling, "The Properties of Gases and Liquids", 4th ed. McGraw-Hill: New York, 1987.
- [16] N. Kaewnopparat, S. Kaewnopparat, A. Jangwang, D. Maneenun, T. Chuchoe, and P. Panichayupakaranant, "Increased solubility, dissolution and physicochemical studies of curcumin-polyvinylpyrrolidone K-30 solid dispersions", *World Acad. Sci. - Eng. Technol.*, vol. 55, pp. 229-234, 2009.
- [17] S.N. Joung, C.W. Yoo, H.Y. Shin, S.Y. Kim, K-P Yoo, C.S. Lee, and W.S. Huh, "Measurements and correlation of high-pressure VLE of binary CO₂-alcohol systems (methanol, ethanol, -methoxyethanol and 2-ethoxyethanol)", *Fluid Phase Equilib.*, vol. 185, pp. 219-230, 2001.
- [18] C.J. Chang, C.-Y. Day, C.-M. Ko, and K.-L.g Chiu, "Densities and P-x-y diagrams for carbon dioxide dissolution in methanol, ethanol, and acetone mixtures", *Fluid Phase Equilib.*, vol. 131, pp. 243-258, 1997.
- [19] H.-Y. Chiu, M.-J. Lee, and H.-M. Lin, "Vapor-Liquid phase boundaries of binary mixtures of carbon dioxide with ethanol and acetone", *J. Chem. Eng. Data*, vol. 53, pp. 2393-2402, 2008.
- [20] Z. Zhang, W. Wu, B. Wang, J. Chen, D. Shen and B. Han, "High-pressure phase behavior of CO₂/acetone/ionic liquid system", *J. Supercrit. Fluids*, vol. 40, pp. 1-6, 2007.

Received: August 15, 2009

Revised: November 06, 2009

Accepted: December 08, 2009

© Giufriada et al.; Licensee Bentham Open.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.