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Solubility of Azadirachtin in Supercritical Carbon Dioxide at Several Temperatures

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ABSTRACT: The solubility data of azadirachtin in supercritical carbon dioxide were measured at several temperatures (308.15, 313.15, 318.15, 323.15, 328.15, and 333.15 K) and at pressure between (10 and 26) MPa. The measurement of solubility data was conducted in static mode. The experimental results were correlated by Chrastil model and Del valle and Aguilera equation. Chrastil model can represent the experimental data well and give a reasonable value for fitting parameters.

INTRODUCTION

Azadirachtin is a chemical compound belonging to the limonoids and one of more than 70 limonoids produced by the neem tree. Azadirachtin has a complex structure, and the IUPAC name of this compound is dimethyl (2aR,3S,4S,R,S,7aS,8S,10R,10a,7-10bR)-10-(acetyloxy)-3,5-dihydroxy-4-[(1S,2S,6S,8S,9R,7-1S)-2-hydroxy-11-methyl-5,7,10-trioxatetracyclo[6.3.1.0^{2,6}.0^{9,11}]dodec-3-en-9-yl]-4-methyl-8-[(2E)-2-methylbut-2-enyl]oxy}octahydro-1H-furo[3',4':4,4a]naphtho[1,8-bc]furan-5,10a(8H)-dicarboxylate. The molecular structure of azadirachtin is given in Figure 1. Azadirachtin has an insecticidal effect; therefore, it can be used as a natural insecticide.^{1–5} Azadirachtin and related limonoids are obtained from neem seeds by solvent extraction followed by several steps of separation and purification to obtain a high purity product. Purification of azadirachtin from the extract or oil can be conducted using various methods such solvent precipitation,⁶ and combination of several chromatography techniques.^{7–10} Extraction of azadirachtin using supercritical fluid technology has also been explored,^{11–13} but this technique did not give complete recovery.¹⁴ The failure of supercritical extraction technology to recovery completely of azadirachtin from its extract may be due to incorrect operation condition because of the lack of information about the solubility of this substance in supercritical carbon dioxide at various temperatures and pressures.

The solubility of solids and liquids in supercritical fluids is very important information for the design of any supercritical extraction processes.¹⁵ Currently, there is no information about the solubility of azadirachtin in supercritical carbon dioxide available in the literature. In this study, solubilities of azadirachtin in supercritical carbon dioxide were measured at several temperatures in a range of pressures from (10 to 26) MPa. The experimental data were then correlated by the Chrastil equation and its modified form.

MATERIAL AND METHODS

Material. Azadirachtin is a microcrystalline powder with a melting point of 447.15 K and -1.4 .¹⁴ Azadirachtin used in this study was obtained as a analytical standard from Sigma-Aldrich

(CAS no: 11141-17-6) and used without any further purification. Food grade carbon dioxide obtained from Aneka Gas Pty Ltd. was used as the supercritical solvent and supplied as liquid CO₂ with a mole fraction purity of 0.999.

EXPERIMENTAL PROCEDURE

The schematic diagram of supercritical equipment used in this study to obtain the solubility data of azadirachtin is given in Figure 2. The supercritical equipment consists of a high pressure pump (Eldex AA-100-S-2-CE, U.S.A.), a pressure transducer (Druck PTX 611, U.S.A.) with a digital process indicator (Druck DPI 280, U.S.A.), a heater and temperature controller (oven Memmert, Germany), a vacuum pump (GAST DOA-PS04 BN, U.S.A.), a volume calibrator (ZEAL DM3B, U.K.), and an equilibration column (Swagelok, U.S.A.). All fitting and tubing used in the system are made of stainless steel (Swagelok, U.S.A.). The maximum working pressure and temperature of the supercritical system are 30 MPa and 373.15 K, respectively. The uncertainties of the pressure and temperature measurements were ± 0.01 MPa and ± 1 K, respectively.

To measure the solubility of azadirachtin in supercritical CO₂, the following procedure was employed:¹⁵ the sample holder in the equilibration column was loaded with azadirachtin. The system was evacuated using a vacuum pump (GAST DOA-PS04 BN, U.S.A.) to remove air, and then the system was heated until the desired temperature was reached. Subsequently, the liquid CO₂ was pumped to the equilibration column using a high pressure pump (Eldex AA-100-S-2-CE, U.S.A.). During the experiments, valves V-3, V-4, and V-5 were closed, while valves V-1 and V-2 were opened. After equilibrium of the desired temperature and pressure was achieved (4 h), the sampling tube was disconnected from the system by closing valve V-2.¹⁵ The sample in the sampling tube was released to the collector containing

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a known amount of methanol to completely separate azadirachtin and carbon dioxide. At least three replicated samples were taken at an experimental condition, and the equilibrium composition was determined by averaging the replications. The uncertainty of each measurement was within $\pm 2\%$. The concentration of azadirachtin in methanol was determined by HPLC technique.

RESULTS AND DISCUSSIONS

The densities of supercritical carbon dioxide at various pressures and temperatures are calculated from the Stryjek and Vera modification of the Peng–Robinson equation of state,¹⁶ and the results are reported in Table 1. The solubilities of azadirachtin in supercritical CO₂ at various pressures and temperatures are given in Table 2. At 10 MPa, the solubility of azadirachtin decreases with increases of temperature. At pressures above 10 MPa, as the temperature increases, the solubility of the compound also increases. This phenomenon indicates that a crossover pressure region is present in the system. Below the crossover region, the effect of density is more dominant than vapor pressure, indicated by a decrease of solubility as the temperature increases, whereas above crossover region, the effect of vapor pressure is more dominant (solubility of azadirachtin increases with increases of temperature). Plots of solubility data of azadirachtin in supercritical carbon dioxide as a function of temperature are given in Figure 3.

The experimental solubility data were correlated by several semi empirical models. The density-based correlation method is

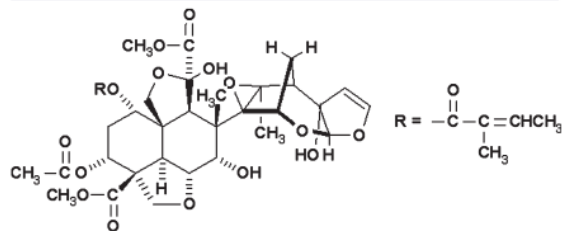


Figure 1. Molecular structure of azadirachtin.

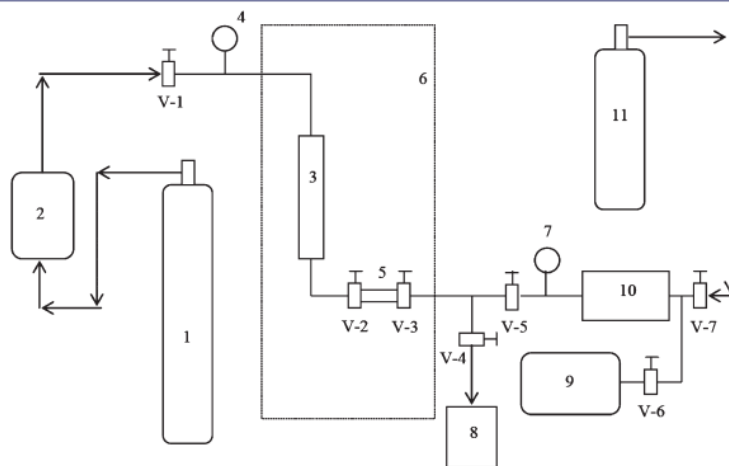


Figure 2. Schematic diagram of supercritical equipment 1. Liquid CO₂ cylinder. 2. High pressure pump system. 3. Equilibration cylinder. 4. High pressure transducer. 5. Sampling tube. 6. Temperature controller. 7. Low pressure transducer. 8. Collecting tank. 9. Vacuum pump. 10. Volume calibrator. 11. Helium cylinder.

widely used to correlate the experimental solubility data. This approach was developed based on the common observation that the logarithm of the solubility is linearly dependent on the density. Chrastil¹⁷ developed a semiempirical model based on this approach; his model has the form as follows:

$$y_2 = \rho^k \exp(a/T + b) \quad (1)$$

where y_2 is the solubility of the solute in gas, ρ is the density of gas, k is an association number, a is a function of the enthalpy of solvation and enthalpy of vaporization, and b is a function of the association number and molecular weights of the solute and supercritical fluids.

The fitting of the solubility experimental data was conducted at each temperature using nonlinear least-squares technique by minimizing the sum of squared errors as objective function

$$\text{SSE} = \left(\frac{\sum (y_{2(\text{exp})} - y_{2(\text{cal})})^2}{N} \right)^{1/2} \quad (2)$$

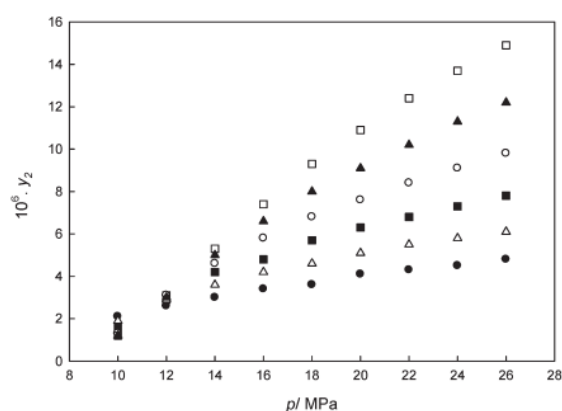
Here $y_{2(\text{exp})}$ is the actual solubility of azadirachtin in supercritical CO₂, $y_{2(\text{cal})}$ is the calculated solubility, and N is the number of experimental data. The nonlinear squares technique involves an

Table 1. Density of Supercritical CO₂ at Various Pressures and Temperatures

P MPa	$\rho/\text{kg}\cdot\text{m}^{-3}$					
	308.15 K	313.15 K	318.15 K	323.15 K	328.15 K	333.15 K
10	655	568	463	378	327	294
12	726	669	605	537	472	417
14	773	727	678	627	574	523
16	809	769	728	685	642	598
18	838	803	767	729	691	653
20	863	831	798	765	730	696
22	885	856	825	794	763	732
24	905	877	849	820	791	762
26	922	896	870	843	816	788

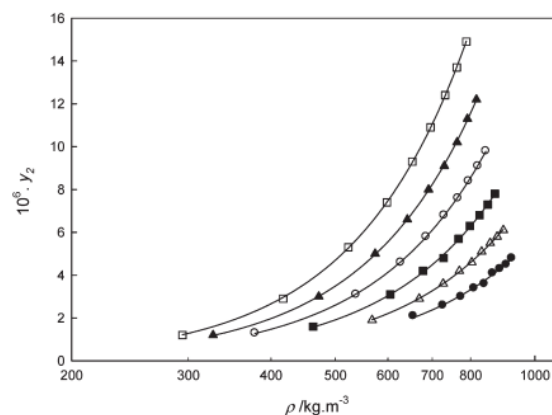
Table 2. Experimental Solubility Data of Azadirachtin in Supercritical Carbon Dioxide

p MPa	$10^6 \times y_2$					
	308.15 K	313.15 K	318.15 K	323.15 K	328.15 K	333.15 K
10	2.1	1.9	1.6	1.3	1.2	1.2
12	2.6	2.9	3.1	3.1	3.0	2.9
14	3.0	3.6	4.2	4.6	5.0	5.3
16	3.4	4.2	4.8	5.8	6.6	7.4
18	3.6	4.6	5.7	6.8	8.0	9.3
20	4.1	5.1	6.3	7.6	9.1	10.9
22	4.3	5.5	6.8	8.4	10.2	12.4
24	4.5	5.8	7.3	9.1	11.3	13.7
26	4.8	6.1	7.8	9.8	12.2	14.9

**Figure 3.** Solubility of azadirachtin on supercritical CO₂ as function of pressure. ●, Experimental data at 308.15 K; △, experimental data at 313.15 K; ■, experimental data at 318.15 K; ○, experimental data at 323.15 K; ▲, experimental data at 328.15 K; □, experimental data at 333.15 K.

iterative curve fitting procedure. In this procedure, an initial set of estimates for the parameters in the equation must be provided, and then calculation of a point by point sum of squares (eq 2) for each iteration will be conducted. The algorithm will modify each parameter value until it satisfies the convergence criteria to obtain a final solution.

Figure 4 shows that the Chrastil equation can represent the experimental solubility data of azadirachtin in supercritical CO₂ very well. The advantage of using the Chrastil equation is the model does not require any physical–chemical property data of the solute. Therefore this equation is applicable in most cases. The optimal parameters from the fitting of the Chrastil model are given in Table 3. The parameters of k , a , and b for the system of CO₂(1) + azadirachtin (2) are almost constant as indicated in Table 3. As mentioned before, k is an association number. Therefore this value should be specific for a given system, and the parameter of k obtained from this study is consistent. The parameter a is a function of the enthalpy of solvation and enthalpy of vaporization, and this parameter should increase with the increase of temperature; however, since the solubilities of azadirachtin in supercritical CO₂ are very small (Table 2), changes in the enthalpy of solvation and enthalpy of vaporization

**Figure 4.** Experimental solubility data as a function of density (shown in logarithmic scale) and those estimated from the Chrastil equation (eq 1) by minimizing eq 2. ●, Experimental data at 308.15 K; △, experimental data at 313.15 K; ■, experimental data at 318.15 K; ○, experimental data at 323.15 K; ▲, experimental data at 328.15 K; □, experimental data at 333.15 K; —, Chrastil model.**Table 3. Fitted Chrastil Equation Parameters for CO₂ (1) + Azadirachtin (2)**

T K	parameter			SSE %
	k	a	b	
308.15	2.511	-6270.1	-9.052	0.18
313.15	2.551	-6303.3	-9.213	0.14
318.15	2.534	-6275.4	-9.191	0.17
323.15	2.535	-6260.1	-9.244	0.09
328.15	2.551	-6264.6	-9.325	0.15
333.15	2.541	-6246.2	-9.308	0.17

are not considered by this equation. Therefore this parameter in the system of CO₂(1) + azadirachtin (2) remains constant. The last parameter b is a function of the association number and the molecular weights of the solute and supercritical fluids. Since the molecular weight of azadirachtin is constant and the association number of the solute is specific for each solute, this parameter should not be influenced by temperature. The fitting values of the parameter b at different temperatures are essentially constant, which is consistent with the physical meaning of this parameter.

Del Valle and Aguilera¹⁸ proposed another density-based model based on Chrastil's equation. Their model considered the change in the enthalpy of vaporization with temperature

$$y_2 = \rho^k \exp\left(b' + \frac{a'}{T} + \frac{d}{T^2}\right) \quad (3)$$

The meaning of the parameters k' , b' , and d' is similar to that of the parameters in the Chrastil model. The parameter d' is a parameter associated with the change in enthalpy of vaporization. This equation can represent the experimental data well, as shown in Figure 5. The parameters of eq 3 obtained from fitting experimental data are given in Table 4. Even if this equation can fit the experimental data well, however, considerably varying values of parameters b' , d' , and d were obvious. This inconsistency indicates a drawback in using this equation to correlate the solubility data of

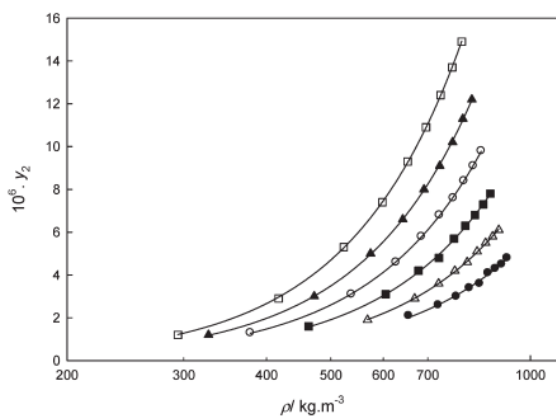


Figure 5. Experimental solubility data as a function of density (shown in logarithmic scale) and those estimated from the Del Valle and Aguilera model (eq 3) by minimizing eq 2. ●, experimental data at 308.15 K; △, experimental data at 313.15 K; ■, experimental data at 318.15 K; ○, experimental data at 323.15 K; ▲, experimental data at 328.15 K; □, experimental data at 333.15 K; —, Del Valle and Aguilera model.

Table 4. Fitted Del Valle and Aguilera Model Parameters for CO₂ (1) + Azadirachtin (2)

T K	parameter				SSE %
	k'	a'	b'	d	
308.15	2.511	19.31	-12590	-745353	0.18
313.15	2.550	42.73	-20101	-772497	0.14
318.15	2.534	-36.13	4808	-799470	0.18
323.15	2.535	-10.49	-3408	-791069	0.13
328.15	2.551	-14.60	-2041	-817174	0.15
333.15	2.541	-9.13	-3773	-843531	0.16

azadirachtin in supercritical carbon dioxide. The deviations of experimental data to the models of Del Valle–Aguilera and Chrastil are close as indicated in Tables 3 and 4. As mentioned before, the Del Valle and Aguilera model was developed based on the Chrastil model; therefore, this model will give a similar trend to the Chrastil equation in predicting the experimental data.

CONCLUSION

New solubility data of azadirachtin in supercritical carbon dioxide were obtained in this study. The solubility data were correlated by the Chrastil model and the Del Valle and Aguilera equation. The Chrastil model can represent the experimental data well and give a reasonable value of the fitting parameters.

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REFERENCES

- Denardi, S. E.; Bechara, G. H.; Oliveira, P. R. D.; Camargo-Mathias, M. I. Azadirachtin induced morphological changes on oocytes of *Rhipicephalus sanguineus* (Latreille, 1806) (Acari: Ixodidae) tick females. *Exp. Parasitol.* **2010**, *126*, 462–70.
- McKenzie, N.; Helson, B.; Thompson, D.; Otis, C.; McFarlane, J.; Buscarini, T.; Meating, J. Azadirachtin: An effective systemic insecticide for control of *agrilus planipennis* (Coleoptera: Buprestidae). *J. Econ. Entomol.* **2010**, *103*, 708–717.
- Cherry, R.; Nuessly, G. Repellency of the biopesticide, azadirachtin, to wireworms (Coleoptera: Elateridae). *Fla. Entomol.* **2010**, *93*, 52–55.
- Lu, H.-Y.; Liu, F.; Zhu, S.-D.; Zhang, Q. Effects of azadirachtin on rice plant volatiles induced by *Nilaparvata lugens*. *Chin. J. Appl. Ecol.* **2010**, *21*, 197–202.
- Ganguly, S.; Bhattacharya, S.; Mandi, S.; Tarafdar, J. Biological detection and analysis of toxicity of organophosphate- and azadirachtin-based insecticides in *Lathyrus sativus* L. *Ecotoxicology* **2010**, *19*, 85–95.
- Melwita, E.; Ju, Y. H. Separation of azadirachtin and other limonoids from crude neem oil via solvent precipitation. *Sep. Purif. Technol.* **2010**, *74*, 219–224.
- Yamasaki, R. B.; Klocke, J. A.; Lee, S. M.; Stone, G. A.; Darlington, M. V. Isolation and purification of azadirachtin from neem (*Azadirachta indica*) seeds using flash chromatography and high performance liquid chromatography. *J. Chromatogr.* **1986**, *356*, 220–226.
- Govindachari, T. R.; Sandhya, G.; Raj, S. P. G. Simple method for the isolation of azadirachtin by preparative high-performance liquid chromatography. *J. Chromatogr.* **1990**, *513*, 389–391.
- Schroeder, D. R.; Nakanishi, K. A simplified isolation procedure for azadirachtin. *J. Nat. Prod.* **1987**, *50*, 241–244.
- Sharma, V.; Walia, S.; Kumar, J.; Nair, M. G.; Parmar, B. S. An efficient method for the purification and characterization of nematocidal azadirachtins A, B, and H using MPLC and ESIMS. *J. Agric. Food Chem.* **2003**, *51*, 3966–3997.
- Ambrosino, P.; Fresa, R.; Fogliano, V.; Monti, S. M.; Ritieni, A. Extraction of azadirachtin from neem seed kernels by supercritical fluid and its evaluation by HPLC and LC/MS. *J. Agric. Food Chem.* **1999**, *47*, 5252–5256.
- Johnson, S.; Morgan, E. D. Supercritical fluid extraction of oil and triterpenoids from Neem seeds. *Phytochem. Anal.* **1997**, *8*, 228–232.
- Brooks, M. W.; Roy, S.; Uden, P. C.; Vittum, P. The extraction and determination of azadirachtin from soil and insects by supercritical fluid extraction. *J. Test. Eval.* **1996**, *24*, 149–153.
- Morgan, E. D. Azadirachtin, a scientific gold mine. *Bioorg. Med. Chem.* **2009**, *17*, 4096–4105.
- Ismađji, S. Solubility of methyl salicylate in supercritical carbon dioxide at several temperatures. *J. Chem. Eng. Data* **2008**, *53*, 2207–2210.
- Stryjek, R.; Vera, J. H. PRSV: An Improved Peng–Robinson Equation of State for Pure Compounds and Mixtures. *Can. J. Chem. Eng.* **1986**, *64*, 323–333.
- Chrastil, J. Solubility of solids and liquids in supercritical gases. *J. Phys. Chem.* **1982**, *86*, 3016–3021.
- del Valle, J. M.; Aguilera, J. M. An improved equation for predicting the solubility of vegetable oils in supercritical CO₂. *Ind. Eng. Chem. Res.* **1988**, *27*, 1551–1553.

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