# Prediction of solubility of biomolecules in supercritical solvents

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## Abstract

The supercritical fluid extraction (SFE) is considered an appropriate alternative for separation of biomolecules from food and pharmaceutical products. A major difficulty in utilizing the SFE for biomolecules has been the difficulty in measurement and prediction of their solubilities in supercritical solvents at various pressures and temperatures for process optimization. Lack of data for intermolecular energy parameters and/or critical properties, acentric factors, and molar refractions limits us to the use of the simple equations of state for prediction of their solubilities in supercritical solvents. In this report, six different cubic equations of state are used to predict the solubility of cholesterol and $\beta$-carotene, as two representative biomolecules, in supercritical fluids. They are the van der Waals, Redlich–Kwong, Mohsen-Nia–Moddaress–Mansoori (MMM), Peng–Robinson (PR) and Patel–Teja and modified PR equations. It is shown that the two-parameter MMM equation is more accurate than five of the other equations and comparable to the modified PR equation in predicting the solubility of cholesterol and $\beta$-carotene in supercritical fluids. © 2001 Elsevier Science Ltd. All rights reserved.

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## 1. Introduction

The advantages of utilizing supercritical solvents for extraction have been well documented (Park, Kwak, & Mansoori, 1987; Schulz, Martinelli, & Mansoori, 1991; Ekhtera, Mansoori, Mensinger, Rehmat, & Deville, 1997). The supercritical fluid extraction (SFE) has interested investigators during the past few decades. Unlike the conventional extraction process which uses liquids, the SFE process uses a supercritical fluid as the solvent. In comparison with conventional solvents, a supercritical fluid has high diffusivity and low viscosity, thus allowing rapid extraction and phase separation. Another attractive feature of supercritical solvents is the fact that their isothermal compressibility is several orders of magnitude greater than that of liquids while their density is the same as liquids. The relatively high supercritical fluid density gives it a good solvent power. As a result a sudden

reduction in temperature or pressure often causes the loss of these special characteristics of the supercritical solvent. Therefore, a solute can be extracted at supercritical condition of the solvent, and separated from the solvent by reducing pressure or temperature below the critical condition of the solvent, yielding a solvent-free extract (Schulz et al., 1991). By using supercritical solvents having low critical temperatures, it is possible to extract thermally labile compounds, especially the pharmaceutical and food products. As an example, cholesterol can be removed from food products using supercritical solvents resulting in minimal protein degradation (Chao et al., 1991). Valuable thermal-labile compounds, such as $\beta$-carotene can also be extracted using supercritical solvents without any degradation observed (Skerget, Knez, & Habulin, 1995). Carbon dioxide is the most widely used gas as the supercritical solvent because it is non-toxic, nonflammable, inexpensive, abundantly available, and has low critical temperature (Schulz et al., 1991).

Cholesterol is a sterol that can be found in many animal tissues, but not in plant tissues. It is the most abundant sterol in human tissues. It is a component of all cell membranes and functions as a precursor of bile acids, steroid hormones, and vitamin D. The

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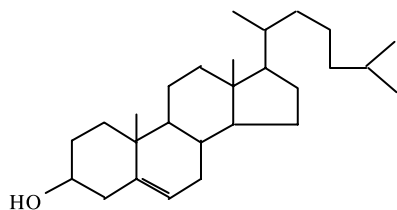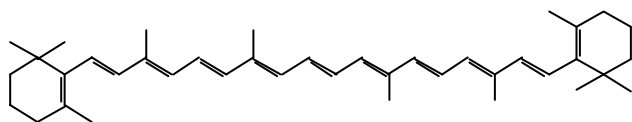
Fig. 1. Structure of cholesterol.



Fig. 2. Structure of β-carotene.

structure of cholesterol is depicted in Fig. 1. Cholesterol is not a dietary essential because it can be synthesized in the body. Typically, the body synthesizes about 600–1500 mg cholesterol per day, whereas the diet supplies about 300–500-mg cholesterol per day. It is transported in the plasma and is delivered to the tissues in the form of lipoprotein particles. The amount of cholesterol in the diet is one of the factors that influence the amount of cholesterol circulating within lipoprotein particles. In humans, the delivery system is less perfect than in animals. As a result, humans experience a gradual deposition of cholesterol in tissues. When the deposition contributes to plaque formation, it can cause the narrowing of blood vessels, known as atherosclerosis (Champe & Harvey, 1994). Therefore, reduction of cholesterol in the diet is beneficial to health. Hardardottir and Kinsella (1998) extracted cholesterol from fish muscle using supercritical carbon dioxide and ethanol as co-solvent. King, Johnson, and Friedrich (1989) used supercritical carbon dioxide to extract cholesterol from meat products. Chao et al. (1991) investigated the feasibility of separating cholesterol and lipids from ground beef. Acosta, Hou, Drake, and Smith (1994) examined the supercritical fluid extraction of fat from model bio-membrane structures. Mohamed, Saldaña, Socantaype, and Kieckbusch (2000) studied the reduction in the cholesterol content of butter oil using supercritical ethane extraction and adsorption on alumina.

β-Carotene is known as provitamin A and an antioxidant that may exert an important protective action against many diseases, including cancer. β-Carotene also enhances immunity and is used in livestock for enhancing fertility (Pfander, 1992). It is also used in food industry as a natural pigment. As many vegetables are sources of carotenoids, by using the SFE process, it is possible to obtain them as natural pigments. The structure of β-carotene is depicted in Fig. 2.

The development of SFE processes needs the understanding of the relevant phase behavior over a wide range of temperature and pressure (Schulz et al., 1991;

Kwon & Mansoori, 1993; Yang, Chen, & Guo, 1997). Many groups of researchers have determined the solubility of cholesterol in supercritical fluids (Chrastil, 1982; Wong & Johnston, 1986; Yeh, Liang, & Hwang, 1991; Singh, Yun, Macnaughton, Tomasko, & Foster, 1993; Yun, Liong, Guardial, & Foster, 1991; Kosal, Lee, & Holder, 1992; Foster, Singh, Yun, Tomasko, & Macnaughton, 1993). Chrastil (1982), Yeh et al. (1991), and Yun et al. (1991) correlated their experimental data using model developed by Chrastil. This model is based on the postulate that, at equilibrium, a solute molecule is associated with a fixed number of solvent molecules to form a solvatocomplex. This model, although simple, relies much on the knowledge of the thermodynamic behavior of the supercritical solvent rather than of the solute and it is mostly capable of correlating, rather than predicting, the solubility. Other groups of researchers correlated the solubility by using equations of state. Wong and Johnston (1986) applied the Hard-Sphere van der Waals equation of state for this purpose using the supercritical fluid density data as the input. Kosal, Lee, and Holder (1992), Singh et al. (1993), and Foster et al. (1993) have used a modified Peng–Robinson (PR) equation of state with additional adjustable parameters to correlate the solubility.

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, vapor pressure and density data of solute involved are needed (Mansoori & Ely, 1985; Hartono, Mansoori, & Suwono, 1999; Kwak & Mansoori, 1986, 1987). For three-parameter equations of state, a third parameter is needed; the PR and Soave-Redlich–Kwong (SRK) equations of state need the data of acentric factor, while the Riazi–Mansoori (RM) equation of state requires molar refraction data. The experimental critical properties, acentric factors, and molar refractions of cholesterol and β-carotene are not available in the literature. These organic compounds decompose at high temperature, making it impossible to measure their critical properties and vapor pressures at high temperature, which are needed for calculation of acentric factor. However, methods for prediction of critical properties are available in the literature. Lydersen's method has been proven to be accurate enough for prediction of critical properties of organic compounds, but it is not intended for larger molecules (Lyman, Reehl, & Rosenblatt, 1990) like cholesterol and β-carotene. Among the methods for prediction of acentric factor, the Edmister's method is considered the most accurate one. But still, Edmister's method gives high errors even for small molecules (such as 9.1% for toluene as reported by Reid & Sherwood, 1966). There are several methods for predicting molar refraction, such as Eisenlohr and Vogel methods (Lyman et al., 1990). These methods have been proven to be accurate enough for predicting the molar refractions of small molecules.

Cholesterol molecule has a phenanthrene skeleton (Champe & Harvey, 1994), while $\beta$-carotene has isoprenoid units (Pfander, 1992). Both Eisenlohr and Vogel methods are not accurate to predict the molar refraction of olefin and polycyclic compounds. As a result equations of state with least number of adjustable parameters are preferred for application to biomolecules.

In the present report, we study the two-parameter equations of state, i.e. the van der Waals, the Redlich–Kwong (Walas, 1985) and the Mohsen-Nia–Modarress–Mansoori (Mohsen-Nia, Moddaress, & Mansoori, 1995) to predict the solubility of cholesterol and $\beta$-carotene in supercritical fluids. These equations of state need only the data of critical pressure and temperature of the compounds involved. We also study the applicability of some three-parameter equations, i.e. the PR, Patel–Teja (PT) and modified Peng–Robinson equations (Singh et al., 1993) for comparison purposes. Critical values used here were predicted using Lydersen's method (Lyman et al., 1990) and are reported by Singh et al. (1993) for cholesterol and Subra, Castellani, Ksibi, and Garrabos (1997) for $\beta$-carotene.

## 2. Supercritical phase equilibrium involving a condensed phase

In predicting the phase equilibrium between a supercritical phase and a condensed phase, the equality of fugacity of each component in each phase is required. The solubility of a condensed ($y_i$) in a vapor phase at supercritical condition is defined as follows (Walas, 1985):

$$y_i = \left(\frac{P_i^{\text{sat}}}{P}\right)\left(\frac{\phi_i^S}{\phi_i^V}\right)\exp\left\{\int_{P_i^{\text{sat}}}^P \frac{v_i^S}{RT}\,dP\right\}. \tag{1}$$

In the derivation of this equation it is assumed that the supercritical solvent does not dissolve in the condensed phase. The saturation pressure of the condensed phase, $P_i^{\text{sat}}$, is usually very small, so that the fugacity coefficient of the condensed phase can be assumed to be $\phi_i^S \sim 1$. If we assume that molar volume of the condensed phase, $v_i^S$, is independent of pressure, Eq. (1) can be converted to the following form:

$$y_i = \left(\frac{P_i^{\text{sat}}}{\phi_i^V P}\right)\exp\left\{\frac{v_i^S(P - P_i^{\text{sat}})}{RT}\right\}. \tag{2}$$

The fugacity coefficient of the condensed phase in the vapor phase, $\phi_i^V$, can be derived from an equation of state through the following expression:

$$RT\ln\phi_i^V = \int_V^\infty\left[\left(\frac{\partial P}{\partial n_i}\right)_{T,V,n_{j\neq i}} - \frac{RT}{V}\right]dV - RT\ln Z, \tag{3}$$

where $Z = Pv/RT$. Three of the equations of state used along with the fugacity coefficients are listed in Table 1. The critical properties of the compounds involved are

Table 1
Various equations of state, mixing rules and their fugacity coefficient

| EOS | Formula and parameters | Mixing rules | Fugacity coefficient |
|---|---|---|---|
| vdW | $P = \dfrac{RT}{v-b} - \dfrac{a}{v^2}$ <br> $a_{ii} = 27R^2 T_{cii}^2/64P_{cii}$ <br> $b_{ii} = RT_{cii}/8P_{cii}$ | $a = \sum_i \sum_j y_i y_j a_{ij}$ <br> $b = \sum_i y_i b_i$ | $\phi_i = \exp\left\{\dfrac{b_i}{v-b} - \ln[z(1-b/v)] - \dfrac{2\sum_j y_j a_{ij}}{RTv}\right\}$ |
| RK | $P = \dfrac{RT}{v-b} - \dfrac{a}{T^{0.5}v(v+b)}$ <br> $a_{ii} = 0.42748R^2 T_{cii}^{2.5}/P_{cii}$ <br> $b_{ii} = 0.08664RT_{cii}/P_{cii}$ | $a = \sum_i \sum_j y_i y_j a_{ij}$ <br> $b = \sum_i y_i b_i$ | $\phi_i = \exp\left\{\dfrac{b_i}{b}(z-1) - \ln[z(1-b/v)]\right.$ <br> $\left. + \dfrac{1}{bRT^{1.5}}\left[\dfrac{ab_i}{b} - 2\sum_j y_j a_{ij}\right]\ln(1+b/v)\right\}$ |
| MMM | $P = \dfrac{RT(v+1.3191b)}{v-b} - \dfrac{a}{T^{0.5}v(v+\sum_i y_i b_{ii})}$ <br> $a_{ii} = 0.48748R^2 T_{cii}^{2.5}/P_{cii}$ <br> $b_{ii} = 0.064662RT_{cii}/P_{cii}$ | $a = \sum_i \sum_j y_i y_j a_{ij}$ <br> $b = (1/4)\left(3\sum_i \sum_j y_i y_j b_{ij} + \sum_i y_i b_{ii}\right)$ | $\phi_i = \exp\left\{2.3191\left[\dfrac{3(2\sum_i y_i b_{ij} - \sum_i \sum_j y_i y_j b_{ij}) + b_{ii}}{4(v-b)} - \ln\left(1-\dfrac{b}{v}\right)\right] - \ln Z\right.$ <br> $\left. + \dfrac{a}{RT^{1.5}\sum_i y_i b_{ii}}\left[\left(\dfrac{b_{ii}}{\sum_i y_i b_{ii}} - \dfrac{2\sum_j y_j a_{ij}}{a}\right)\ln\left(1+\dfrac{\sum_i y_i b_{ii}}{v}\right) - \dfrac{b_{ii}}{v+\sum_i y_i b_{ii}}\right]\right\}$ |

Table 2
Critical properties of compounds used in this study

| Compound | $T_c$ (K) | $P_c$ (bar) | $v^S$(L/mol) | Ref. |
|---|---|---|---|---|
| Carbon dioxide ($CO_2$) | 304.12 | 73.740 | | Ferreira de França, Reber, Meireles, Machado, & Brunner (1999) |
| Ethane ($C_2H_6$) | 305.42 | 48.800 | | Frenkel et al. (1997) |
| Ethylene ($C_2H_4$) | 282.34 | 50.400 | | Frenkel et al. (1997) |
| Nitrous oxide ($N_2O$) | 309.60 | 72.55 | | Ferreira de França et al. (1999) |
| Cholesterol ($C_{27}H_{46}O$) | 778.70 | 12.200 | 0.3624 | Sakaki (1992) |
| $\beta$-Carotene | 801.00 | 8.090 | 0.5368 | Schulz et al. (1991) |

Table 3
Literature survey of solid solubility measurement in supercritical solvent

| Authors | Method to attain equilibrium[a] | Sampling technique[b] | Determination of concentration |
|---|---|---|---|
| *Cholesterol* | | | |
| Chrastil (1982) | Static | Slow flow into a pippet | n.a.[c] |
| Wong and Johnston (1986) | Pure gas circulation | Expansion into a sample loop | Chromatographic |
| Yun et al. (1991) | Pure gas circulation | Expansion into a cold trap | Gravimetric |
| Kosal et al. (1992) | Pure gas circulation | Expansion into a cold trap | Chromatographic |
| Singh et al. (1993) | Pure gas circulation | Expansion into a cold trap | Gravimetric |
| *β-carotene* | | | |
| Chang and Randolph (1989) | Pure gas circulation | Fast expansion into a heated glass | Gravimetric |
| Cygnarowicz et al. (1990) | Gas phase recirculation | Recirculation | UV; on line |
| Sakaki (1992) | Pure gas circulation | Expansion into a sample loop | Chromatographic |
| Skerget et al. (1995) | Static | Expansion into a cold trap[d] | Spectrophotometric |
| Johannsen and Brunner (1997) | Static | Fast expansion into a gas flow leading to GC | Chromatographic |
| Subra et al. (1997) | Gas phase recirculation | Recirculation | Chromatographic; on line |

[a] According to Fornari et al. (1990).
[b] According to Dieter and Schneider (1986).
[c] Not available; information is not given in the reference.
[d] From Johannsen and Brunner (1994).

shown in Table 2. The critical properties of ethane, ethylene, and carbon dioxide were taken from *TRC Thermodynamic Tables-Hydrocarbon*, while those of nitrous oxide were from *TRC Thermodynamic Tables-Non-Hydrocarbon* (Frenkel et al., 1997). The molar volumes of cholesterol and $\beta$-carotene were taken from *CRC Handbook of Chemistry and Physics* (Weast, Astle, & Beyer, 1984). The interpolated sublimation pressure of cholesterol were taken from the paper of Wong and Johnston (1986), while that of $\beta$-carotene was calculated using the correlation developed by Cygnarowicz, Maxwell, and Seider (1990). The experimental data of solubility of cholesterol and $\beta$-carotene in supercritical solvents were taken from literature from various groups of researchers as reported in Table 3. The three equations of state reported in Table 1 are used to predict solubilities of cholesterol and $\beta$-carotene in various supercritical solvents.

## 3. Results and discussion

The solubility of cholesterol in supercritical carbon dioxide as predicted by MMM, RK and vdW equations and compared with the experimental data is shown in

Fig. 3. According to this figure, the MMM equation of state is in good agreement with the experimental data. The solubility of cholesterol calculated using the RK equation is 2–3 orders of magnitude lower than the experimental data, while that calculated using the vdW equation is 4–7 orders of magnitude also lower than the experimental data. In all these calculations, $k_{ij} = 0$ is assumed. As it is also shown in Fig. 3 there is a considerable inconsistency in the experimental data from various sources. The inconsistency could be due to the differences in the experimental techniques employed. All of the investigators used analytical method, but different approaches to attain the equilibrium, sampling techniques to determine concentrations of cholesterol, as shown in Table 3. Chrastil (1982) used the static method to attain the equilibrium and withdrew the sample using a sampling pippet. According to Dohrn and Brunner (1995), withdrawing a large sample from the equilibrium cell in an experiment using the static method could create large pressure drop, which disturb the phase equilibrium significantly. The sampling techniques used by the other authors are the techniques that do not affect the overall composition and without disturbing the equilibrium in the equilibration cell (Dieter & Schneider, 1986).
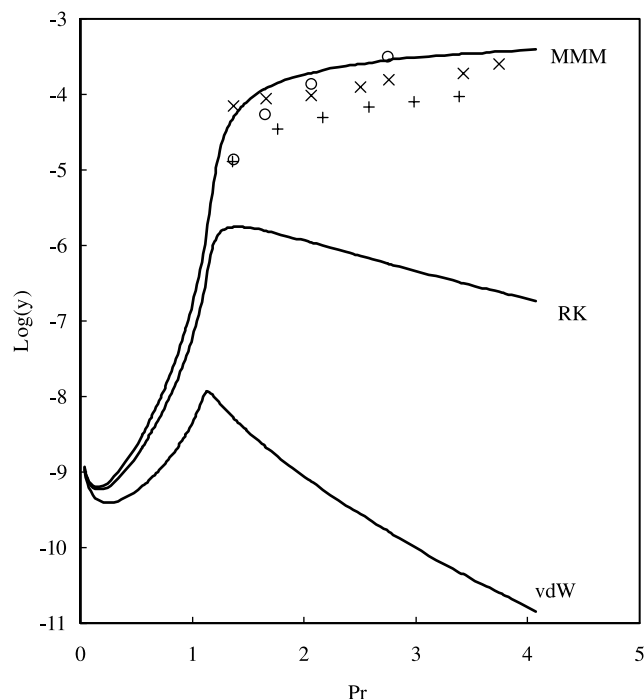
Fig. 3. Solubility of cholesterol in supercritical carbon dioxide at 313 K: (O) Chrastil (1982) data, ($\times$) Wong and Johnston (1986) data, ($+$) Yun et al. (1991) data.. The lines are the results obtained by using various equations of state with $k_{ij} = 0$.



Fig. 4. Solubility of cholesterol in supercritical ethane. The experimental data are taken from Singh et al. (1991): (O) 313 K, ($\times$) 333 K. The lines are the results obtained by using various equations of state with $k_{ij} = 0$.



Fig. 5. Solubility of $\beta$-carotene in supercritical carbon dioxide at 313 K: (O) Cygnarowicz et al. (1990) data, ($\times$) Johannsen and Brunner (1997) data, ($+$) Sakaki (1992) data, ($\Delta$) Skerget et al. (1995) data. The lines are the results obtained by using various equations of state with $k_{ij} = 0$.

The solubility of cholesterol in supercritical ethane as predicted by MMM. RK and vdW equations and compared with experimental data is shown in Fig. 4. According to this figure, the MMM equation of state is in good agreement with the experimental data, even though in this calculation $k_{ij} = 0$. The effect of temperature on the solubility is shown in this figure. The experimental data shows that there is a cross over region. The MMM equation shows the same trend. The RK equation also produces a cross over region, but the solubility prediction of this equation is about two orders of magnitude lower than the experimental data. The vdW equation does not show a cross over region, and its prediction is 4–7 orders of magnitude lower than the experimental data.

The predicted solubility of $\beta$-carotene in supercritical carbon dioxide by various equations along with the experimental data at 313 and 340 K are shown in Figs. 5 and 6, respectively. According to Fig. 6 there is an inconsistency among the reported experimental data. The solubility data of Cygnarowicz et al. (1990) are 1–2 orders of magnitude lower than the other data. The inconsistency also exists between the data obtained by using the same experimental method, i.e. Johannsen and Brunner's data and Skerget's data. The discrepancy could be attributed to the very low solubility of $\beta$-carotene, where accurate measurements become rather sensitive to the methodology (Subra et al., 1997). According to Figs. 5 and 6,
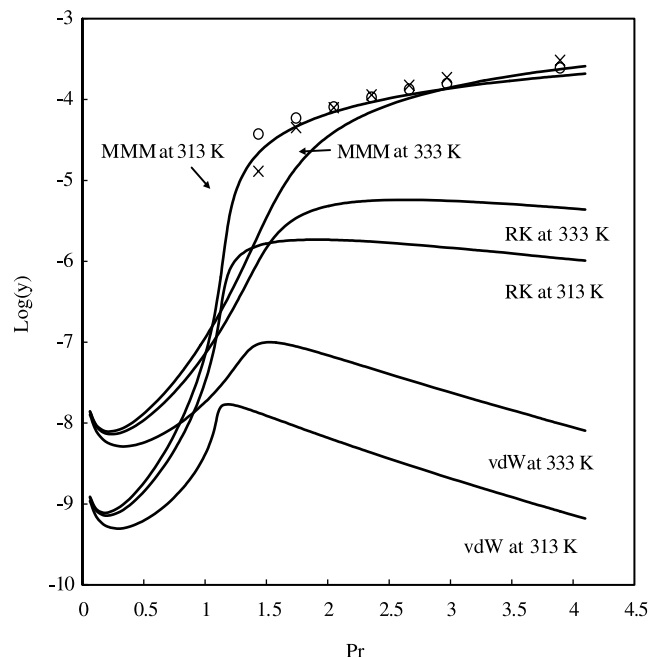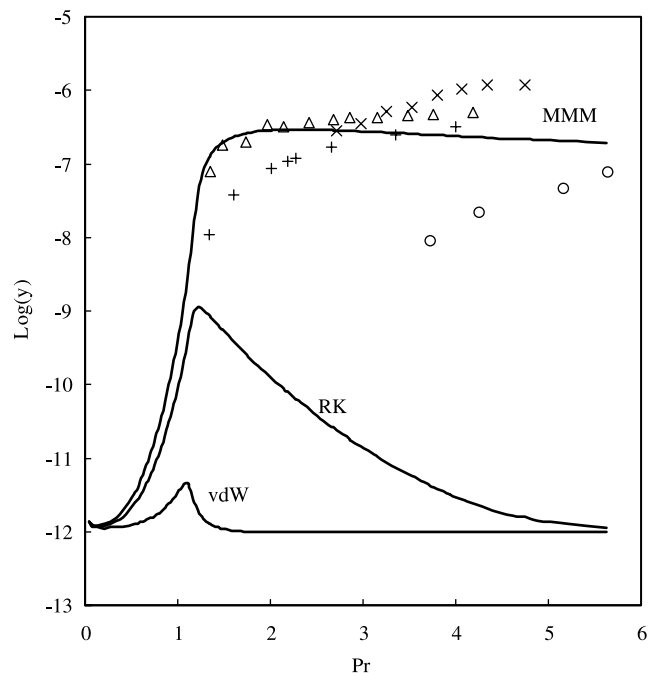
the experimental solubility increases as the pressure increases. The MMM equation prediction is in good agreement with experimental data, while predictions by the
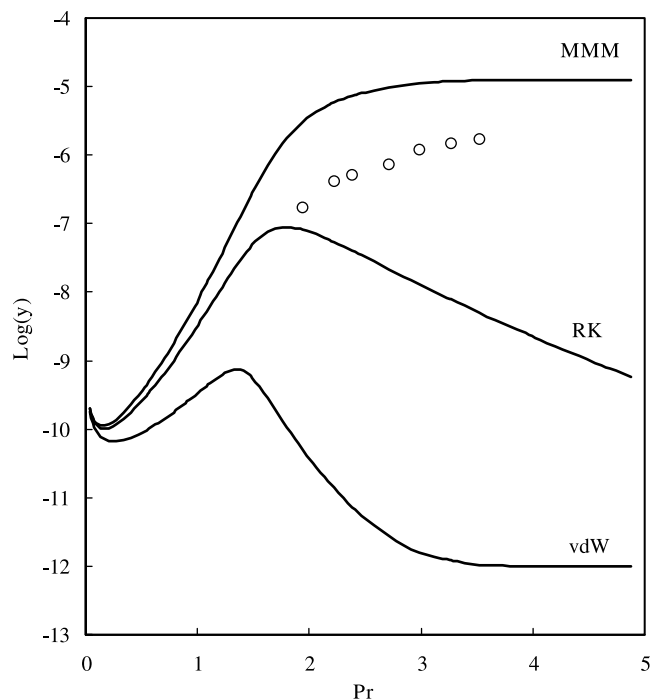
Fig. 6. Solubility of $\beta$-carotene in supercritical carbon dioxide at 340 K. The experimental data (Subra et al., 1997) are given by open circles. The lines are the results obtained by using various equations of state with $k_{ij} = 0$.

vdW and RK equations do not agree with experimental data. In all these calculation, $k_{ij} = 0$ is used.

The solubilities of $\beta$-carotene in supercritical ethylene in 313 and 323 K are shown in Fig. 7. The experimental data shows that there is a cross over region. None of the equations of state show this phenomena when $k_{ij} = 0$ is used in the calculation. However, the MMM equation is much better than the other two equations in predicting the solubility of $\beta$-carotene in supercritical solvents. The MMM equation also has the right trend with pressure variation as the experimental data, while the RK and vdW equations do not. The RK predicted solubility values are 2–5 orders of magnitude lower then the experimental data, while those predicted using the vdW are 5–7 orders of magnitude lower than the experimental data.

The solubilities of $\beta$-carotene in supercritical nitrous oxide are depicted in Fig. 8. It is clear from this figure that the MMM equations of state is in good agreement with the experimental data, while the vdW and RK equations are not. In all these calculation, also $k_{ij} = 0$ is used for the sake of comparison without curve fitting.

The solubility of cholesterol and $\beta$-carotene in supercritical solvents is very small, especially near the critical point of the solvent. Dieter and Schneider (1986) stated that the analytical method could not be applied in the vicinity of the critical points, where the equilibrium is disturbed by sampling. The experimental results of Subra et al. (1997) indicated that the uncertainty of the solu-
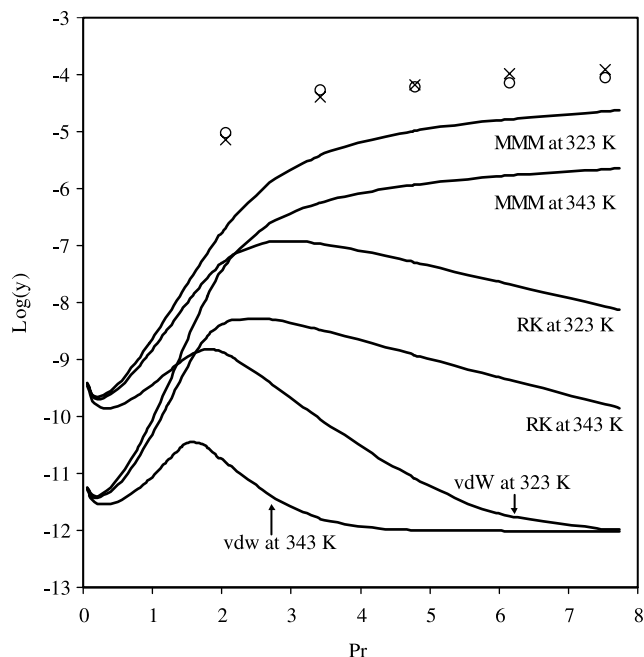


Fig. 7. Solubility of $\beta$-carotene in supercritical ethylene at various temperatures. The experimental data are taken from Chang and Randolph (1989): (O) 323 K, ($\times$) 343 K. The lines are the results obtained by using various equations of state with $k_{ij} = 0$.
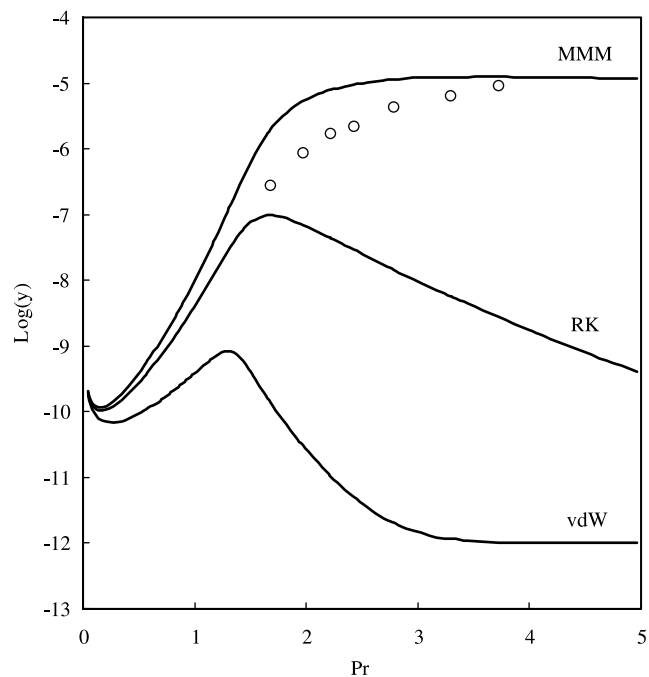


Fig. 8. Solubility of $\beta$-carotene in supercritical in supercritical nitrous oxide at 340 K. The experimental data (Subra et al., 1997) are given by open circles. The lines are the results obtained by using various equations of state with $k_{ij} = 0$.

bility measurements became higher at lower pressures. At pressures close to the critical pressure of the solvent, the solubility of the condensed phase is very low, especially those of $\beta$-carotene. The interaction parameter ($k_{ij}$)
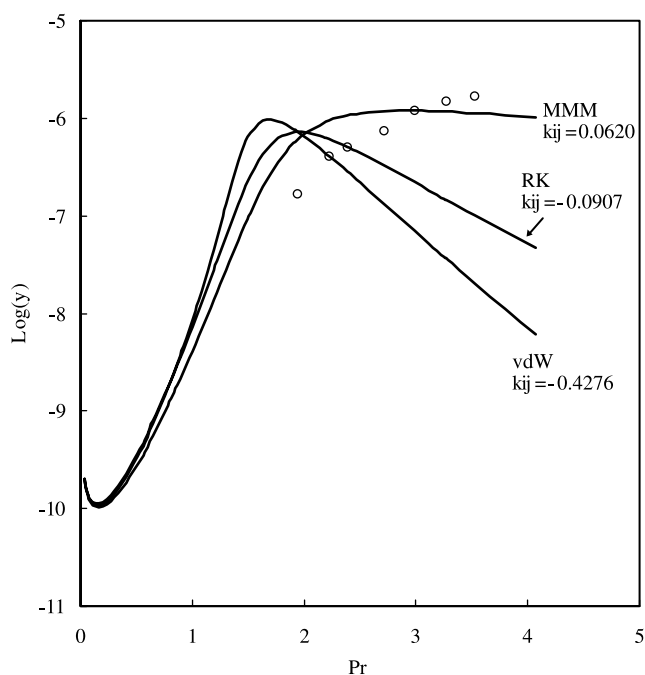
Fig. 9. Solubility of cholesterol in supercritical carbon dioxide at 313 K: (O) are taken from Chrastil (1982), (×) Wong and Johnston (1986), and (+) Yun et al. (1991). The lines are the results obtained by various equations of state with $k_{ij} \neq 0$.
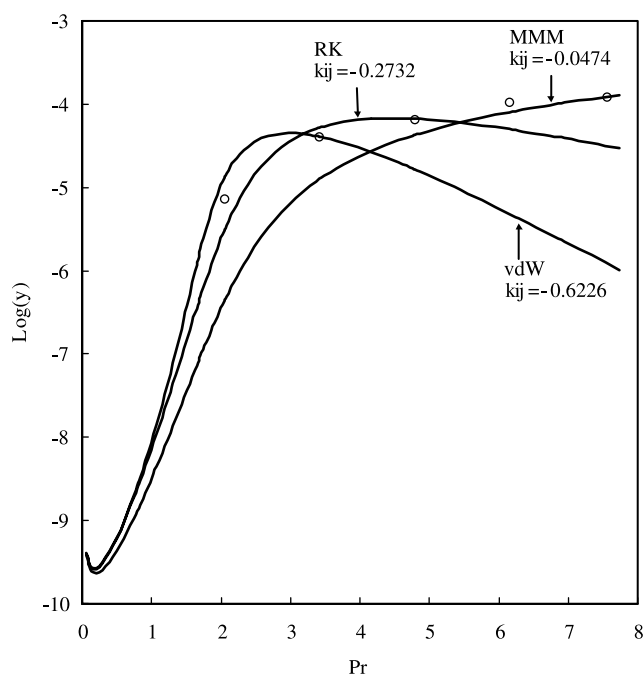


Fig. 10. Solubility of cholesterol in supercritical ethane at 313 K. The experimental data are taken from Singh et al. (1991) and given by open circles. The lines are the results obtained by various equations of state with $k_{ij} \neq 0$.

of each EOS was calculated by minimizing the average deviation (AD) that is defined by

$$\text{AD} = \frac{1}{N} \sum_{i=1}^{N} |y_{2,i}^{\text{calc}} - y_{2,i}^{\text{exp}}|, \qquad (4)$$

where $N$ is the number of experimental data. The results are shown in Table 4. According to this table, the $k_{ij}$ absolute values of the MMM equation are one order of magnitude smaller than those of the other two equations compared. The smaller the absolute value of interaction parameter, the more accurate is the equation of state. The AD of the MMM equation of state is also smaller than those of the other equations. The solubility of cholesterol and $\beta$-carotene in the supercritical solvents calculated using various equations of state with optimized value of $k_{ij}$ is reported in Figs. 9–11 and in Table 4. According to Figs. 9–11 and Table 4 the MMM equations of state predicts the solubilities more accurately than the other equations.

For the sake of comparison of The MMM equation of state to the other well-known equations, i.e. the PR and PT equations, the interaction parameter of the MMM equation of state was then calculated by minimizing the percentage of average absolute deviation (%AAD). The interaction parameters calculated by minimizing the %AAD, along with the %AAD of the PR, PT, and modified PR (MPR) equations of state are shown in Table 5. According to this table, the MMM equation is better than the other equations having one adjustable parameter, i.e.
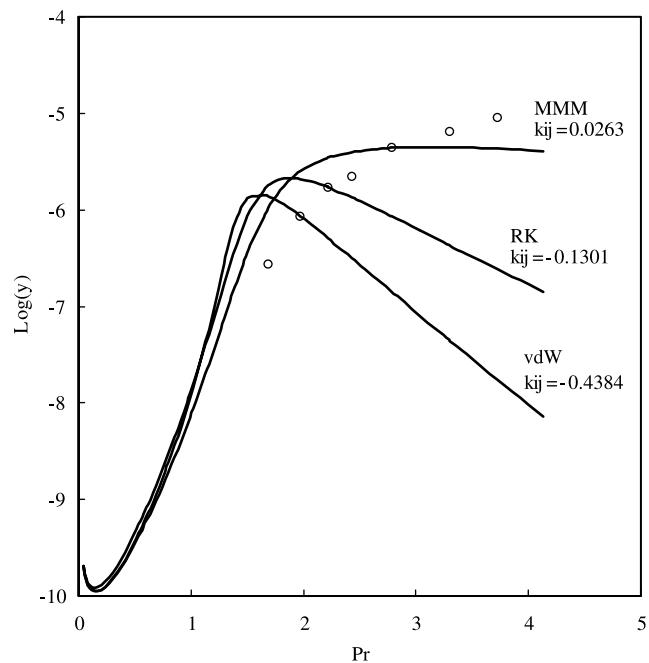


Fig. 11. Solubility of $\beta$-carotene in supercritical carbon dioxide at 340 K. The experimental (Subra et al., 1997) are given by circles. The lines are the results obtained by using various equations of state with $k_{ij} \neq 0$.

the PR and PT equations. The interaction parameter and the %AAD of the MMM are much smaller than those of both equations. The other advantage is that the MMM

Table 4
Interaction parameters and average deviations (AD) of various simple cubic equations of state at different temperatures

| System | $T$ (K) | $k_{12}$ | | | AD | | | No. of data points | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| | | vdW | RK | MMM | vdW | RK | MMM | | |
| $CO_2$ (1)-cholesterol (2) | 308 | −0.4708 | −0.1352 | 0.0416 | $3.01 \times 10^{-5}$ | $2.42 \times 10^{-5}$ | $8.07 \times 10^{-6}$ | 7 | Skerget et al. (1995) |
| | 313 | −0.4910 | −0.1561 | 0.0191 | $8.21 \times 10^{-5}$ | $6.50 \times 10^{-5}$ | $4.42 \times 10^{-5}$ | 17 | Cygnarowicz et al. (1990), Subra et al. (1997), Weast et al. (1984) |
| | 323 | −0.4543 | −0.1389 | 0.0327 | $4.85 \times 10^{-5}$ | $3.25 \times 10^{-5}$ | $7.50 \times 10^{-6}$ | 6 | Weast et al. (1984) |
| | 328 | −0.4586 | −0.1593 | 0.0196 | $1.02 \times 10^{-4}$ | $6.24 \times 10^{-5}$ | $1.02 \times 10^{-5}$ | 7 | Kosal et al. (1992) |
| | 333 | −0.4526 | −0.1430 | 0.0141 | $1.11 \times 10^{-4}$ | $8.18 \times 10^{-5}$ | $5.13 \times 10^{-5}$ | 17 | Cygnarowicz et al. (1990), Kosal et al. (1992), Subra et al. (1997), Weast et al. (1984) |
| $C_2H_6$ (1)-cholesterol (2) | 313 | −0.5142 | −0.1746 | −0.0050 | $5.87 \times 10^{-5}$ | $3.38 \times 10^{-5}$ | $2.88 \times 10^{-6}$ | 8 | Riazi and Mansoori (1993) |
| | 323 | −0.5110 | −0.1804 | −0.0157 | $7.19 \times 10^{-5}$ | $3.85 \times 10^{-5}$ | $5.20 \times 10^{-6}$ | 8 | Riazi and Mansoori (1993) |
| | 333 | −0.4790 | −0.1693 | −0.0172 | $9.23 \times 10^{-5}$ | $4.73 \times 10^{-5}$ | $3.64 \times 10^{-6}$ | 7 | Riazi and Mansoori (1993) |
| $CO_2$ (1)-$\beta$-carotene (2) | 308 | −0.4994 | −0.1418 | −0.0009 | $1.19 \times 10^{-7}$ | $1.18 \times 10^{-7}$ | $6.60 \times 10^{-8}$ | 5 | Park et al. (1987) |
| | 310 | −0.4835 | −0.1293 | 0.0152 | $8.20 \times 10^{-8}$ | $8.07 \times 10^{-8}$ | $4.69 \times 10^{-8}$ | 7 | Mansoori, Schulz, and Martinelli (1988) |
| | 313 | −0.5491 | −0.1930 | 0.0074 | $2.00 \times 10^{-7}$ | $1.86 \times 10^{-7}$ | $1.18 \times 10^{-7}$ | 32 | Dieter and Schneider (1986), Johannsen and Brunner (1997), Park et al. (1987), Sakaki (1992) |
| | 318 | −0.4937 | −0.1303 | 0.0280 | $1.64 \times 10^{-7}$ | $1.59 \times 10^{-7}$ | $1.22 \times 10^{-7}$ | 6 | Park et al. (1987) |
| | 320 | −0.5017 | −0.1383 | 0.0256 | $2.02 \times 10^{-7}$ | $1.89 \times 10^{-7}$ | $8.48 \times 10^{-8}$ | 6 | Mansoori, et al. (1988) |
| | 323 | −0.3949 | −0.1145 | 0.0418 | $2.17 \times 10^{-7}$ | $2.06 \times 10^{-7}$ | $1.38 \times 10^{-7}$ | 7 | Park et al. (1987) |
| | 330 | −0.4708 | −0.1283 | 0.0654 | $2.54 \times 10^{-7}$ | $2.23 \times 10^{-7}$ | $1.22 \times 10^{-7}$ | 7 | Mansoori, et al. (1988) |
| | 333 | −0.5349 | −0.1460 | 0.0616 | $4.56 \times 10^{-7}$ | $4.28 \times 10^{-7}$ | $3.51 \times 10^{-7}$ | 13 | Dieter and Schneider (1986), Johannsen and Brunner (1994) |
| | 340 | −0.4276 | −0.0907 | 0.0620 | $8.10 \times 10^{-7}$ | $7.28 \times 10^{-7}$ | $4.07 \times 10^{-7}$ | 7 | Mansoori, et al. (1988) |
| | 343 | −0.4333 | −0.1032 | 0.0715 | $1.08 \times 10^{-6}$ | $1.07 \times 10^{-6}$ | $8.27 \times 10^{-7}$ | 7 | Dieter and Schneider (1986) |
| | 353 | −0.4266 | −0.0581 | 0.1207 | $1.27 \times 10^{-6}$ | $1.14 \times 10^{-6}$ | $8.30 \times 10^{-7}$ | 7 | Johannsen and Brunner (1997) |
| $C_2H_4$ (1)-$\beta$-carotene (2) | 323 | −0.7625 | −0.3507 | −0.0893 | $4.20 \times 10^{-5}$ | $1.84 \times 10^{-5}$ | $2.04 \times 10^{-5}$ | 5 | Champe and Harvey (1994) |
| | 343 | −0.6227 | −0.2732 | −0.0474 | $5.52 \times 10^{-5}$ | $3.21 \times 10^{-5}$ | $1.67 \times 10^{-5}$ | 5 | Champe and Harvey (1994) |
| $N_2O$ (1)-$\beta$-carotene (2) | 308 | −0.6035 | −0.2711 | −0.0557 | $1.71 \times 10^{-6}$ | $1.59 \times 10^{-6}$ | $8.27 \times 10^{-7}$ | 6 | Park et al. (1987) |
| | 313 | −0.6071 | −0.2269 | −0.0432 | $1.80 \times 10^{-6}$ | $1.73 \times 10^{-6}$ | $9.86 \times 10^{-7}$ | 7 | Park et al. (1987) |
| | 318 | −0.5691 | −0.1987 | −0.0318 | $2.24 \times 10^{-6}$ | $2.16 \times 10^{-6}$ | $1.13 \times 10^{-6}$ | 7 | Park et al. (1987) |
| | 320 | −0.5977 | −0.2175 | −0.0214 | $1.97 \times 10^{-6}$ | $1.79 \times 10^{-6}$ | $8.34 \times 10^{-7}$ | 6 | Mansoori, et al. (1988) |
| | 323 | −0.5615 | −0.1907 | −0.0204 | $2.55 \times 10^{-6}$ | $2.45 \times 10^{-6}$ | $1.38 \times 10^{-6}$ | 7 | Park et al. (1987) |
| | 330 | −0.5315 | −0.1679 | −0.0088 | $3.68 \times 10^{-6}$ | $3.48 \times 10^{-6}$ | $1.47 \times 10^{-6}$ | 6 | Mansoori, et al. (1988) |
| | 340 | −0.4384 | −0.1301 | 0.0263 | $3.43 \times 10^{-6}$ | $3.15 \times 10^{-6}$ | $1.82 \times 10^{-6}$ | 7 | Mansoori, et al. (1988) |

Table 5
Equation of state correlation for ethane–cholesterol binary system

| $T$ (K) | PR[a] | | PT[a] | | MPR[a] | | MMM | |
|---|---|---|---|---|---|---|---|---|
| | Parameter | %AAD[b] | Parameter | %AAD[b] | Parameters | %AAD[b] | Parameter | %AAD[b] |
| 313 | $k_{12}=0.111$ | 20.6 | $k_{12}=0.0862$ | 10.5 | | | $k_{12}=-0.0050$ | 6.0 |
| 323 | $k_{12}=0.113$ | 20.6 | $k_{12}=0.0881$ | 13.9 | | | $k_{12}=-0.0166$ | 11.3 |
| 333 | $k_{12}=0.110$ | 23.2 | $k_{12}=0.0879$ | 17.9 | | | $k_{12}=-0.0172$ | 6.4 |
| 313–333 | | | | | $K_1=-469557$ $K_2=4.1052\times10^8$ $b_2=269.3$ | 5.9 | | |
| Average | | 21.5 | | 13.9 | | 5.9 | | 7.9 |

[a]From Singh et al. (1993).

[b]%AAD is defined as

$$\%\text{Add}=\frac{1}{N}\sum_{i=1}^{N}\left|\frac{y_{2,i}^{\text{calc}}-y_{2,i}^{\text{exp}}}{y_{2,i}^{\text{exp}}}\right|100\%.$$

equation is a two-parameter equation of state, while the PR and PT equations are three-parameter ones. Having only one adjustable parameter, the MMM equation is comparable to the one having three adjustable parameters, i.e. the MPR equation proposed by Singh et al. (1993).

According to all the calculations and comparison presented in this report of the five cubic equations of state, the MMM equation of state is in much better agreement with the experimental data than the other equations of state. Having only two adjustable parameters and one interaction parameter, the prediction by the MMM equation is comparable to the modified PR equation that has four adjustable parameters and two interaction parameters.

## Notation

| | |
|---|---|
| $k_{ij}$ | binary interaction parameter |
| $P$ | pressure, bar |
| $R$ | gas universal constant |
| $T$ | temperature, K |
| $v$ | molar volume, l/mol |
| $y$ | mole fraction |
| $Z$ | compressibility factor |

*Greek letter*

| | |
|---|---|
| $\phi$ | fugacity coefficient |

*Superscripts*

| | |
|---|---|
| $L$ | liquid phase |
| $V$ | vapor phase |
| $S$ | solid phase |
| sat | saturation |

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