SOLUBILITY OF CHOLESTEROL IN SUPERCRITICAL CARBON DIOXIDE

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Supercritical fluid (SCF) extraction offers a good alternative to the current methods of extraction that normally involve the use of organic solvents. To perform this technique it is very important to know the solubility of the drug in the supercritical fluid, usually carbon dioxide.
Several set of solubility data of cholesterol in supercritical CO_2 have been reported in literature: however there is a considerable inconsistency in the experimental results.
In this work, the solubility of cholesterol in supercritical carbon dioxide at 313, 323 and 333 K and at pressures between 110-170 bar has been determined.
The experimental data obtained have been compared with literature data and correlated with the Peng Robinson and the PHSC equations of state.

INTRODUCTION

In human nutrition the role of cholesterol is very important since its amount in the blood can be connected with coronary diseases. Several methods, as for example steam distillation [1, 2], complex formation and/or adsorption [3, 4], and supercritical extraction, have been proposed for the reduction of cholesterol content in dairy products.
Extraction with supercritical carbon dioxide (SF-CO_2) requires high investment but it can be highly selective, without leaving objectionable residues (such as solvents) or suffering the risk of thermal degradation.
Reduction in cholesterol content using SF-CO_2 extraction has been reported for dehydrated meat and chicken samples [5] and for dried and liquid eggs [6, 7]. Furthermore the possibility of producing low-cholesterol milk fat, while maintaining the original color and flavor in the extracted product, with the use of supercritical CO_2 has been suggested [8, 9].
In order to facilitate the development of a commercial-scale SCF extraction plant, solubility data are required. Wong and Johnston [10], Yun et al. [11] and Kosal et al. [12] have already measured the solubility of cholesterol in supercritical CO_2 in the temperature range 308-333 K and at pressures between 100 and 280 bar. However there is considerable inconsistency in these experimental solubility data, obtained by different techniques, and for this reason a new study has been considered necessary.

EXPERIMENTAL SECTION

Materials. The cholesterol used was obtained from Sigma. CO_2 with a purity of 99.9% was supplied by SIAD.
Equipment and procedures. The solubility has been determined using a static method. The used equipment is a variable-volume equilibrium cell with a sapphire window [13] as shown in Fig.1. The total cell volume might vary between 38.84 and 72.32 cm^3. A DELTA OHM HD 9124 digital thermometer (± 0.1°C) checks the temperature inside the cell while a DRUCK DPI 280 pressure transducer (± 0.1 bar) monitors the pressure.

At the beginning of each experiment a weighed amount of cholesterol, about 0.01 grams, is introduced into the cell. Moving the piston in order to have the cell at the minimum volume condition, the CO_2 is slightly flowed inside the opened cell to remove air. After few seconds, the system containing the solution and a small amount of CO_2 is closed by means of an appropriate screw plug.

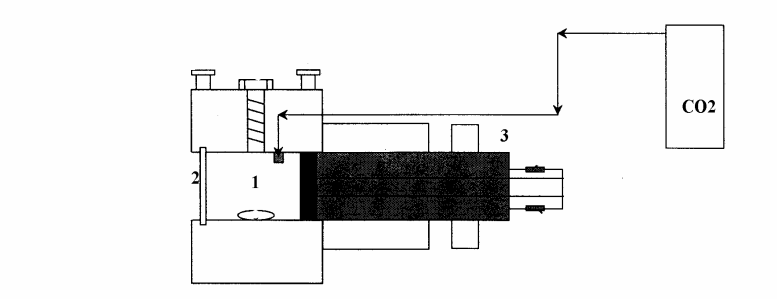

Figure 1. Equilibrium cell (1), window (2), movable piston (3)

The cell is filled with CO_2 and thermostated at the proper working temperature. After closing the CO_2 bottle, the system in the cell is stirred until the pressure and the temperature stabilized. At this point, the piston is moved very slowly in order to increase the total volume and decrease the pressure until the cholesterol starts to precipitate. The system is successively compressed and then expanded again to define the narrowest range of pressure at which the precipitation phenomena occurs. At the end of each experiment the cell is opened by means of a needle valve

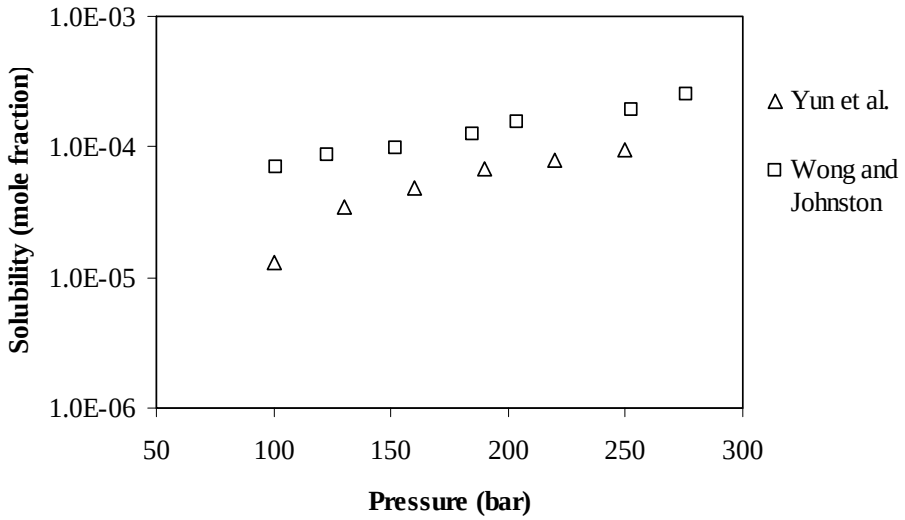

Figure 2. Literature solubility data of cholesterol in supercritical CO_2 at 313 K

and the gaseous carbon dioxide is sent into a calibrated wet gas meter, in order to measure the total amount of gas present and to obtain the global composition of the system. Experiments have been performed at 313, 323 and 333 K and at pressures in the range, 110-170 bar.

RESULTS

Literature solubility data of cholesterol in SF-CO_2 [10, 11], at 313 K, are reported in Fig.2.

The inconsistency between the data can be related to the different experimental techniques used by the authors: Wong and Johnston [10] utilized a microsampling technique while Yun et al. [11] employed a continuous-flow apparatus and the reliability of the data was verified by repeating the experiments at different solvent flow rates.

Fig. 3 reports the solubility experimental data available at 333 K: at this temperature there is less discrepancy between the literature data. The solubility values obtained by Kosal et al. [12] seem to be in good agreement with the ones reported by Wong and Johnston.

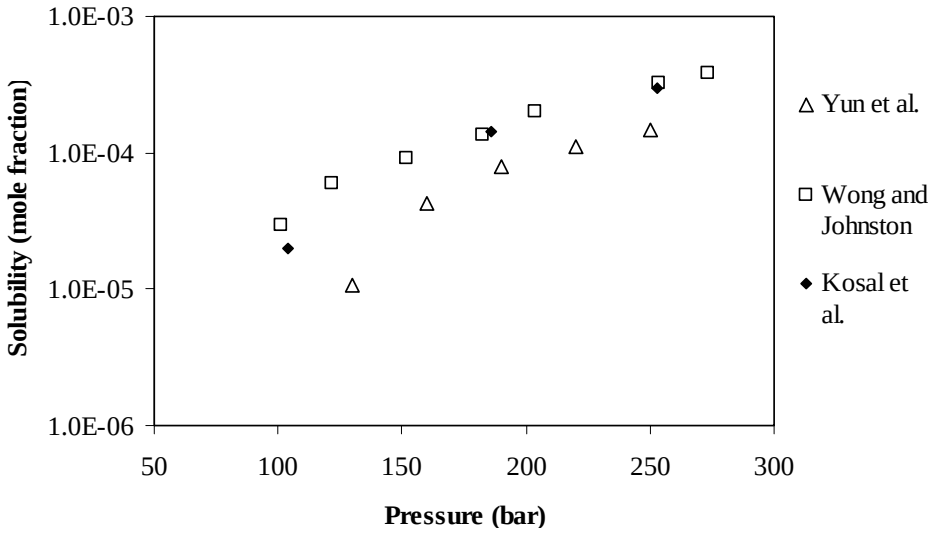

Figure 3. Literature solubility data of cholesterol in supercritical CO_2 at 333 K

The aim of this work was to investigate once more the binary system cholesterol-supercritical carbon dioxide by using the above described experimental technique in order to overcome the incongruities and to find new solubility data values.

The results obtained are presented in Table 1. The results are in good agreement with the data obtained by Yun et al. especially at 323 and 333 K, as shown in Fig. 4. The solubility isotherms show the typical trend for a solid/SCF system with a crossover point located at approximately 160 bar. It is important to consider also that the slope of the solubility isotherm is steeper at 333 than at 313 K. This observable fact has important implication for industrial SF extraction and fractionation processes because the extraction pressure can be highly decreased with an increase in temperature of simply 20 degrees with a strong effect on the economy of the process.

The data obtained in this work, together with the Yun et al. data, have been correlated using Peng Robinson (PR) and PHSC equations of states [14].

For PR model, the melting temperature and heat of fusion of cholesterol must be known together with critical temperature T_c, critical pressure P_c, acentric factor *w* of both pure compounds. The values of melting temperature and heat of fusion used are obtained from literature [15]. The critical parameters can be estimated using group contributions methods: T_c has been estimated by Fedors' method, P_c by Ambrose's method and *w* was calculated using Lee- Kesler equation.

From the fitting, binary interaction parameter k_{ij} and l_{ij} between have been determined, using classical Van der Waals mixing rules. The results of the fitting are reported in Table 2.

	Pressure/bar		
Mole fraction	**313 K**	**323 K**	**333 K**
3.05 E-05	112.9	133.2	143.4
3.32 E-05	113.1	136.2	146.9
4.30E-05	125.8	144.8	152.5
4.85E-05	136.2	149.4	159.6
5.02E-05	144.1	154.3	160.7

Table 1. Solubility of cholesterol in supercritical CO_2

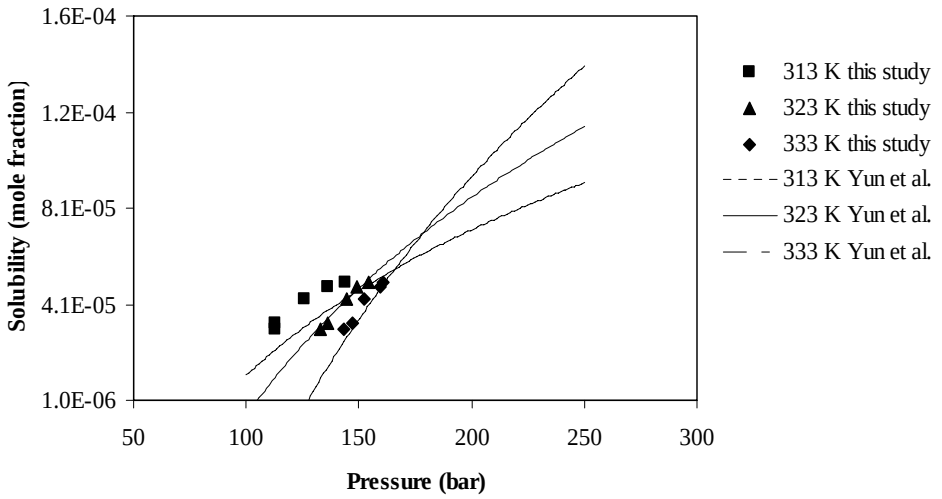

Figure 4. Solubility of cholesterol in SF-CO_2 at 313, 323 and 333 K

PHSC model requires the knowledge of three characteristic parameters, characteristic area, volume and energy, that are calculated by fitting experimental density and vapor pressure data if available. The pure component parameters for cholesterol were calculated using a group contribution method [14] This equation fits the experimental data by means of a unique interaction parameter k_{ij}. In the Tables 3 the result of the fitting with PHSC model is reported.

	T_c	P_c	*w*
CO_2	304.2	73.8	0.224
Cholesterol	971.9	12.8	0.831
k_{ij} parameter	**l_{ij} parameter**	**AAD (%)**	
0.133	0.039	18.82	

Table 2. Parameters and fitting result for PR-EOS.

It's very interesting to note that the PHSC model is able to fit the experimental data, with a deviation comparable to the one obtained with PR-EOS, but using only one fitting parameter.
In Fig. 5 the correlations with the two models, at 323 K, are reported. It appears evident the good agreement between experimental and calculated data.

	A*	V*	E*
CO_2	41.82	16.35	42955
Cholesterol	396.72	284.9	274378
k_{ij} parameter		**AAD (%)**	
0.222		20.68	

Table 3. Parameters and fitting result for PHSC EOS.

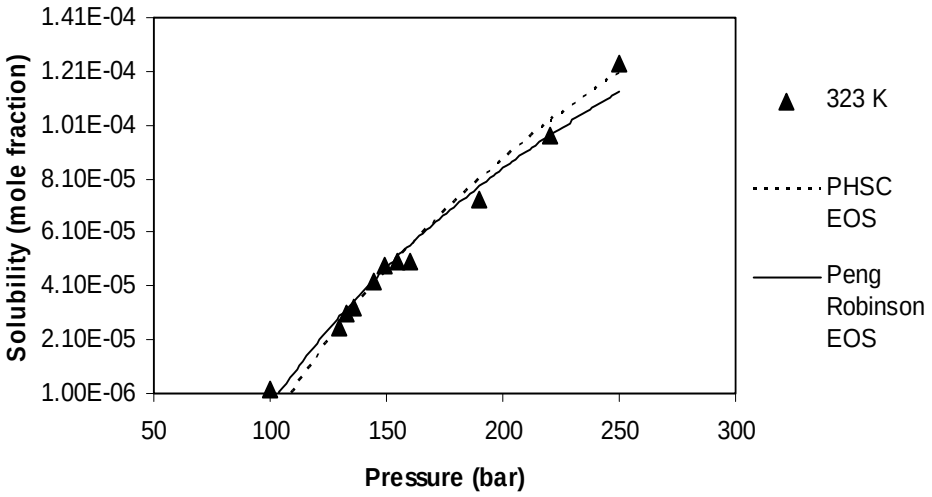

Figure 5. Fitting of experimental data at 323 K.

CONCLUSIONS

The solubility of cholesterol in carbon dioxide at 313, 323 and 333 K has been determined and the results were found to be in good agreement with the literature data published by Yun et al. The fitting of the experimental data has been done using Peng Robinson and PHSC EOS. The second method, by means of a single parameter, is able to fit the experimental data with a standard deviation comparable to the one obtained by PR-EOS.

ACKNOWLEDGEMENTS

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