

## Review Article

# Correlating Solubilities of Some Parabens in Supercritical Carbon Dioxide using Modified Wilson's Model

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Email: chandrasehar@ptunivedu.in**Received:** May 25, 2023**Accepted:** June 24, 2023**Published:** July 01, 2023**Abstract**

Modelling and measuring of solubilities of compounds in supercritical fluids is an important area of research and is gaining significant importance in the recent times. It is being exploited in the particle micronization. Parabens are some of the crucial industrial compounds as their roles in the cosmetics, food, pharmaceutical etc., industries are indispensable. The present work deals with the inception of new model correlations for the solubilities of ethyl, methyl and propyl parabens in Supercritical Carbon Dioxide (ScCO<sub>2</sub>), wherein, the correlation constant's predictions were compared with the existing data reported in the literature [Asghari-Khiavi, M.; Yamini, Y. J. Chem. Eng. Data 48,61-65 (2003); Li, W.; Jin, J.; Tian, G.; Zhan, Z. Fluid Phase Equilib. 264, 93-98 (2008); Cheng, K-W.; Tang, M.; Chen, Y.-P. Fluid Phase Equilib. 201, 79-96 (2002)]. The solubility model used in this work was based on thermodynamic solid-liquid phase equilibrium criteria. In the present model, ScCO<sub>2</sub> was considered as an expanded liquid and the activity coefficient of the solute at infinite dilution is represented with the Wilson's model. Correlation efficacy of the model was evaluated with corrected Akaike's information criterion (AIC<sub>c</sub>). From the correlation results, the present model was able to correlate the data below 6.13%, 7.93% and 4.04% and the corresponding AIC<sub>c</sub> were -793.145, -356.868 and -462.107 for methyl, ethyl and propyl parabens respectively. Further, conventional density model proposed by Chrastil has been evaluated for comparison. The correlation results of Chrastil model were 10.09%, 5.217% and 11.12% and the corresponding AIC<sub>c</sub> were -773.932, -301.787, -526.112 for methyl, ethyl and propyl paraben respectively.

**Keywords:** Chrastil model; Ethylparaben; Methylparaben; Modified Wilson's model; Propylparaben; Solid liquid equilibrium criteria

**Introduction**

Parabens are the esters of para hydroxyl benzoic acids. They are extensively used in pharmaceutical, food, personal hygiene etc., industries as preservative compounds, additives and bacterial and mold growth inhibitors in the cosmetic industry. Methylparaben's industrial usage as an anti-fungal agent in both the personal hygiene and cosmetic industries and as a food preservative (E218) is noticeable. For ethylparaben, its anti-fungal and anti-microbial properties are appreciable along with its usage as a phytoestrogen and as a plant metabolite. In the case of propylparaben, its industrial uses are common as a food preservative and as a preservative, specifically in the water-based cosmetics. It is to be noted that paraben compounds have low solubility in the aqueous phase but they tend to dissolve in a maximum number of systems at temperatures above 333.15 K. At room temperature, the above parabens are solids. Their

utilization, effectively, is managed by controlling the particle's size of the compound. This is generally known as micronization of particles. The process of micronization may be effectively performed with organic solvents or supercritical solvents. The process that utilizes supercritical fluids is known as green process and it is given due importance. In nature we have several supercritical compounds, however, carbon dioxide is increasingly being used and it is represented as ScCO<sub>2</sub>. It has impressive solubility characteristics and distinctive physical properties such as alterable density, non-flammability, low cost for more purity, non-toxicity, inert nature, precise and efficient separation as a green solvent and more. Supercritical solvents dissolve paraben compounds to varying extent depending on pressure and temperature. There is a limited amount of paraben solubility data in ScCO<sub>2</sub> is available in literature and measuring solubility at every

point is a difficult task, therefore, the modelling the solubility data is essential [1-4].

In this work, a new four parameter solubility model based on solid liquid phase equilibrium criteria is evaluated. For comparison, popular Chrastil model [5] is considered and the efficacy of the model is evaluated in terms of corrected Akaike's information criterion (AIC<sub>c</sub>). More details about the models and AIC<sub>c</sub> are presented in the following sections.

**Theory (expanded liquid model)**

According to solid-liquid phase equilibrium criteria, at equilibrium, fugacity of the solute (paraben) in the solid phase is equal to fugacity of solute in the liquid phase. Density of ScCO<sub>2</sub> is close to that of the liquid's density, therefore, the supercritical gas phase can be treated approximately as an expanded liquid. When solubility of ScCO<sub>2</sub> in solid phase is negligible, solubility of solid component in ScCO<sub>2</sub>, at infinite dilution is expressed as [6,7].

$$y_2 = \frac{1}{\gamma_2^\infty} \frac{f_2^S}{f_2^L} \tag{1}$$

Where,  $\gamma_2^\infty$  is the solute's activity coefficient at infinite dilution in ScCO<sub>2</sub>;  $f_2^S/f_2^L$  is the ratio of fugacity of pure solid and liquid, [8].

$$\ln\left(\frac{f_2^S}{f_2^L}\right) = \frac{\Delta H_2^m}{RT} \left(\frac{T}{T_m} - 1\right) - \int_{T_m}^T \frac{1}{RT^2} \left[ \int_{T_m}^T [\Delta C_p] dT \right] dT \tag{2}$$

Where,  $\Delta C_p$  is the net change of heat capacities between the solid and ScCO<sub>2</sub> phases. On substituting eq.(2) in eq.(1) we get, eq (3)

$$y_2 = \frac{1}{\gamma_2^\infty} \exp\left[ \frac{\Delta H_2^m}{R} \left(\frac{T}{T_m} - 1\right) - \int_{T_m}^T \frac{1}{R} \left[ \int_{T_m}^T [\Delta C_p] dT \right] dT \right] \tag{3}$$

The final expression for solubility depends on the activity coefficient and the integral expression in the eq.(3) When the integral term in eq. (3) is neglected and the expression for the solubility is

$$y_2 = \exp\left[ \frac{\Delta H_2^m}{R} \left(\frac{T}{T_m} - 1\right) \right] / \gamma_2^\infty$$

in order to use eq (3), we need an appropriate model for activity coefficient. In this work, a modified Wilson's activity coefficient model is used. The relevant equations are presented as follows [6,7].

$$\ln(\gamma_2^\infty) = 1 - \Lambda_{12} - \ln(\Lambda_{12}) \tag{5}$$

Where,

$$\Lambda_{12} = \frac{v_2}{v_1} \exp\left(-\frac{\lambda_{12}'}{RT}\right) \tag{6}$$

$$\Lambda_{21} = \frac{v_2}{v_1} \exp\left(-\frac{\lambda_{21}'}{RT}\right) \tag{7}$$

$$\Lambda_{12} = v_2 \rho_{c1} \rho_r \exp\left(-\frac{\lambda_{12}'}{T_r}\right) \tag{8}$$

$$\Lambda_{12} = \frac{1}{v_2 \rho_{c1} \rho_r} \exp\left(-\frac{\lambda_{21}'}{T_r}\right) \tag{9}$$

$$\lambda_{12}' = \frac{\lambda_{12}}{RT_{c1}} \text{ and } \lambda_{21}' = \frac{\lambda_{21}}{RT_{c1}}$$

$$v_2 = \alpha \rho_r + \beta \tag{10}$$

$v_1$  and  $v_2$  are molar volumes of the solute and solvent respectively; On combining eqs.(6) to (10), we get

$$\Lambda_{12} = (\alpha \rho_r + \beta) \rho_{c1} \rho_r \exp\left(-\frac{\lambda_{12}'}{T_r}\right) \tag{12}$$

$$\Lambda_{21} = \frac{1}{(\alpha \rho_r + \beta) \rho_{c1} \rho_r} \exp\left(-\frac{\lambda_{21}'}{T_r}\right) \tag{13}$$

$\lambda_{21}'$  and  $\lambda_{12}'$  are the energies of interaction between the molecules respectively. Finally, the expression for dilute activity coefficient is

$$\ln(\gamma_2^\infty) = 1 - (\alpha \rho_r + \beta) \rho_{c1} \rho_r \exp\left(-\frac{\lambda_{12}'}{T_r}\right) - \ln\left(\frac{1}{(\alpha \rho_r + \beta) \rho_{c1} \rho_r} \exp\left(-\frac{\lambda_{21}'}{T_r}\right)\right) \tag{14}$$

Combining eq.(3) and eq.(14) gives an expression for solubility.

$$y_2 = \exp\left[ \frac{\Delta H_2^m}{R} \left(\frac{T}{T_m} - 1\right) \right] / \exp\left[ 1 - (\alpha \rho_r + \beta) \rho_{c1} \rho_r \exp\left(-\frac{\lambda_{12}'}{T_r}\right) - \ln\left(\frac{1}{(\alpha \rho_r + \beta) \rho_{c1} \rho_r} \exp\left(-\frac{\lambda_{21}'}{T_r}\right)\right) \right] \tag{15}$$

Thus eq.(15) is a four parameter model.

**Chrastil Model**

Chrastil [5] has proposed a solubility model based on solvato complex theory which was the first density-based model and it is being used for a variety of solute-solvent systems. Chrastil model is represented according to the following equation in terms of mole fraction

$$y_2 / \text{mole fraction} = \frac{M_{SF}}{M_{Solite}} (\rho_1 / k \cdot m^{-3})^{k-1} \exp\left(A_1 + \frac{B_1}{T/K}\right) \left[ 1 + \frac{M_{SF}}{M_{Solite}} (\rho_1 / k \cdot m^{-3})^{k-1} \exp\left(A_1 + \frac{B_1}{T/K}\right) \right] \tag{15}$$

The model constants in eqs (12), (13) and (14) are estimated with following objective function (OF) eq.(15) [4-9].

$$\theta = \sum_{i=1}^N \frac{|y_{2i}^{\text{exp}} - y_{2i}^{\text{calc}}|}{y_{2i}^{\text{exp}}} \tag{16}$$

The results are reported in terms of average absolute relative deviation percentage (AARD %).

$$\text{AARD}(\%) = \left(100 / N\right) \sum_{i=1}^N \frac{|y_{2i}^{\text{exp}} - y_{2i}^{\text{cal}}|}{y_{2i}^{\text{exp}}} \tag{16}$$

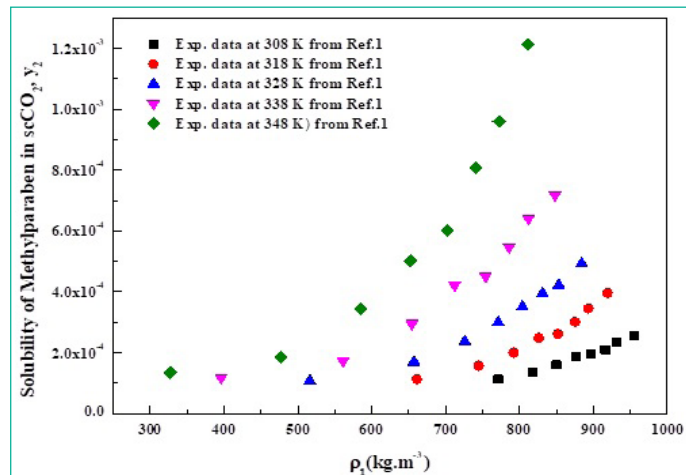
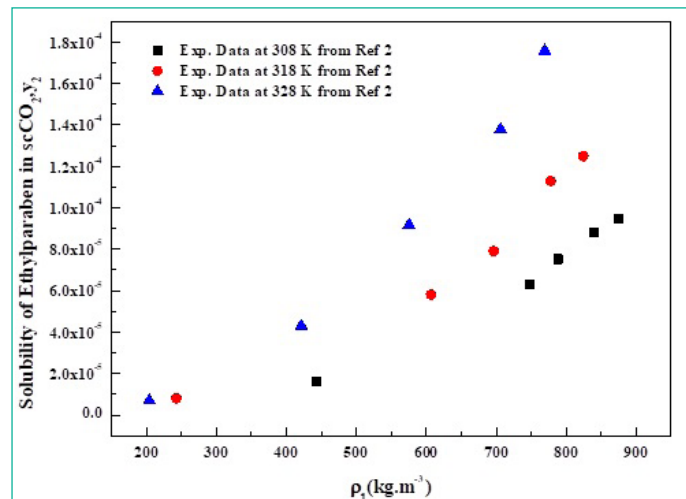
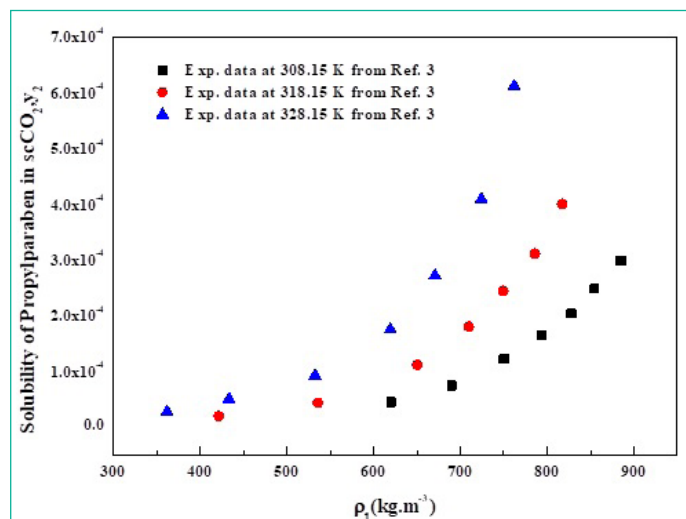
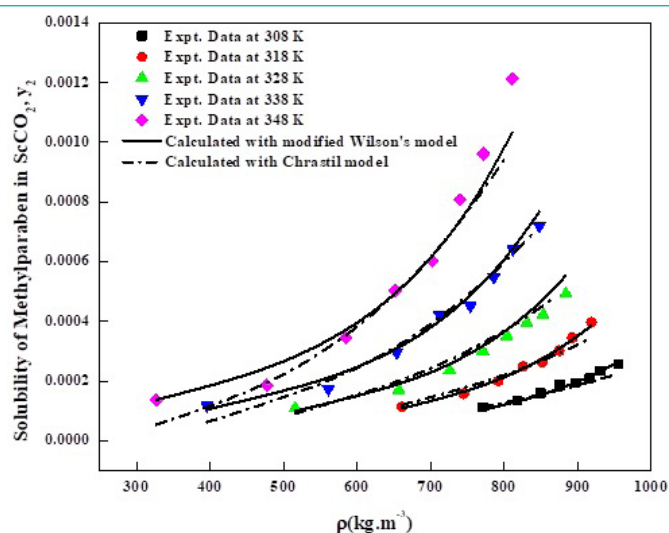
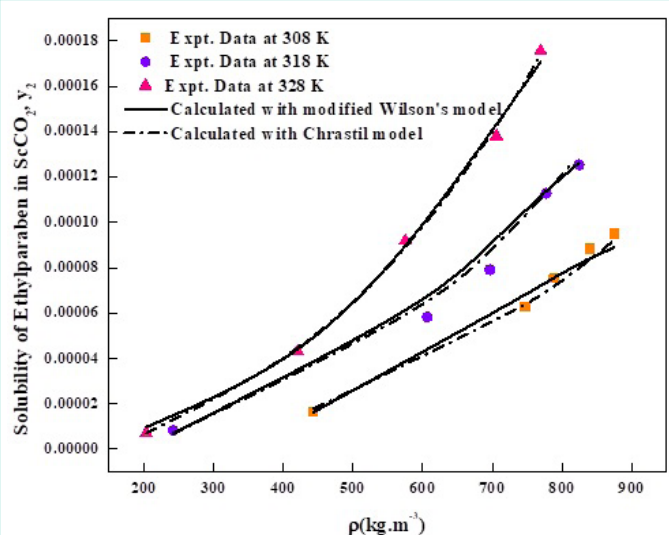
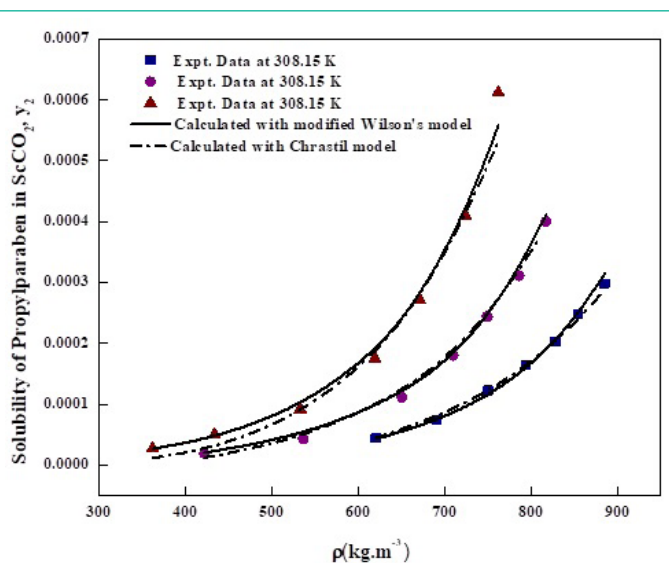
If meltingenthalpy ( $\Delta H_2^m$ ) and melting point ( $T_m$ ) a suitable group contribution method such as Jain et al. [10] may be used. The regression is done with MATLAB's inbuilt fminsearch algorithm.

**Table 1:** Correlation constants of modified Wilson's model and Chrastil model.

Name of the model/Compound	Correlation constants				AARD %
<b>Modified Wilson's model</b>					
	$\alpha$	$\beta$	$\lambda_{12}'$	$\lambda_{21}'$	
Methylparaben	$6.6982 \times 10^{-4}$	$5.0734 \times 10^{-3}$	0.16784	9.3740	6.13
Ethylparaben	$-9.0137 \times 10^{-4}$	$3.7672 \times 10^{-3}$	-1.3686	12.746	7.93
Propylparaben	$-6.6627 \times 10^{-4}$	$1.5332 \times 10^{-2}$	0.41238	11.172	4.04
<b>Chrastil model</b>					
	$k$	$C_1$	$C_2$		
Methylparaben	<b>3.877</b>	-10.15752	-5170.3		10.09
Ethylparaben	<b>3.3749</b>	-8.5741	-4770.5		5.217
Propylparaben	<b>5.5618</b>	-14.791	-7099.6		11.12

**Table 2:** Statistical parameters of modified Wilson's model and Chrastil model.

Model/Compound	SSE	AIC	AIC <sub>c</sub>
<b>Modified Wilson's model</b>			
Methylparaben	$8.28 \times 10^{-8}$	-794	-793.145
Ethylparaben	$4.04 \times 10^{-10}$	-359	-356.868
Propylparaben	$4.09 \times 10^{-9}$	-464	-462.107
<b>Chrastil model</b>			
Methylparaben	$1.34 \times 10^{-7}$	-775	-773.932
Ethylparaben	$1.59 \times 10^{-8}$	-304	-301.787
Propylparaben	$1.94 \times 10^{-10}$	-528	-526.112

**Figure 1:** Solubility of Methylparaben in ScCO<sub>2</sub> [1].**Figure 2:** Solubility of Ethylparaben in ScCO<sub>2</sub> [2].**Figure 3:** Solubility of Propylparaben in ScCO<sub>2</sub> [3].**Figure 4:** Solubility of Methylparaben vs ScCO<sub>2</sub> density. Symbols indicate experimental data at different temperatures obtained from literature. Solid lines are calculated modified Wilson's model. Dash-dot lines are calculated Chrastil model.**Figure 5:** Solubility of Ethylparaben vs ScCO<sub>2</sub> density. Symbols indicate experimental data at different temperatures obtained from literature. Solid lines are calculated modified Wilson's model. Dash-dot lines are calculated Chrastil model.**Figure 6:** Solubility of Propylparaben vs ScCO<sub>2</sub> density. Symbols indicate experimental data at different temperatures obtained from literature. Solid lines are calculated modified Wilson's model. Dash-dot lines are calculated Chrastil model.

## Results and Discussion

For modelling, the available solubility data of methyl (at 308, 318, 328 and 338 K), ethyl (at 308, 318 and 328 K) and propyl (at 308, 318 and 328 K) parabens are considered from the literature (Chen et al. [1], Asghari Khiavi and Yamini [2] and Li et al. [3]). Figure 1, 2 and 3 show the solubility data of the parabens. The experimental data are modelled with modified Wilson's model and Chrastil model. The correlation results along with the statistical parameters are reported in Table 2. Figures (4) to (6) indicate the correlating ability of the models. From the tables and figures, it is clear that modified Wilson's model is able to correlate the data better. The success of modified Wilson's model may be attributed to its number of parameters. The statistical methodology is applied to know the best model. Since our experimental data set was less (less than 40 data points), we have considered the corrected Akaike's information criterion (AIC), and it is known as  $AIC_c$  [8,9]. The following expression denotes  $AIC_c$

$$AIC_c = AIC + \frac{2Q(Q+1)}{N-Q-1} \quad (17)$$

Where

$$AIC = N \ln(\sigma^2) + 2Q \quad (18)$$

In eqs.(17) and (18),  $\sigma$ ,  $N$  and  $Q$  represent the variance of deviations, number of observations, and model parameters, respectively. The calculated  $AIC_c$  values are shown in Table 1. From the  $AIC_c$  values, we can conclude that whichever the model is having the least value is the better model. From table 2 modified Wilson's model is observed to be better for the 3 paraben compounds.

## Conclusion

In this study, the new correlations for the solubility of the paraben compounds in  $ScCO_2$  are reported. The models used are modified Wilson's model and Chrastil model. Akaike's information criteria revealed that the modified Wilson's model shows better correlating ability than the Chrastil model.

## References

1. Cheng KW, Tang M, Chen YP, Solubilities of benzoin, propyl 4-hydroxybenzoate and mandelic acid in supercritical carbon dioxide. *Fluid Phase Equilib.* 2002; 201: 79–96.
2. Asghari-Khiavi M, Yamini Y, Solubility of the drugs bisacodyl, methimazole, methylparaben, and iodoquinol in supercritical carbon dioxide. *J Chem Eng Data.* 2003; 48: 61–65.
3. Li W, Jin J, Tian G, Zhan Z. Single-component and mixture solubilities of ethyl p-hydroxybenzoate and ethyl p-aminobenzoate in supercritical CO<sub>2</sub>. *Fluid Phase Equilib.* 2008; 264: 93–98.
4. Mahesh G, Garlapati C. Modelling of solubility of some parabens in supercritical carbon dioxide and new correlations. *Arab J Sci Eng.* 2021; 47: 5533-5545.
5. Chrastil J. Solubility of solids and liquids in supercritical gases. *J Phy Chem.* 1982; 86: 3016-3021.
6. Nasri L. Modified Wilson's model for correlating solubilities in supercritical fluids of some polycyclic aromatic solutes. *Polycycl Aromat Compd.* 2018; 38: 244-256.
7. Sodeifian G, Garlapati C, Nooshabadi MA, Razmimanesh, F, Tabibzadeh A. Solubility measurement and modeling of hydroxychloroquine sulfate (antimalarial medication) in supercritical carbon dioxide, *Scientific Reports.* 2023; 13: 8112.
8. Sodeifian G, Garlapati C, Razmimanesh F, Sodeifian F, Solubility of Amlodipine Besylate (Calcium Channel Blocker Drug) in Supercritical Carbon Dioxide: Measurement and Correlations. *J Chem Eng Data.* 2021; 66: 1119-1131.
9. Sodeifian G, Garlapati C, Razmimanesh F, Nateghi H, Experimental solubility and thermodynamic modeling of empagliflozin in supercritical carbon dioxide. *Scientific Reports.* 2022; 12: 9008.
10. Jain A, Yang G, Yalkowsky SH. Estimation of melting points of organic compounds. *Ind Eng Chem Res.* 2004; 43: 7618-7621.