

## Modelling of liquid-solid equilibria and determination of a new group interaction parameters for unifac method

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### **Abstract**

The objective of this study is to predict solid-liquid equilibria by means of the UNIFAC model for systems containing certain groups like (AC-Cl) and (CHO) for which the interaction parameters are not available. The model is tested on four systems such as (Hexachlorobenzene – dibutylether), (Hexachlorobenzene – MTBE), (Chloro benzoic acid – diisopropylether) and (Chloro benzoic acid – dibutylether). The agreement between the predicted results and the experimental values was very encouraging. The obtained interaction parameters will be further test on other systems.

**Keywords :** Solid-Liquid equilibria, UNIFAC, group interaction parameters.

### **Résumé**

L'objectif de ce travail est de prédire les équilibres solide-liquide en utilisant le modèle UNIFAC pour des systèmes contenant des groupes tels que (AC-Cl) et (CHO) dont les paramètres d'interaction pour ce modèle ne sont pas disponibles. Le modèle a été testé pour quatre systèmes (Hexachlorobenzène – dibutyléthère), (Hexachlorobenzène – MTBE), (4-Chlorobenzoïque acide – diisopropyléthère) et (4-Chlorobenzoïque acide - dibutylether). La déviation entre les résultats calculés et les valeurs expérimentales est assez encourageante et les paramètres interaction obtenus seront testés en considérant d'autres systèmes.

**Mot Clé :** équilibre Solide - Liquide, UNIFAC, paramètres d'interaction de groupe.

### **1. Introduction**

Thermodynamic models are increasingly used by the pharmaceutical industry at different stages of the product and process development and optimization processes. At the product development and formulation stage, various solvents are screened for new pharmaceutical molecules. At the later stage of process development and optimization, appropriate selection of a solvent or a mixture of solvents is critical for the crystallization and other processes. Most of the pharmaceutical molecules are significantly more complex than molecules encountered in oil and chemical industry, with multiple functional polar and hydrogen bonding groups. At the same time, experimental physical property data for most of the pharmaceutical molecules of interest are substantially more limited than data for hydrocarbons and other compounds relevant to oil and gas industries. Generally the solubility of pharmaceutical compounds in various solvents is a key parameter. Its measuring is not always easy and may also be an arduous task when several systems are to be tested. Consequently in this work, the modeling of the solubility of Hexachlorobenzene and 4-chlorobenzoic acid reported in the literature [1] and [2] was carried out using the group contribution method UNIFAC (UNIversal Functional group Activity Coefficients) [3]

## 2. Methodology

### 2.1 Thermodynamics of Solid – Liquid equilibrium

Similarly to other phase Equilibria, the required thermodynamic relations for solid –liquid can be derived starting from the isofugacity criterion [4]:

$$f_i^s = f_i^l \quad (1)$$

Where  $s$  refers to solid state and  $l$  to the liquid state. The fugacity of the solute in the liquid phase may be expressed as [5]:

$$f_i^l = x_i^l \gamma_i^l f_i^{\circ l} \quad (2)$$

With  $f_i^{\circ l}$  representing the fugacity of the pure solute in a subcooled liquid state below its melting point. When the solvent does not enter the solid phase, the fugacity of the solid solute remains that of pure solid:

$$f_i^s = f_i^{\circ s} \quad (3)$$

Using Eq. (1), the solubility of the solute  $i$  in the liquid phase can be calculated by:

$$x_i^l \gamma_i^l = \frac{f_i^{\circ s}}{f_i^{\circ l}} \quad (4)$$

An expression for the ratio of the standard fugacities can be obtained via a thermodynamic cycle and after some justified simplifications (Gmehling and al, 1992), as follows:

$$\ln \frac{f_i^{\circ s}}{f_i^{\circ l}} = \frac{\Delta H_m}{R} \left( \frac{1}{T_m} - \frac{1}{T} \right) \quad (5)$$

With the subscript  $m$  denoting the melting point.

Substituting Eqn. 4 into 5 gives:

$$\ln(x_i^l \gamma_i^l) = \frac{\Delta H_m}{R} \left( \frac{1}{T_m} - \frac{1}{T} \right) \quad (6)$$

And hence the solubility  $x_i^l$  of a solute in a solvent or solvent mixture which is expressed as:

$$x_i^l = \frac{\exp\left[\frac{\Delta H_m}{R} \left( \frac{1}{T_m} - \frac{1}{T} \right)\right]}{\gamma_i^l} \quad (7)$$

For the determination of the solubility, knowing the melting point  $T_m$  and the heat of fusion  $\Delta H_m$  the only required parameter is the activity coefficient of component  $i$ . While the pure component data can directly be read from the Dortmund Data Bank (DDBST) [5], which presents one of the most reliable data banks for pure component and mixture properties. The activity coefficient  $\gamma_i$  can be calculated by means of thermodynamic models.

### 2.2 Modeling section

UNIFAC is based on the group contribution concept, which assumes that a mixture does not consist of molecules but of functional groups. This reliable and fast technique is described in detail by Fredenslund et al (1977) [3]. According to this model the activity coefficient is expressed as follows:

$$\ln \gamma_i = \ln \gamma_i^C + \ln \gamma_i^R \quad (8)$$

The first term  $\ln \gamma_i^C$  concerns the combinatorial part and takes into account the differences in sizes and shapes of the molecules. It can be calculated using van der Waals volumes  $R_k$  and surface areas  $Q_k$  of the functional groups. The second term  $\ln \gamma_i^R$  is the residual part which takes into account the intermolecular forces. The determination of these two contributions requires the knowledge of volume ( $R_k$ ) and surface area ( $Q_k$ ) group parameters as well as binary interaction parameters ( $a_{mn}$ ) which may or may not be available in the corresponding tables reported in the literature base [6].

### 2.3 Estimated interaction parameters procedure

The binary group interaction parameters involving ACCL group with ether groups, required for the UNIFAC model were retrieved in the present work using the Nelder-Mead method [14] for the minimization of the following objective function ( $F_{obj}$ ) defined as the sum of the squared deviations between the experimental and calculated mole fractions:

$$F_{obj} = \sum_{i=1}^N (x_{i(exp)} - x_{i(cal)})^2 \quad (9)$$

with N denoting the number of data points.

### 3. Results and discussion:

Table 1 shows the solubility data results obtained by means of UNIFAC equation and the experimental data reported by Acree Jr (2013) for the considered systems presented in this work, which are assessed by calculating the average absolute relative deviation (AARD) defined as follows:

$$AARD = \frac{1}{n} \sum_{i=1}^n \left| \frac{x_{i(exp)} - x_{i(cal)}}{x_{i(exp)}} \right| \quad (10)$$

Where  $n$  is the number of experimental points;  $x_{i(cal)}$  is the solubility calculated using UNIFAC equation;  $x_{i(exp)}$  is the experimental solubility reported in literature. This comparison is also shown by Figures 1 where clearly the predicted results using UNIFAC model are in very good agreement with the experimental values.

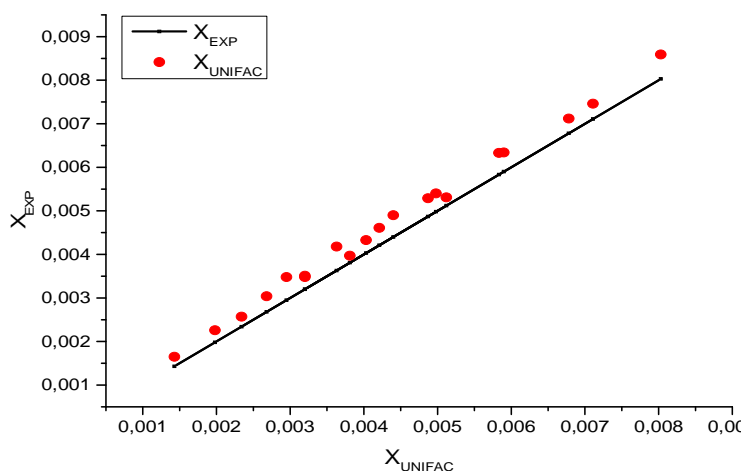


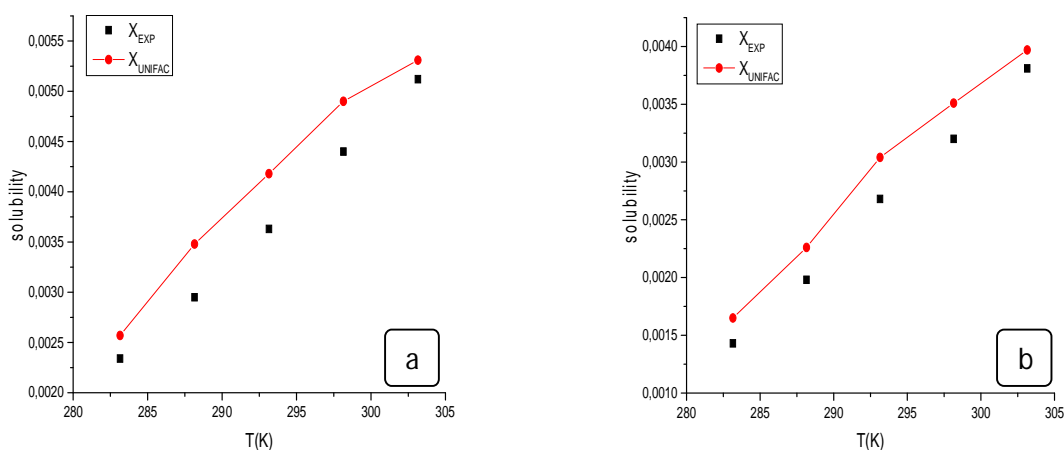
Figure 1: Assessment of UNIFAC model.

**Table 1:** Comparison of experimental and calculated solubilities.

SOLUTE	SOLVENT	T(K)	X <sub>EXP</sub>	X <sub>UNIFAC</sub>	AARD (%)
Hexachlorobenzene	Dibutylether	283.15	0.00234	0.00257	9.8290
		288.15	0.00295	0.00348	17.9661
		293.15	0.00363	0.00418	15.1515
		298.15	0.0044	0.0049	11.3636
		303.15	0.00512	0.00531	3.7109
Hexachlorobenzene	MTBE	283.15	0.00143	0.00165	15.3846
		288.15	0.00198	0.00226	14.1414
		293.15	0.00268	0.00304	13.4328
		298.15	0.0032	0.00351	9.6875
		303.15	0.00381	0.00397	4.1994
4-chlorobenzoic acid	disopropylether	283.15	0.00421	0.00461	9.5011
		288.15	0.00498	0.0054	8.4337
		293.15	0.0059	0.00634	7.4576
		298.15	0.00678	0.00712	5.0147
		303.15	0.00803	0.00859	6.9738
4-chlorobenzoic acid	Dibutylether	283.15	0.0032	0.00348	8.75
		288.15	0.00403	0.00433	7.4441
		293.15	0.00487	0.00529	8.6242
		298.15	0.005833	0.00633	8.5204
		303.15	0.00711	0.00746	4.9226

The estimated interaction parameters of (ACCl /CH<sub>2</sub>O) and 1 (CH<sub>2</sub>O / ACCl) were 2273.81 and 3031.74, respectively and their use led to solubility results in a quite good agreement with the data reported in the literature

For a better representation of solid-liquid phase equilibrium, the corresponding diagrams are shown for chosen systems. Figures 2(a & b) and 3(a & b) show the comparisons of the obtained results by means of UNIFAC model with the experimental values. UNIFAC results were in a very good agreement with the experimental values.



**Figure 2:** Solid-liquid equilibrium for Hexachlorobenzene in a)Dibutylether and b) MTBE

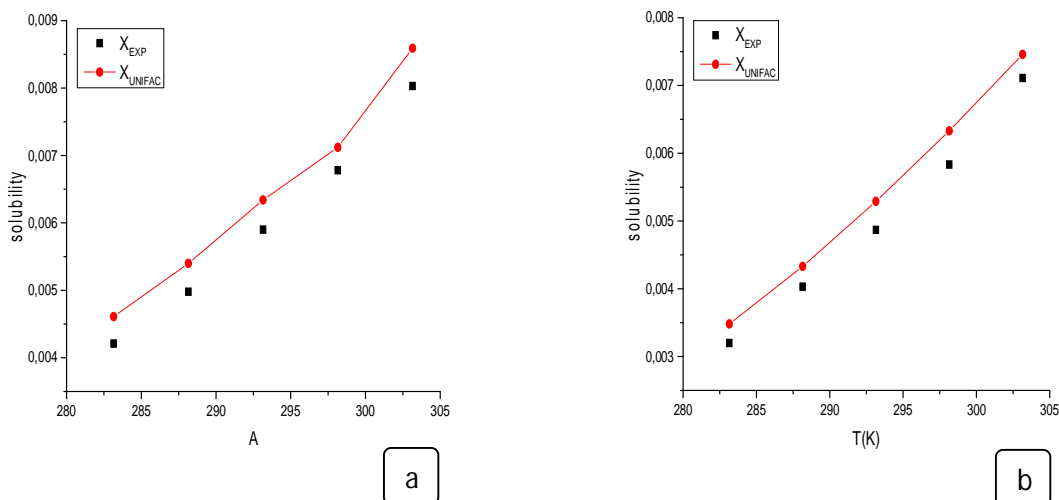


Figure 3: Solid-liquid equilibrium for 4-Chlorobenzoic acid in a) Diisopropylether and b) Dibutylether

#### 4. Conclusion :

The present study has clearly demonstrated the importance of modeling solid-liquid phase equilibria, particularly for sensitive industrial fields like pharmaceuticals. However, the influence of the molecular structure decomposition into groups, on the accuracy of activity models like the UNIFAC has also been showed. Globally the models using molecular interaction parameters led to more accurate results compared to models using group interaction parameters like the UNIFAC. This is perhaps due to the fact that any group contribution approach is assumed approximately to be additive.

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