Modeling Solubilities of Sugars in Alcohols Based on Original Experimental Data

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Solubility of six different carbohydrates in methanol, ethanol, 1-propanol, and 2-propanol were measured at 22, 30, and 40°C. Ketose sugars (fructose, tagatose, and lactulose) show higher solubilities than aldoses (glucose, galactose, and lactose). The binary solid–liquid equilibrium data obtained was satisfactory represented by using the A-UNIFAC model. Additionally, the capability of the model to predict the carbohydrate solubility in alcohol–alcohol and alcohol–water mixed solvents was explored. © 2007 American Institute of Chemical Engineers *AIChE J,* 53: 2411–2418, 2007
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Introduction

Carbohydrates have a wide range of applications in a variety of industries (textile, plastics, food, pharmaceutical, etc.) and are also used in biological applications. Particularly, since the introduction of the prebiotic concept as a nondigestible oligosaccharide that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon,[1] an increased interest in the use of carbohydrates for manipulating the intestinal microflora composition, in order to improve the activity of the gastrointestinal tract, has been observed.[2–5]

Tagatose and lactulose (4-*O*-*β*-D-galactopyranosyl-D-fructose) are considered as prebiotic carbohydrates and can be used in a wide variety of functional foods and dietary supplements as well as in medicine.[6–8] Both carbohydrates are ketoses and are currently produced by alkaline isomerization of the corresponding aldose,[6–9] i.e. galactose and lactose, respectively. The biological manufacture of tagatose from galactose[10] and lactulose from lactose[11] has also been studied and although considerable levels and purity of the corresponding ketose have been reported, the main difficulty in the production process is its separation from the unreacted aldose.

Water–alcohol and alcohol–alcohol solvents can be used in the isolation, by precipitation, of expensive sugars in mixture with other sugars. To study and develop industrial processes related to this kind of systems, both experimental solubility data and accurate thermodynamic modeling are required.

Solubility data for different sugars in water have been measured and published since the late years of the 19th century.[12] Additionally, the solubility of common sugars (glucose, fructose, lactose, and sucrose) in methanol–water and ethanol–water mixtures is also available in the literature.[13–17] Earlier studies on the solubility of lactose and lactulose in alcohols at room temperature and water contents up to 5%[18] showed that the solubility of lactulose is higher than that of lactose.

This article presents an extensive experimental study on the solubility of different aldoses (glucose, galactose, and lactose) and ketoses (fructose, tagatose, and lactulose) in four different alcohols (methanol, ethanol, isopropanol, and 1-propanol) at 22, 30, and 40°C. A total of 72 solubility data points are reported.

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Several authors[19–21] have applied different UNIFAC-based[22] methods to represent sugar solubilities in aqueous and alcoholic mixtures. Generally, the modifications studied include different combinatorial and residual terms, but the version presented by Ferreira et al.,[23] the A-UNIFAC model, takes into consideration association effects between carbohydrates, water, and alcohols by introducing a specific term in the original UNIFAC equation based on Wertheim associating theory.[24] Thus, this model was preferred to represent the extensive binary solubility data measured in this work, and to explore its capability to predict the sugar solubility in ternary sugar–alcohol–alcohol and sugar–alcohol–water mixtures.

Materials and Methods

Samples and reagents

Tagatose (D-(−)-tagatose minimum 99%), fructose (D(−)-fructose 99+%), glucose (D-(+)-glucose, ACS reagent), lactulose employed in solubility analysis, internal standard (phenyl-β-glucoside), methanol, and two derivatizing reagents (*N*-trimethylsylilimidazole and chlorotrimethylsilane redistilled) were obtained from Sigma (St. Louis, MO). Galactose (D(+) galactose for bacteriology) and the other derivatizing agent, dried pyridine, were supplied by Merck (Darmstadt, Germany). Lactose (mono-hydrate pure), molecular sieve (3 Å, pearl shaped 2–3 mm), 1-propanol extra pure, and 2-propanol extra pure were purchased from Scharlau Chemie S.A. (Barcelona, Spain). Ethanol absolute was from Prolabo (Fontenay sous Bois, France). Hexane (purex analytical grade) used during derivatization was supplied by Carlo Erba Reagenti (Limito, Italy). Ultrapure water quality (18.2 MΩ cm) with 1–5 ppb total organic carbon (TOC) and <0.001 EU/mL pyrogen levels (Milli-Q) was produced in-house using a laboratory water purification Milli-Q Synthesis A10 system (Millipore, Bellerica, MA) and was used throughout.

Solubility measurements

Solubility of lactose, lactulose, galactose, tagatose, glucose, and fructose in methanol, ethanol, 1-propanol, and 2-propanol at 22, 30, and 40°C were determined. For this purpose, a slight excess of each carbohydrate—with respect of its expected solubility limit—was weighed, respectively, in an analytical balance AB-104 (Mettler Toledo, OH) with a 0.1-mg precision. Then, 5 mL of methanol, ethanol, 1-propanol, and 2-propanol (every alcohol with molecular sieve) were added to the different vials containing carbohydrates and sealed. The accuracy of the temperature measurements was ±0.1°C.

Vials were stirred in an incubation shaker (Type AT200 Multitron HT Infors AG, Bottmingen-Basel, Switzerland) at 150 rpm at constant temperature (22, 30, and 40°C, respectively) for 48 h. Then, the solution was allowed to stand at constant temperature (Typ VTR 5036 Heraeus Holding GMBH, Hanau, Germany) for about 24 h to enable any finely dispersed solids to settle down.

The time needed until equilibrium was reached and excess carbohydrate settled down was established in previous experiments by measuring the solubility in 24-h intervals. Equilibrium is considered to have been reached when the difference in the value of solubility in 24-h intervals is less than the experimental uncertainty of the gas chromatography method followed in the present work (5%).

The solubility measurements were carried out by triplicate; the absolute average deviation for the data reported is 0.7%, being the highest deviation 2.4%.

Table 1. Carbohydrates Physical Properties[23]

	T_m, K	ΔH_m, J/mol	ΔC_p, J/mol K
Glucose	423.15	32,248	120
Fructose	378.15	26,030	120
Galactose	436.15	43,778	120
Tagatose	407.15*	29,700†	120
Lactose	474.15	75,306	239
Lactulose	442.15*	57,506†	239

*www.sigmaaldrich.com.
†Estimated by the method of Jain et al.[25]

GC determination of carbohydrates

Sample Preparation. The solution of carbohydrate (0.5 mL) in alcohol was carefully taken from the surface and added with 0.5 mL of a solution of 0.01% (w:v) phenyl-β-D-glucoside in methanol/water (70:30, v/v) as internal standard. Prior to derivatization, this sample was dried at 38–40°C in a Rotavapor R-200 (from Büchi Labortechnik AG, Flawil, Switzerland).

Derivatization and GC Analysis of Lactose and Lactulose. The dried mixtures were added with 100 μL of *N*-trimethylsilylimidazole to sylilate the carbohydrates; the reaction was completed in 30 min at 65°C. Sylilated carbohydrates were extracted with 0.1 mL of hexane and 0.2 mL of water. Volumes in the range of 1–2 μL of the organic phase containing sylil derivates were injected into the GC system.

The trimethylsilyl ethers were separated using a 30 m × 0.32 mm inside diameter and 0.5 μm film fused silica capillary column SPBTM–17, bonded, crosslinked phase poly (50% diphenyl/50% dimethylsiloxane) (Supelco, 595 North Harrison Road, Bellefonte, PA). Separation was performed at 235°C for 10 min, followed for an increase up to 270°C at rate of 20°C/min and keeping this temperature for 5 min. Temperature of injector and detector was 300°C during the analysis. Injections were carried out in split mode 1:50. Data were acquired by means of HP ChemStations (Agilent Technologies, Wilmington, DE).

Derivatization and GC Analysis of Tagatose, Galactose, Glucose, and Fructose. The dried mixtures were added with 100 μL of pyridine, 100 μL of *N*-trimethylsilylimidazole, and 100 μL of chlorotrimethylsilane for silylation; the reaction was carried out instantly at room temperature. Silylated carbohydrates were extracted with 0.1 mL of hexane and 0.2 mL of water. Volumes in the range of 1–2 μL of the organic phase containing silyl derivatives were injected into the GC system.

The trimethylsilyl ethers were analyzed using a 30 m × 0.32 mm internal diameter and 0.5 μm film fused silica capillary column SPBTM–17, as described previously. Separation was performed at 165°C for 13 min, followed for an increase up to 270°C at rate of 50°C/min and keeping this tempera-

Table 2. Experimental Solubilities (g/L) of Different Carbohydrates in Methanol, Ethanol, Isopropanol, and 1-Propanol at 22, 30, and 40°C

	Methanol			Ethanol			Isopropanol			1-Propanol		
	22	30	40	22	30	40	22	30	40	22	30	40
Glucose	23.5	27.1	31.6	1.96	3.84	4.21	0.66	0.77	1.42	0.63	0.95	1.59
Fructose	141.5	193.8	229.7	17.4	22.5	36.3	4.43	6.61	13.1	5.95	8.68	14.2
Galactose	4.09	5.50	8.78	0.43	0.63	1.07	0.10	0.15	0.39	0.12	0.21	0.41
Tagatose	34.1	53.8	73.6	6.21	8.24	12.0	2.14	2.51	5.42	2.20	3.35	5.34
Lactose	0.96	1.50	1.87	0.07	0.08	0.12	0.006	0.012	0.019	0.008	0.019	0.025
Lactulose	19.4	25.4	31.4	1.09	1.31	1.90	0.18	0.29	0.40	0.26	0.37	0.50

ture for 5 min. Temperature of injector and detector was 280°C and 300°C, respectively. Injections were carried out in split mode 1:50. Data were acquired by means of HP ChemStations.

Thermodynamic Modeling Framework

Assuming that water is not present in the solid carbohydrate phase and no temperature dependence for ΔC_p (the difference between the heat capacity of the pure liquid and solid carbohydrate), the anhydrous sugar mole fraction x_s in the liquid phase (i.e. the sugar solubility) can be calculated using the following expression:

$$\ln(x_s/\gamma_s) = -\frac{\Delta H_m}{RT_m}\left(\frac{T_m}{T}-1\right)+\frac{\Delta C_p}{R}\left(\frac{T_m}{T}-1\right)+\frac{\Delta C_p}{R}\ln\left(\frac{T}{T_m}\right)$$

where T_m and ΔH_m are, respectively, the carbohydrate normal melting temperature and enthalpy and γ_s is its activity coefficient in the liquid alcoholic phase. Thus, to calculate the sugar solubility, pure sugar physical properties and a thermodynamic model to calculate γ_s are required. The values for the pure component properties (T_m, ΔH_m, and ΔC_p) for the six carbohydrates studied in this work are given in Table 1.

Regarding the calculation of the sugar activity coefficient in the aqueous phase (γ_s), the A-UNIFAC model was employed to represent the extensive binary solubility data measured in this work. Furthermore, the model capability to predict the sugar solubility in ternary sugar–alcohol–alcohol and sugar–alcohol–water mixtures is explored. The A-UNIFAC equations are given in Appendix A. A detailed explanation of the model is given elsewhere.[23,26]

The group composition of the different carbohydrates was defined following Ferreira et al.,[23] i.e. introducing three main groups to represent sugar molecules. The new defined main groups and corresponding subgroups are given in Appendix B, together with the group composition of all six carbohydrates studied in this work.

Results and Discussion

Experimental

Table 2 reports the solubility data obtained in the experimental assays carried out for the carbohydrates (glucose, fructose, galactose, tagatose, lactose, and lactulose) in all four alcohols (methanol, ethanol, 1-propanol, and 2-propanol) at 22, 30, and 40°C. As expected, solubility increased with temperature and decreased with the carbon chain length of the alcohol. Also, the solubility of ketose sugars was higher than those corresponding to aldoses. Additionally, for all carbohydrates and temperatures explored, the solubility was higher in isopropanol (2-propanol) than in 1-propanol.

ANOVA test has been used to check the statistical significance of the differences found in the smallest solubilities reported in Table 2, i.e. lactose solubility in 1-propanol and isopropanol. Results showed that the solubility values were significantly different from each other. Statistica program version 7.1 (Statsoft 2005, www.statsoft.com) for Windows was used for data processing.

The experimental solubility data reported in Table 2 correspond to weight-to-volume values (e.g. g/L). To express solubility as molar fractions (x_s, mol sugar/mol mixture), the density of the solution is required. Table 3 gives the values of

Table 3. Measured Density for some Carbohydrate + Alcohol Mixtures at Different Temperatures

Sugar + Alcohol	Solubility, g/L	T, °C	Mixture Density, g/L	Pure Alcohol Density,* g/L	Density Difference,† %
Fructose + methanol	229.7	40	0.867	0.774	10.7
Fructose + methanol	193.8	30	0.857	0.784	8.5
Tagatose + methanol	73.6	40	0.828	0.774	6.5
Tagatose + methanol	53.8	30	0.813	0.784	3.6
Glucose + methanol	31.6	40	0.816	0.774	5.2
Glucose + methanol	27.1	30	0.803	0.784	2.4
Glucose + ethanol	4.2	40	0.784	0.772	1.6
Galactose + ethanol	1.1	40	0.802	0.772	3.7
Glucose + 1-propanol	0.9	30	0.781	0.796	1.9
Galactose + ethanol	0.627	30	0.7889	0.781	1.00

*Valtz et al.[27]
†100 × (mixture density − pure alcohol density)/mixture density.

Table 4. Group Interaction Parameters Reported by Ferreira et al.[23] and Revised in this Work

a_{mn}, K	PYR/FUR	—O—	CH_2	OH	CH_3OH	H_2O	OH_{ring}
PYR/FUR	0.0	0.0	0.0	50.4 (176.5)	−33.8	−154.3	0.0
—O—	0.0	0.0	0.0	0.0 (−721.0)	0.0 (−323.5)	−508.0	0.0
CH_2	0.0	0.0	0.0	50.4	122.7	380.5	−60.2
OH	387.4	0.0 (−876.6)	387.4	0.0	110.9	−127.3	72.2
CH_3OH	−139.7 (−197.2)	205.8 (−278.7)	−19.78	60.2	0.0	−167.6	31.9
H_2O	108.4	155.3	136.8	70.7	251.2	0.0	87.8
OH_{ring}	0.0	0.0	703.4	715.1	681.8	−174.4	0.0

Values in parentheses show the new values obtained for the parameters revised in this work.

density measured in this work for some sugar–alcohol systems at different temperatures together with the corresponding solubility value and pure alcohol density. As can be observed in Table 3, when the carbohydrate solubility is low, a reasonable assumption is to consider that the density of the mixture is equal to the pure alcohol density; this means that the inaccuracy introduced in the mole fraction calculation lower than 5%. Thus, the measured mixture density was employed in this work to convert high g/L sugar solubility into sugar mole fraction, while the pure alcohol density was used for low carbohydrate solubilities.

Solubility representation using A-UNIFAC model

As mentioned previously, the A-UNIFAC model was selected to represent the binary solubility data reported in this work, together with additional binary data obtained from the literature comprising sugar solubility in different alcohols and water. Additionally, the A-UNIFAC model was employed to predict the solubility of sugars in alcohol–alcohol and alcohol–water mixtures.

The group composition of the six carbohydrates is given in Appendix B. As mentioned, the pure component properties for the carbohydrates studied, and employed in the solubility calculations, are given in Table 1. Although glucose and galactose are isomers (idem for fructose and tagatose) and have exactly the same group composition (see Appendix B), the A-UNIFAC model makes a distinction between these molecules by considering a different number of associative hydroxyl groups $\left(v^{OH}\right)$ for each isomer molecule. For steric reasons, only part of the real number of OH_{ring} groups present in the sugar chemical structure can actually associate. The v^{OH} values regressed by Ferreira et al.[23] are reported in Appendix B; the reader is referred to this work in order to be familiar with the methodology applied to estimate the reported v^{OH} values.

Calculation of Carbohydrate Solubility in Pure Alcohols. Ferreira et al.[23] employed 22 binary solubility data points (glucose, fructose, and sucrose in methanol or ethanol, in the temperature range of 25–60°C) in the optimization of interaction parameters between the sugar groups and the alcoholic (CH_3OH and OH) groups. These parameters were initially employed to predict the solubility data measured in this work. Although the results obtained were not bad, we revised several binary interaction parameters (a_{mn} and a_{nm}) including the extensive data base presented in this work (72 data points), along with solubility data reported in the literature.[13–17] The new values obtained for the revised parameters are given in Table 4, together with the original values reported by Ferreira et al.[23]

The number of associative hydroxyl groups (v^{OH}) for methanol and ethanol alcohols was reasonably set to be 1, but for isopropanol and 1-propanol it was required a v^{OH} value of 0.5 (i.e. lower than 1) in order to maintain for the hydroxyl (OH) group the same associative and dispersive interaction parameters.

Table 5 reports the average absolute deviations (AAD%) obtained between the solubilities measured in this work and A-UNIFAC calculations. Deviations obtained with both the original parameters[23] and those estimated in this work are given in Table 5; deviations were considerably reduced by using the new set of parameters. Nevertheless, it has to be pointed out that the large deviations calculated with the original parameters contain alcohols and carbohydrates, which were not included in the regression procedure carried out by Ferreira et al.[23] For example, using the original parameters deviations are around 25–30% for glucose in methanol or ethanol, but errors are greater than 100% for glucose in 1-propanol or 2-propanol. Thus, when the v^{OH} value for 1-propanol and 2-propanol was reduced from 1 to 0.5, a better correlation with AAD% values between 15 and 35% (see Table 5) could be achieved. This means that not only lower v^{OH} values than the real number of OH_{ring} groups present in the carbohydrate chemical structure are necessary (as reported by Ferreira et al.[23]) but also, lower v^{OH} values are required while increasing the alcohol molecular size. This indicates that the association strength in sugar + alcohol mixtures, which was assumed to be equal to those used to

Table 5. Average Absolute Deviation (AAD%) between the Experimental Solubility Data Measured in this Work and A-UNIFAC Calculations

	Calculated AAD%	
	Using the Parameters Reported by Ferreira et al.[23]	Using the Parameters Regressed in this Work
Sorted by carbohydrate studied		
Glucose	56.2	24.1
Fructose	33.9	22.9
Galactose	96.9	33.9
Tagatose	30.3	15.8
Lactose	52.6	22.2
Lactulose	60.6	18.7
Sorted by alcohol studied		
Methanol	53.8	20.1
Ethanol	48.9	14.4
1-Propanol	63.7	25.7
2-Propanol	75.1	36.8

$$AAD\% = 100 \times \sum \left| (x_s^{exp} - x_s^{cal})/x_s^{exp} \right|$$

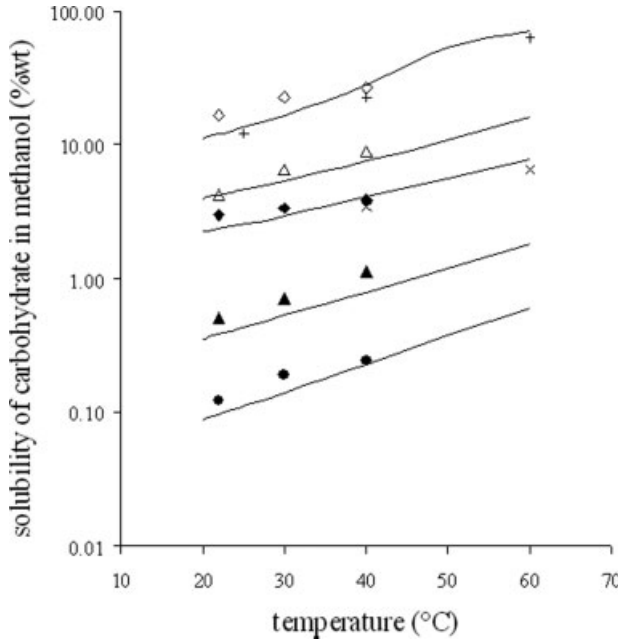

Figure 1. Solubility of carbohydrates in methanol.

Experimental data: this work (◆) glucose, (◇) fructose, (▲) galactose, (△) tagatose, and (●) lactose; Ref. 14 (+) fructose; Ref. 13 (×) glucose; lines: A-UNIFAC calculations.

model alcohol + water mixtures,[23] should be smaller. Nevertheless, this conclusion cannot be generalized considering the solubility of sugars in methanol, ethanol, 1-propanol, and isopropanol, and more reliable solubility data related with alcohols with larger carbon number is required.

Experimental and calculated sugar solubility in methanol, ethanol, 1-propanol, and isopropanol as a function of temperature are depicted in Figures 1–4. To avoid misunderstanding of symbols (experimental data) and lines (model calculations) not all carbohydrates were represented in these figures, but the global performance of the A-UNIFAC approach in representing the 72 solubility measurements reported in this work is given as a log–log plot of experimental versus calculated values (Figure 5). The results observed in Figures 1–5 indicate that a quantitative representation and reasonable distinction between the solubility of the different carbohydrates in the four alcohols studied could be achieved with the A-UNIFAC model.

Calculation of Carbohydrate Solubility in Water. The solubility of carbohydrates (mono and disaccharides) in water was predicted using the original interaction parameters given in Ref. 23 and reported in Table 4. The extensive experimental data set employed by Ferreira et al.[23] to estimate the parameters between the sugar groups and water (including not only solubility data but also freezing and boiling point, osmotic coefficient, vapor pressure, and water activity data of binary glucose–water mixtures) allow very accurate calculations as reproduced in Figure 6 for some of the carbohydrates studied in this work.

Prediction of Carbohydrate Solubility in Ternary Sugar–Alcohol–Alcohol and Sugar–Alcohol–Water Mixtures. The experimental solubility data of the sugar–alcohol and sugar–water binary mixtures was appropriately represented using the A-UNIFAC model and the binary group interaction pa-

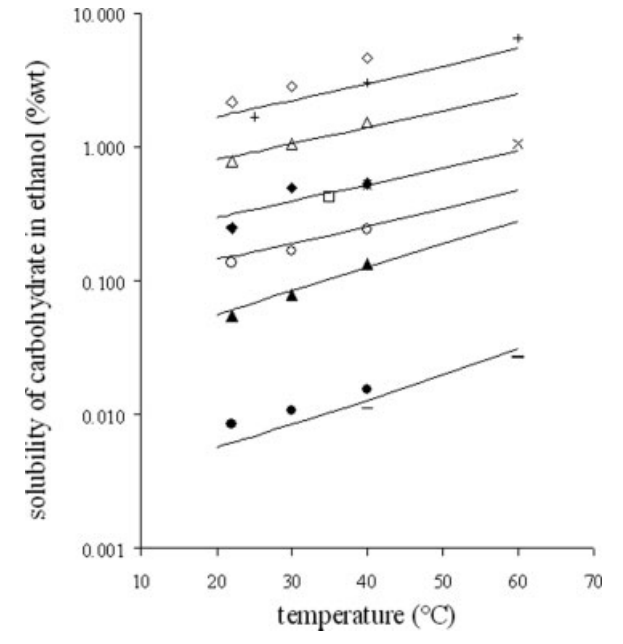

Figure 2. Solubility of carbohydrates in ethanol.

Experimental data: this work (◆) glucose, (◇) fructose, (▲) galactose, (△) tagatose, (●) lactose, and (○) lactulose; Ref. 14 (+) fructose; Ref. 13 (×) glucose; Ref. 28 (□) glucose; Ref. 15 (−) lactose; lines: A-UNIFAC calculations.

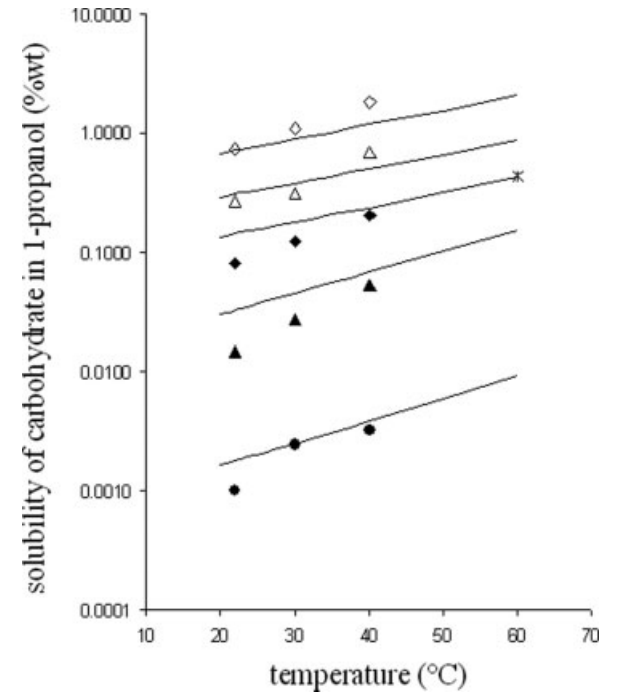

Figure 3. Solubility of carbohydrates in 1-propanol.

Experimental data: this work (◆) glucose, (◇) fructose, (▲) galactose, (△) tagatose, and (●) lactose; Ref. 17 (∗) glucose; lines: A-UNIFAC calculations.

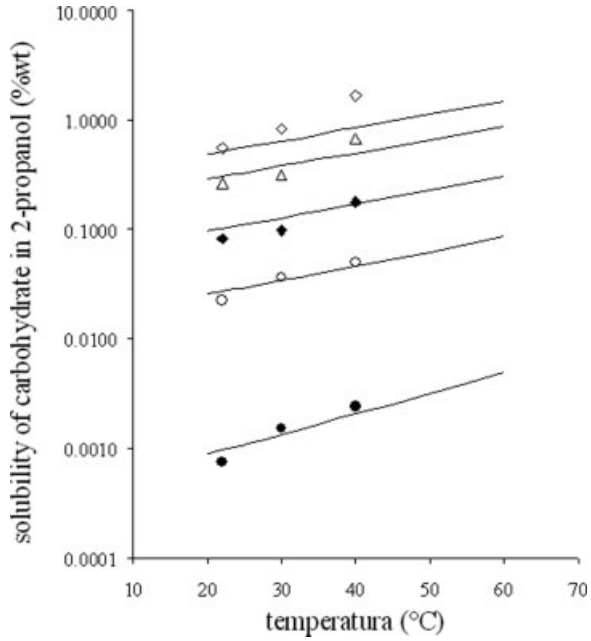

Figure 4. Solubility of carbohydrates in 2-propanol.

Experimental data: this work (◆) glucose, (◇) fructose, (△) tagatose, (●) lactose, and (○) lactulose; lines: A-UNIFAC calculations.

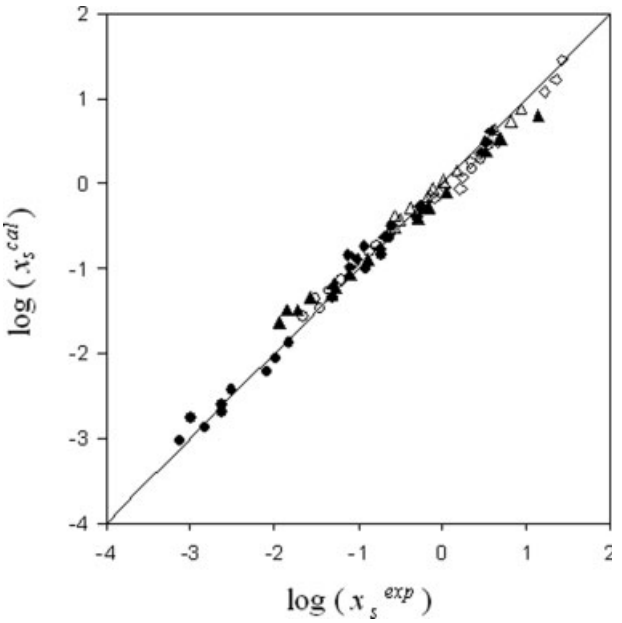

Figure 5. Log–log representation of calculated versus experimental values of carbohydrate solubility in methanol, ethanol, isopropanol, and 1-propanol.

Experimental data (this work): (◆) glucose, (◇) fructose, (▲) galactose, (△) tagatose, (●) lactose, and (○) lactulose.

rameters reported in Table 4. Thus, the model was employed in a completely predictive mode to calculate the solubility of carbohydrates in alcohol–water and alcohol–alcohol mixed solvents. Some of the results obtained are depicted in Figure 7 and show a satisfactory prediction of the sugar solubility with the A-UNIFAC model for all the carbohydrates tested.

Conclusions

This work reports new experimental solubility data of carbohydrates in four different alcohols at 22, 30, and 40 °C. Besides glucose and fructose, sugars for which already exists solubility information in the literature, prebiotic carbohydrates (tagatose and lactulose) were studied together with the corresponding aldoses (galactose and lactose) used in the prebiotic-sugar manufacture.

The A-UNIFAC model presented by Ferreira et al.[23] was employed to correlate the experimental data obtained in this work. Interaction parameters between the alcohol groups and the carbohydrates constituent groups were revised. In this way, important improvements in the solubility calculation were obtained for all systems studied. For the purpose of choosing between alternative ways of separating carbohydrates, accuracy of predicted data should be sufficient (deviations around 15–35%). However, for process design more accurate predicted data will be needed.

Results presented in the present work demonstrate the usefulness of the A-UNIFAC method to model the solubility behavior not only in the binaries alcohol–sugar and water–sugar mixtures but also in the ternaries carbohydrate–alcohol–alcohol or carbohydrate–alcohol–water. The fairly good fitting of the experimental data obtained in our laboratory assures the accuracy of the predictions; therefore, the proposed thermodynamic model can be used to choose the best solvent to selectively purify one sugar in a mixture with different sugars. At present, studies are being conducted in our laboratory to develop a thermodynamic model able to predict

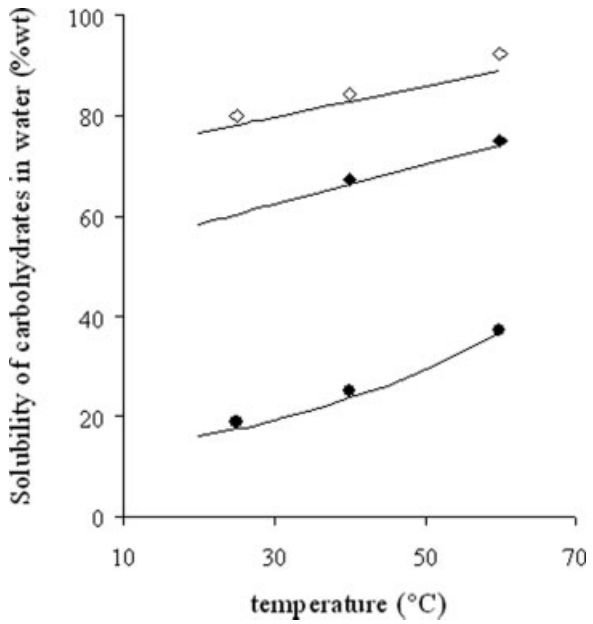

Figure 6. Solubility of carbohydrates in water.

Experimental data: Ref. 13 (◆) glucose, Ref. 14 (◇) fructose and Ref. 15 (●) lactose; lines: A-UNIFAC calculations.

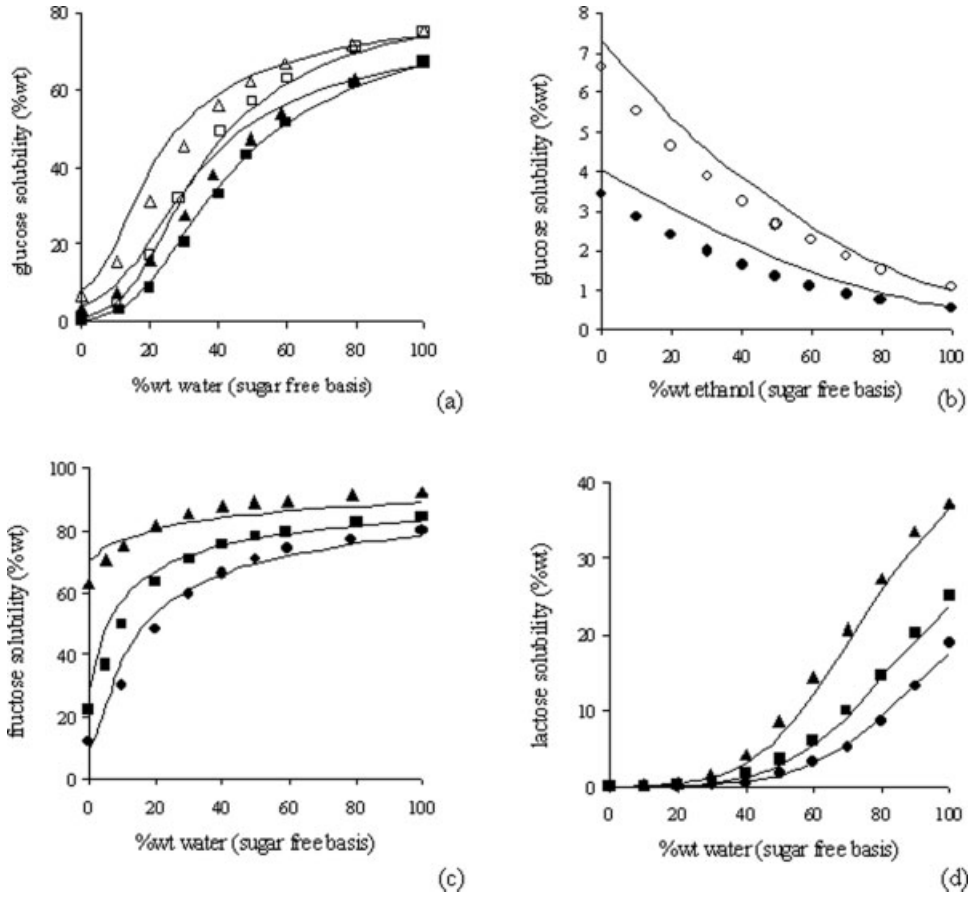

Figure 7. Comparison between experimental solubility data[13–15] of sugars in alcohol–alcohol and alcohol–water mixed solvents and A-UNIFAC predictions.

(a) Glucose–methanol–water at (▲) 40°C and (△) 60°C; glucose–ethanol–water mixture at (■) 40°C and (□) 60°C. (b) Glucose–methanol–ethanol at (●) 40°C and (○) 60°C. (c) Fructose–methanol–water at (●) 25°C (■) 40°C, and (▲) 60°C. (d) Lactose–ethanol–water at (●) 25°C (■) 40°C, and (▲) 60°C.

the solubility of different carbohydrates in more complex reaction mixtures.

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Appendix A

The general expression for the activity coefficient of component i is given by:

$$\gamma_i = \gamma_i^{comb}\gamma_i^{res}\gamma_i^{assoc}$$

In this expression, the combinatorial (comb) and residual (res) contributions are those of the original UNIFAC model,[22] and the association (assoc) term is derived from an expression for the residual Helmholtz energy[25] as a function of the fraction of nonbonded sites in the solution and in the pure-component i.

The simplest expression corresponds to mixtures in which only one associating group with two bonding sites is present. A typical example is hydrogen bonding, due to the interaction between an electropositive hydrogen site and an electronegative oxygen site. In the present work, the association effects corresponding to the sugar OH_{ring} group has been assumed to be identical to that of the OH group present in water and alcohols. Therefore, in these solutions there will be a single associative group with association strength Δ_{OH} characterized by energy ε_{OH} and volume κ_{OH} parameters:

$$\Delta_{OH} = \kappa_{OH}[\exp(\varepsilon_{OH}/kT) - 1]$$

On the basis of these assumptions, the association contribution to the sugar (component i) activity coefficient in sugar–alcohol–water mixtures is given by:

$$\ln\gamma_i^{assoc} = v^{OH,i}\left[2\ln\frac{X_{OH}}{X_{OH,i}} + \left(X_{OH,i} - X_{OH}\right)\right] - (1 - X_{OH})\left(v^{OH,i} - r_i\rho_{OH}\right)$$

where $v^{OH,i}$ is the number of associating groups present in component i. The fractions of nonbonded sites in the mixture (X_{OH}) and in the pure-component i ($X_{OH,i}$) are given by:

$$X_{OH} = \frac{-1 + \sqrt{1 + 4\rho_{OH}\Delta_{OH}}}{2\rho_{OH}\Delta_{OH}}$$

$$X_{OH,i} = \frac{-1 + \sqrt{1 + 4(\rho_{OH})_i\Delta_{OH}}}{2(\rho_{OH})_i\Delta_{OH}}$$

where ρ_{OH} and $\rho_{OH,i}$ are respectively the density of the associative OH group in the solution and in the pure-component i, given by:

$$\rho_{OH} = \sum_{i=1}^{NC} v^{OH,i}x_i \Big/ \sum_{i=1}^{NC} r_i x_i$$

$$(\rho_{OH})_i = v^{OH,i}/r_i$$

x_i is the molar fraction of component i in the mixture and r_i is its molecular volume evaluated from UNIFAC group volume parameters.

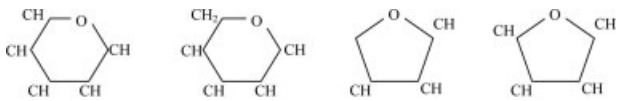
Appendix B

The A-UNIFAC main groups defined by Ferreira et al.[23] to characterize monosaccharides and disaccharides are the following:

Main Groups:

1. Sugar ring [pyranose (PYR) or furanose (FUR) ring]
2. Hydroxyl group attached to the sugar ring (OH_{ring})
3. Osidic bond (—O—)

Additionally, the sugar ring main group has four subgroups:



Taking into account these main groups and subgroups defined, the group composition of the carbohydrates studied in this work is given by:

	PYR1	PYR2	FUR1	FUR2	CH_2	—O—	OH_{ring}	v^{OH}
Glucose	1	0	0	0	1	0	5	2.6
Fructose	0	1	0	0	1	0	5	2.6
Galactose	1	0	0	0	1	0	5	2.4
Tagatose	0	1	0	0	1	0	5	2.4
Lactose	2	0	0	0	2	1	8	4.3
Lactulose	1	0	1	0	3	1	8	4.3

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