

1 **Preferential solvation of xylitol in ethanol + water co-solvent mixtures according to the IKBI and**
2 **QLQC methods**

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4 *Daniel R. Delgado¹, Edgar F. Vargas², Fleming Martínez^{1*}*

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6 ¹ Grupo de Investigaciones Farmacéutico Físicoquímicas, Departamento de Farmacia, Facultad de
7 Ciencias, Universidad Nacional de Colombia, A.A. 14490, Bogotá D.C., Colombia.

8 *E-mail address: fmartinezz@unal.edu.co.

9 ² Grupo de Termodinámica de Soluciones, Departamento de Química, Facultad de Ciencias, Universidad
10 de los Andes, Bogotá D.C., Colombia.

11
12 **Summary**

13 The preferential solvation parameters, i.e., the differences between the local around the solute and bulk
14 mole fractions of the solvents in solutions of xylitol in ethanol + water binary mixtures are derived from
15 their thermodynamic properties by means of the inverse Kirkwood-Buff integrals (IKBI) and quasi-lattice
16 quasi-chemical (QLQC) methods. According to IKBI method it is found that xylitol is sensitive to
17 solvation effects, so the preferential solvation parameter $\delta x_{E,S}$, is slightly positive in water-rich and
18 negative in mixtures beyond 0.25 in mole fraction of ethanol. In different way, according to QLQC
19 method negative values of $\delta x_{E,S}$ are found in all the compositions evaluated. The more solvation by
20 ethanol observed in water-rich mixtures could be due mainly to polarity effects. Otherwise, the preference
21 of this compound for water in ethanol-rich mixtures could be explained in terms of the bigger acidic
22 behavior of water interacting with hydrogen-acceptor hydroxyl groups in xylitol.

23 **Key words:** xylitol, ethanol, solubility, IKBI, QLQC, preferential solvation.

24
25 **Resumen**

26 **Solvatación preferencial del xilitol en mezclas cosolventes etanol + agua según los métodos IKBI y**
27 **QLQC**

28 Partiendo de algunas propiedades termodinámicas clásicas en este trabajo se calcularon los parámetros de
29 solvatación preferencial del xilitol ($\delta x_{E,S}$) en mezclas etanol + agua mediante el método de las integrales
30 inversas de Kirkwood-Buff (IKBI) y el método cuasi-enrejado-cuasi-químico (QLQC). Los parámetros
31 $\delta x_{E,S}$ corresponden a las diferencias entre las fracciones molares locales alrededor del soluto y en el
32 grueso de la solución. Con base en estos valores se encuentra que este compuesto es altamente sensible a
33 los efectos específicos de solvatación según la composición cosolvente. Así, según el método IKBI los
34 valores de $\delta x_{E,S}$ son positivos en mezclas ricas en agua pero negativos en composiciones desde 0.25 en

35 fracción molar de etanol hasta el etanol puro. Sin embargo, según el método QLQC los valores de $\delta x_{E,S}$
36 son negativos en todas las composiciones co-solventes analizadas. En mezclas ricas en agua la mayor
37 solvatación por las moléculas de etanol podría deberse principalmente a efectos de polaridad. De otro
38 lado, la preferencia que manifiesta este compuesto por el agua en mezclas ricas en etanol podría
39 explicarse en términos del mayor comportamiento ácido del agua que estaría interactuando con los grupos
40 aceptores de hidrógeno presentes en el soluto.

41 **Palabras clave:** xilitol, etanol, solubilidad, IKBI, QLQC, solvatación preferencial.

42

43

RESUMO

44 Solvatação preferencial do xilitol no misturas cosolventes etanol + água acordo o métodos IKBI e 45 QLQC

46 Começando a partir de algumas propriedades termodinâmicas clássicos neste trabalho, foram calculados
47 os parâmetros de solvatação preferenciais de xilitol ($\delta x_{E,S}$) em misturas etanol + água pelo método de
48 integrais inversas de Kirkwood-Buff (IKBI) e o método quase-reticulado quase-químicas (QLQC).
49 Parâmetros $\delta x_{E,S}$ correspondem às diferenças entre as frações molares locais ao redor do soluto na
50 solução e a granel. Com base nestes valores se verifique que este composto é extremamente sensível aos
51 efeitos específicos de solvatação por composição de cosolvente. Assim, de acordo com o método IKBI
52 valores $\delta x_{E,S}$ são positivas em misturas ricas em água, mas negativas em composições 0,25 de fração
53 mole de etanol a etanol puro. No entanto, de acordo com o método QLQC os valores de $\delta x_{E,S}$ são
54 negativas em todas as composições testadas. Solvatação de xilitol por moléculas de etanol em misturas
55 ricas em água pode ser devido por polaridade. Por outro lado, a preferência de este composto por água em
56 misturas em etanol pode ser explicada em termos de comportamento ácido de água com os grupos
57 aceitadores de hidrogénio presentes no soluto.

58 **Palavras-chave:** xilitol, etanol, a solubilidade, IKBI, QLQC, solvatação preferencial.

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60

61

INTRODUCTION

62

63 Xylitol ((2R,4S)-Pentane-1,2,3,4,5-pentol, CAS RN 87-99-0, Fig. 1), is an alditol commonly used as
64 additive in several cosmetic and nutraceutical formulations and products. As nutrient agent it is given as
65 oral and intravenous way (1). This compound has been used as a sweetener for diabetic patients and it is
66 actively beneficial for dental health by reducing caries to a third when used regularly. Thus, this
67 sweetening agent is finding increasing application in chewing gum, mouth-rinses, and toothpastes. Unlike

68 sucrose, xylitol is not fermented into cariogenic acid end products (2). According to the US Pharmacopeia
69 it is classified as an official pharmaceutical aid (3).

70

71

Figure 1

72

73 Normally xylitol is obtained from xylose by following several biotechnological procedures (4-6). In its
74 industrial manufacture, xylitol is purified through crystallization from solution as the final step and
75 dilution crystallization generally is preferable. Aqueous alcoholic mixtures are widely used with this
76 purpose. Because the knowledge about solubility is crucial for crystallization processes Wang et al. (7)
77 studied the xylitol solubility in several ethanol + water mixtures at several temperatures.

78

79 Solubility of drugs and other pharmaceutical ingredients, as well as cosmetically and food ingredients, in
80 co-solvent mixtures knowledge is very important for scientists involved in several development stages
81 such as drug and excipients purification and design of liquid medicines (8). Although co-solvency has
82 been employed in pharmacy for several decades it is recently that the mechanisms involved to increase or
83 decrease organic compounds solubility have been approached from a physicochemical point of view (9).
84 In this way, a recent thermodynamic work has been published based on the enthalpic and entropic
85 contributions to the Gibbs energy of solution of this sweetener agent (7). Nevertheless, the preferential
86 solvation, i.e. the co-solvent specific composition around the xylitol molecules has not been studied.
87 Therefore, the main goal of this paper is to evaluate the preferential solvation of xylitol in ethanol + water
88 co-solvent mixtures, based on some classical thermodynamic definitions. Thus this work is similar to the
89 ones presented previously in the literature for some analgesic drugs in similar co-solvent mixtures (10-
90 13).

91

92 The inverse Kirkwood-Buff integral (IKBI) is a powerful tool for evaluating the preferential solvation of
93 nonelectrolytes in solvent mixtures, describing the local compositions around a solute with respect to the
94 different components present in the solvent mixture (14-16). In similar way, quasi-lattice quasi-chemical
95 (QLQC) approach is also useful to do this although is not too much exact as IKBI is (17).

96

97 The first treatment depends on the values of the standard molar Gibbs energies of transfer of the solute
98 xylitol from neat water to the ethanol + water co-solvent mixtures and the excess molar Gibbs energy of
99 mixing for the co-solvent binary mixtures. As has been indicated previously, this treatment is very
100 important in pharmaceutical sciences to understand the molecular interactions solute-solvent because
101 most of the solubility studies developed have been directed towards correlating or modeling the

102 solubilities, and possibly predicting them, from the solubilities in the neat solvents, but not to analyze the
103 local environment around the solute molecules describing the local fraction of the solvent components (E
104 or W) in the surrounding of solute (S) (18, 19).

105
106 In the second case, the QLQC method, proposed by Marcus (17), supposes that the number of nearest
107 neighbors a molecule has (the lattice parameter Z) is the weighted mean of the lattice parameter of the
108 pure components. It also presumes that the interaction energy of a molecule of any component with others
109 is independent of the nature of the other neighbors. The model also assumes that ideal volumes and
110 entropies of mixing take place ($V^{Exc} = 0$; $S^{Exc} = 0$). The main advantage of this method is that non
111 derivative functions are required as in the case of IKBI method (17).

112
113 In this work the IKBI and QLQC approaches are applied to evaluate the preferential solvation of xylitol in
114 the binary mixtures conformed by ethanol (E or EtOH) and water (W). The results are expressed in terms
115 of the preferential solvation parameter $\delta x_{E,S}$ of the solute by the two solvent components.

118 THEORETICAL

119
120 The KBIs (Kirkwood-Buff integrals, $G_{i,S}$) are given by the following expression:

$$121 \quad 122 \quad G_{i,S} = \int_0^{r_{cor}} (g_{i,S} - 1) 4\pi r^2 dr \quad [1]$$

123
124 Here $g_{i,S}$ is the pair correlation function for the molecules of the solvent i in the ethanol + water mixtures
125 around the solute xylitol, r the distance between the centers of the molecules of xylitol and ethanol or
126 water, and r_{cor} is a correlation distance for which $g_{i,S}(r > r_{cor}) \approx 1$. Thus, for all distances $r > r_{cor}$ up to
127 infinite, the value of the integral is essentially zero. Therefore, the results are expressed in terms of the
128 preferential solvation parameter $\delta x_{i,S}$ for the solute in solution by the component solvents ethanol and
129 water (20). For ethanol (E) this parameter is defined as:

$$130 \quad 131 \quad \delta x_{E,S} = x_{E,S}^L - x_E = -\delta x_{W,S} \quad [2]$$

132

133 Where x_E is the mole fraction of ethanol in the bulk solvent mixture and $x_{E,S}^L$ is the local mole fraction of
 134 ethanol in the environment near to the solute. If $\delta x_{E,S} > 0$ then the solute xylitol is preferentially solvated
 135 by ethanol; on the contrary, if it is < 0 the solute is preferentially solvated by water, within the correlation
 136 volume, $V_{cor} = (4\pi/3)r_{cor}^3$, and the bulk mole fraction of ethanol, x_E . Values of $\delta x_{E,S}$ are obtainable from
 137 those of $G_{E,S}$, and these in turn, from thermodynamic data of the co-solvent mixtures with the solute
 138 dissolved on it, as shown below (18).

139
 140 Algebraic manipulation of the basic expressions presented by Newman (20) leads to expressions for the
 141 Kirkwood-Buff integrals (in $\text{cm}^3 \text{mol}^{-1}$) for the individual solvent components in terms of some
 142 thermodynamic quantities as shown in equations [3] and [4] (15, 18, 19):

$$143 \quad G_{E,S} = RT\kappa_T - V_S + x_W V_W D/Q \quad [3]$$

$$144 \quad G_{W,S} = RT\kappa_T - V_S + x_E V_E D/Q \quad [4]$$

145
 146
 147
 148 Where κ_T is the isothermal compressibility of the ethanol + water solvent mixtures (in GPa^{-1}), V_E and V_W
 149 are the partial molar volumes of the solvents in the mixtures (in $\text{cm}^3 \text{mol}^{-1}$), similarly, V_S is the partial
 150 molar volume of xylitol in these mixtures (in $\text{cm}^3 \text{mol}^{-1}$). The function D is the derivative of the standard
 151 molar Gibbs energies of transfer of the solute (from neat water to ethanol + water mixtures) with respect
 152 to the solvent composition (in kJ mol^{-1} , as also is RT) and the function Q involves the second derivative
 153 of the excess molar Gibbs energy of mixing of the two solvents (G_{E+W}^{Exc}) with respect to the water
 154 proportion in the mixtures (also in kJ mol^{-1}) (18-21):

$$155 \quad D = \left(\frac{\partial \Delta_{tr} G_{(S,W \rightarrow E+W)}^0}{\partial x_E} \right)_{T,p} \quad [5]$$

$$156 \quad Q = RT - x_E x_W \left(\frac{\partial^2 G_{E,W}^{Exc}}{\partial x_W^2} \right)_{T,p} \quad [6]$$

157
 158
 159

160 Because the dependence of κ_T on composition is not known for a lot of the systems investigated and
 161 because of the small contribution of $RT \kappa_T$ to the IKBI the dependence of κ_T on composition could be
 162 approximated by considering additive behavior according to the equation [7] (22):
 163

$$164 \quad \kappa_{T,\text{mix}} = \sum_{i=1}^n x_i \kappa_{T,i}^0 \quad [7]$$

165
 166 Where x_i is the mole fraction of component i in the mixture and $\kappa_{T,i}^0$ is the isothermal compressibility of
 167 the pure component i .
 168

169 Ben-Naim (15) showed that the preferential solvation parameter can be calculated from the Kirkwood-
 170 Buff integrals as follows:
 171

$$172 \quad \delta x_{E,S} = \frac{x_E x_W (G_{E,S} - G_{W,S})}{x_E G_{E,S} + x_W G_{W,S} + V_{\text{cor}}} \quad [8]$$

173
 174 The correlation volume, V_{cor} , is obtained by means of the following expression proposed by Marcus (10,
 175 19):
 176

$$177 \quad V_{\text{cor}} = 2522.5 \left(r_s + 0.1363 (x_{E,S}^L V_E + x_{W,S}^L V_W) \right)^3 - 0.085 \quad [9]$$

178
 179 Where r_s is the radio of the solute (in nm), calculated as:
 180

$$181 \quad r_s = \left(\frac{3 \cdot 10^{21} V_s}{4\pi N_{\text{Av}}} \right)^{1/3} \quad [10]$$

182
 183 Here, N_{Av} is the Avogadro number. However, the definitive correlation volume requires iteration, because
 184 it depends on the local mole fractions. This iteration is done by replacing $\delta x_{E,S}$ in the equation [2] to
 185 calculate $x_{E,S}^L$ until a non-variant value of V_{cor} is obtained.
 186

187 For the QLQC method, the local mole fraction of solvent component ethanol around the xylitol molecules
 188 is defined as (17, 19):

$$189 \quad x_S^L = 1 / \left[1 + (N_{EE} / N_{WW})^{0.5} \exp(\Delta E_{EW,S} / 2RT) \right] \quad [11]$$

$$191 \quad N_{EE} / N_{WW} = [x_E - N_{EW} / Z(N_E + N_W)] / [x_W - N_{EW} / Z(N_E + N_W)] \quad [12]$$

$$193 \quad \frac{N_{EW}}{Z(N_E + N_W)} = \frac{1 - [1 - 4x_E x_W (1 - \exp\{-\Delta E_{EW} / RT\})]^{0.5}}{2[1 - \exp(-\Delta E_{EW} / RT)]} \quad [13]$$

$$195 \quad \Delta E_{EW,S} = \Delta_{tr} G_{(S,W \rightarrow E)}^0 / Z \quad [14]$$

$$197 \quad \exp(\Delta E_{EW} / RT) = \left[\left(2 \exp\left\{ -G_{EW(x=0.5)}^{Exc} / ZRT \right\} \right) - 1 \right]^2 \quad [15]$$

199 In these equations, the lattice parameter Z is usually assumed as 10. N_E and N_W are the number of
 200 molecules of both components in the bulk, whereas, N_{EE} , N_{WW} , and N_{EW} are the number of neighboring
 201 pairs of these molecules in the quasi lattice. Equation [14] expresses the difference in the molar neighbor
 202 interaction energies of xylitol with the solvents ethanol and water, $\Delta E_{EW,S}$, by the molar Gibbs energy of
 203 transfer from water to ethanol per neighboring lattice. ΔE_{EW} denotes the molar energy of interaction of
 204 solvent on neighboring quasi-lattice sites. It is important to note that only the Gibbs energy of the xylitol
 205 transfer between the neat solvents and the excess Gibbs energy of mixing at equimolar composition of
 206 both solvents are required for this method.
 207

208 RESULTS AND DISCUSSION

209 The solubility of xylitol in ethanol + water mixtures (Table 1) was taken from Wang et al. (7). Xylitol
 210 solubility diminishes with the increasing the proportion of ethanol in the mixtures at all the temperatures
 211 studied. It is for this reason that this compound is purified by precipitation after adding ethanol to its
 212 aqueous solutions.
 213

214 ***Table 1***

218

219 Standard molar Gibbs energy of transfer of this sweetening agent from neat water to ethanol + water
220 mixtures is calculated and correlated to regular quartic polynomials from the drug solubility data by using
221 equation [16]. Figure 2 shows the Gibbs energy of transfer behavior at several temperatures whereas
222 Table 2 show the behavior at all the temperatures studied. Otherwise, polynomials coefficients are shown
223 in Table 3.

224

$$225 \quad \Delta_{tr} G_{S,W \rightarrow E+W}^0 = RT \ln \left(\frac{x_{S,W}}{x_{S,E+W}} \right) = a + bx_E + cx_E^2 + dx_E^3 + ex_E^4 \quad [16]$$

226

227 ***Fig. 2, Tables 2 and 3***

228

229 Thus D values are calculated from the first derivative of the polynomial models (Equation [17]) solved
230 according to the co-solvent mixtures composition. This procedure was done varying by 0.05 in mole
231 fraction of ethanol but in the following tables the respective values are reported varying only by 0.10 in
232 mole fraction. D values are reported in Table 4.

233

$$234 \quad D = b + 2cx_E + 3dx_E^2 + 4ex_E^3 \quad [17]$$

235

236 ***Table 4***

237

238 In order to calculate the Q values the excess molar Gibbs energies of mixing $G_{E,W}^{Exc}$ at all the temperatures
239 considered are required. Nevertheless, normally these values are reported only at one temperature, i.e.
240 298.15 K. For this reason, it is necessary to calculate it at other temperatures. In this way, $G_{E,W}^{Exc}$ values
241 were calculated at 298.15 K by using the equation [18] as reported by Marcus (18). On the other hand, the
242 $G_{E,W}^{Exc}$ values at the other temperatures were calculated by using the equation [19], where, $H_{E,W}^{Exc}$ is the
243 excess molar enthalpy of the co-solvent mixtures, T_1 is 298.15 K and T_2 is one of the other temperatures
244 under consideration (18). In turn, $H_{E,W}^{Exc}$ values were calculated by using the equation [20] at 298.15 K as
245 also reported by Marcus (18).

246

$$247 \quad G_{E,W}^{Exc} = x_E x_W \left(2907 - 777(1 - 2x_E) + 494(1 - 2x_E)^2 \right) \quad [18]$$

248

$$G_{E,W}^{Exc}(T_2) = G_{E,W}^{Exc}(T_1) - T \int_{T_1}^{T_2} H_{E,W}^{Exc} d\left(\frac{1}{T}\right) \approx \frac{T_2}{T_1} G_{E,W}^{Exc}(T_1) + H_{E,W}^{Exc} \left(1 - \frac{T_2}{T_1}\right) \quad [19]$$

250

$$H_{E,W}^{Exc} = x_E x_W (-1300 - 3567(1 - 2x_E) - 4971(1 - 2x_E)^2) \quad [20]$$

252

253 It is important to note that quartic regular polynomials of $G_{E,W}^{Exc}$ as a function of the mole fraction of water
254 were obtained. Q values at all temperatures are shown in Table 5. On the other hand, Table 6 shows the
255 $RT \kappa_T$ values calculated by assuming additive behavior of κ_T (Equation [7]) with the values 1.153 and
256 0.457 GPa^{-1} , for ethanol and water, respectively (22).

257

Tables 5 and 6

259

260 The partial molar volumes of ethanol (Table 7) and water (Table 8) were calculated by means of
261 equations [21] and [22] from the density (ρ) values of ethanol + water mixtures reported by Jiménez *et al.*
262 at all the temperatures under study (23). In these equations V is the molar volume of the mixtures and it is
263 calculated as $V = (x_E M_E + x_W M_W) / \rho$. M_E and M_W are 46.06 and 18.02 g mol^{-1} , respectively (1).

264

$$\bar{V}_E = V + x_W \frac{dV}{dx_E} \quad [21]$$

266

$$\bar{V}_W = V - x_E \frac{dV}{dx_E} \quad [22]$$

268

Table 7 and 8

270

271 Partial molar volumes of non-electrolyte drugs are not frequently reported in the literature. This is
272 because this property is dependent on temperature and composition and therefore it requires a lot of
273 experiments. For this reason, in a first approach the molar volume of xylitol is considered here as
274 independent of co-solvent composition and temperature, and equal to that presented in solid state, just as
275 it is calculated by considering the density value reported in the literature (1.52 g cm^{-3}) (2) obtaining the

276 value $100.10 \text{ cm}^3 \text{ mol}^{-1}$. Additionally, from this volume value the radius of the drug molecule (required
277 for equation [9]) was calculated by using the equation [10] as $r_s = 0.341 \text{ nm}$.

278
279 Table 9 shows that all the $G_{E,S}$ values are negative with the maximum in $x_{\text{EtOH}} = 0.60$. In different way,
280 Table 10 shows that $G_{W,S}$ values are negative in water-rich mixtures but positive beyond the mixture with
281 $x_{\text{EtOH}} = 0.40$ reaching maximum value in the mixture with $x_{\text{EtOH}} = 0.80$. This could be interpreted as the
282 preference of xylitol by water in ethanol-rich mixtures.

283
284 ***Tables 9 and 10***

285
286 In order to use the IKBI method, the correlation volume was iterated three times by using the equations
287 [2], [8] and [9] to obtain the values reported in Table 11. It is interesting to note that this value is almost
288 independent on temperature in water-rich mixtures but increases in some extent in ethanol-rich mixtures.
289 This could be a consequence of the greater molar expansibility of ethanol in comparison with water (23).

290
291 ***Table 11***

292
293 The values of $\delta x_{E,S}$ vary non-linearly with the ethanol concentration in the aqueous mixtures at all the
294 temperatures studied (Table 12 and Fig. 3). In the beginning, the addition of ethanol to water tends to
295 make positive the $\delta x_{E,S}$ values of xylitol from the pure water up to the mixture 0.25 in mole fraction of
296 ethanol reaching a maximum of 4.8×10^{-3} . This maximum diminishes with the temperature increasing.

297
298 ***Table 12 and Figure 3***

299
300 From this ethanol proportion up to neat ethanol, the local mole fraction of the ethanol around the solute
301 decreases, being the $\delta x_{E,S}$ values negative, and therefore, xylitol is preferentially solvated by water.

302
303 Xylitol acts in solution as a Lewis acid due to the hydrogen atoms in its $-\text{OH}$ groups (Fig. 1) in order to
304 establish hydrogen bonds with proton-acceptor functional groups in the solvents (oxygen atoms in $-\text{OH}$).
305 In addition, this drug could act as a Lewis base due to free electron pairs in oxygen atoms of hydroxyl
306 groups to interact with acidic hydrogen atoms in both solvents.

307
308 According to the preferential solvation results, it is conjecturable that in water-rich mixtures, the xylitol is
309 acting as Lewis acid with ethanol molecules because this co-solvent is more basic than water, i.e. the

310 Kamlet-Taft hydrogen bond acceptor parameters are $\beta = 0.75$ for ethanol and 0.47 for water (24). On the
311 other hand, in ethanol-rich mixtures, where the solute is preferentially solvated by water, this compound
312 is acting mainly as a Lewis base in front to water because the Kamlet-Taft hydrogen bond donor
313 parameters are, $\alpha = 1.17$ for water and 0.86 for ethanol, respectively (25). Thus, water is more acidic than
314 ethanol. In this way, the specific and nonspecific interactions between xylitol and the co-solvent decrease
315 in these mixtures (12, 26).

316
317 On the other hand, in order to use the QLQC method, the excess Gibbs energy of mixing of equimolar
318 mixture of both solvents was used as follows: 0.709, 0.727, 0.744, 0.762, and 0.780 kJ mol⁻¹, at
319 temperatures from 293.15 to 313.15 K, respectively (12). According to QLQC method (Table 13 and
320 Figure 3) xylitol is preferentially solvated by water in all the mixtures and the $\delta x_{E,S}$ values are bigger (as
321 negative magnitude) than the ones obtained by using the IKBI method in mixtures with composition 0.25
322 $< x_{EtOH} < 0.50$ but they are lower in the other mixtures ($0.50 < x_{EtOH} < 1.00$). Therefore, as has been
323 indicated in the literature the IKBI method is more indicate than QLQC to discriminate the effect of co-
324 solvent composition on the local mole fraction around the drugs molecules (12, 13). Nevertheless, it is
325 important to keep in mind that QLQC requires only two specific values, i.e. Gibbs energy of transfer of
326 xylitol from water to ethanol and the excess Gibbs energy of mixing at $x_{EtOH} = 0.50$, so it is more easy to
327 use.

328
329 ***Table 13***

330 331 332 CONCLUSIONS

333
334 Explicit expressions for local mole fraction of ethanol and water around of xylitol were derived on the
335 basis of the IKBI and QLQC methods applied to equilibrium solubility values of this sweetening agent in
336 ethanol + water mixtures. Thus, this compound is preferentially solvated by ethanol in water-rich
337 mixtures but preferentially solvated by water in mixtures beyond 0.25 in mole fraction of ethanol at all
338 temperatures considered. These results are in agreement with that described previously and base in more
339 classical thermodynamic treatments (7).

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Table 1. Mole fraction solubility ($1000 x_s$) of xylitol at several temperatures. ^a

x_{EtOH}^b	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.0000	162.5	180.6	204.2	234.4	265.5
0.0706	121.5	138.0	172.9	198.7	226.2
0.1741	97.0	108.5	136.8	167.8	202.3
0.2821	80.1	97.2	119.8	145.9	173.2
0.3654	60.0	73.6	90.9	114.8	141.8
0.4777	38.2	48.5	61.7	77.6	101.8
0.6101	16.2	24.0	31.0	40.9	53.4
0.7000	10.1	12.4	15.9	20.7	25.1
0.7827	6.7	8.8	11.0	14.7	19.4
1.0000	2.1	2.5	3.1	4.2	5.7

^a Data from Wang et al. (7).

^b x_{EtOH} is the mole fraction of ethanol in the ethanol + water co-solvent mixtures free of xylitol.

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Table 2. Gibbs energy of transfer (kJ mol^{-1}) of xylitol from neat water to ethanol + water co-solvent mixtures at several temperatures.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.0000	0.00	0.00	0.00	0.00	0.00
0.0706	0.71	0.67	0.42	0.42	0.42
0.1741	1.26	1.26	1.01	0.86	0.71
0.2821	1.72	1.54	1.34	1.21	1.11
0.3654	2.43	2.23	2.04	1.83	1.63
0.4777	3.53	3.26	3.02	2.83	2.50
0.6101	5.62	5.00	4.75	4.47	4.18
0.7000	6.77	6.64	6.43	6.22	6.14
0.7827	7.77	7.49	7.36	7.09	6.81
1.0000	10.60	10.61	10.55	10.30	10.00

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Table 3. Coefficients of the Equation [16] (kJ mol^{-1}) applied to Gibbs energy of transfer of xylitol from neat water to ethanol + water co-solvent mixtures at several temperatures.

Coefficient	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
<i>a</i>	0.09	0.06	0.01	0.03	0.03
<i>b</i>	7.87	9.22	7.15	6.25	6.25
<i>c</i>	-16.49	-26.61	-19.41	-18.19	-22.44
<i>d</i>	44.71	60.28	50.63	49.72	58.59
<i>e</i>	-25.61	-32.36	-27.85	-27.52	-32.46

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Table 4. D values (kJ mol^{-1}) of xylitol in ethanol + water co-solvent mixtures at several temperatures.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	7.87	9.22	7.15	6.25	6.25
0.10	5.81	5.57	4.68	4.00	3.39
0.20	5.82	4.77	4.57	4.06	3.27
0.30	7.28	6.03	6.17	5.79	5.11
0.40	9.58	8.58	8.80	8.52	8.12
0.50	12.10	11.63	11.79	11.59	11.53
0.60	14.24	14.42	14.48	14.34	14.57
0.70	15.37	16.17	16.20	16.11	16.44
0.80	14.88	16.09	16.28	16.24	16.38
0.90	12.15	13.42	14.05	14.07	13.60
1.00	6.58	7.38	8.84	8.93	7.33

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Table 5. Q values (kJ mol^{-1}) of ethanol + water co-solvent mixtures at several temperatures.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	2.437	2.479	2.520	2.562	2.604
0.10	2.077	2.039	2.000	1.962	1.924
0.20	1.855	1.813	1.771	1.729	1.687
0.30	1.668	1.658	1.648	1.638	1.627
0.40	1.460	1.487	1.515	1.543	1.570
0.50	1.220	1.272	1.324	1.377	1.429
0.60	0.985	1.040	1.095	1.149	1.204
0.70	0.838	0.875	0.912	0.949	0.986
0.80	0.906	0.918	0.930	0.942	0.953
0.90	1.365	1.367	1.370	1.372	1.374
1.00	2.437	2.479	2.520	2.562	2.604

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Table 6. $RT \kappa_T$ values ($\text{cm}^3 \text{mol}^{-1}$) of ethanol + water co-solvent mixtures at several temperatures.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	1.114	1.133	1.152	1.171	1.190
0.10	1.283	1.305	1.327	1.349	1.371
0.20	1.453	1.478	1.503	1.527	1.552
0.30	1.623	1.650	1.678	1.706	1.733
0.40	1.792	1.823	1.853	1.884	1.915
0.50	1.962	1.995	2.029	2.062	2.096
0.60	2.132	2.168	2.204	2.241	2.277
0.70	2.301	2.341	2.380	2.419	2.458
0.80	2.471	2.513	2.555	2.597	2.639
0.90	2.641	2.686	2.731	2.776	2.821
1.00	2.810	2.858	2.906	2.954	3.002

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Table 7. Partial molar volume ($\text{cm}^3 \text{mol}^{-1}$) of ethanol in ethanol + water co-solvent mixtures at several temperatures.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	52.49	52.77	53.38	53.95	54.30
0.10	54.05	54.37	54.86	55.30	55.68
0.20	55.31	55.65	56.06	56.40	56.79
0.30	56.29	56.65	56.99	57.28	57.68
0.40	57.03	57.40	57.70	57.96	58.37
0.50	57.57	57.93	58.22	58.47	58.87
0.60	57.94	58.28	58.57	58.83	59.23
0.70	58.16	58.50	58.79	59.07	59.45
0.80	58.28	58.61	58.91	59.21	59.58
0.90	58.33	58.65	58.95	59.28	59.64
1.00	58.34	58.65	58.96	59.29	59.66

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Table 8. Partial molar volume ($\text{cm}^3 \text{mol}^{-1}$) of water in ethanol + water co-solvent mixtures at several temperatures.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	18.05	18.07	18.09	18.11	18.14
0.10	17.97	17.99	18.01	18.04	18.07
0.20	17.75	17.77	17.80	17.85	17.88
0.30	17.42	17.44	17.49	17.55	17.58
0.40	17.03	17.04	17.11	17.19	17.21
0.50	16.59	16.60	16.69	16.77	16.80
0.60	16.15	16.17	16.27	16.34	16.37
0.70	15.73	15.78	15.86	15.90	15.95
0.80	15.38	15.46	15.52	15.48	15.56
0.90	15.12	15.25	15.25	15.12	15.24
1.00	14.99	15.18	15.11	14.83	15.00

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Table 9. $G_{\text{E,S}}$ values ($\text{cm}^3 \text{mol}^{-1}$) for xylitol in ethanol + water co-solvent mixtures at several temperatures.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	-40.7	-31.8	-47.6	-54.7	-55.3
0.10	-53.6	-54.6	-60.9	-65.7	-70.1
0.20	-54.3	-61.3	-61.9	-65.1	-70.9
0.30	-45.2	-54.0	-52.6	-54.9	-59.8
0.40	-31.1	-39.2	-38.5	-41.1	-44.7
0.50	-15.7	-22.0	-23.6	-27.2	-30.0
0.60	-4.6	-8.2	-11.7	-16.3	-18.5
0.70	-11.4	-10.5	-13.3	-16.9	-18.0
0.80	-47.4	-43.5	-43.5	-44.4	-44.2
0.90	-84.1	-82.5	-81.8	-81.9	-82.3
1.00	-97.3	-97.2	-97.2	-97.1	-97.1

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Table 10. $G_{w,s}$ values ($\text{cm}^3 \text{mol}^{-1}$) for xylitol in ethanol + water co-solvent mixtures at several temperatures.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	-99.0	-99.0	-98.9	-98.9	-98.9
0.10	-83.7	-83.9	-85.9	-87.5	-88.9
0.20	-64.0	-69.4	-69.7	-72.1	-76.5
0.30	-24.8	-36.6	-34.4	-37.6	-44.1
0.40	51.4	34.2	35.9	29.9	22.6
0.50	187.5	166.8	161.2	148.4	139.7
0.60	404.2	386.9	367.1	342.7	332.1
0.70	648.5	658.5	632.9	603.6	595.8
0.80	667.0	723.7	726.4	718.2	720.2
0.90	369.2	420.2	446.1	449.2	433.4
1.00	60.2	77.3	109.6	109.6	70.9

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Table 11. Correlation volume ($\text{cm}^3 \text{mol}^{-1}$) for xylitol in ethanol + water co-solvent mixtures at several temperatures after three iterations.

x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	583	583	584	584	585
0.10	650	651	652	653	654
0.20	713	714	716	717	719
0.30	773	775	778	780	782
0.40	826	830	833	836	839
0.50	872	876	880	884	888
0.60	910	914	920	925	930
0.70	954	957	962	967	972
0.80	1030	1030	1033	1037	1041
0.90	1133	1136	1138	1142	1147
1.00	1219	1223	1228	1232	1238

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Table 12. $100 \delta x_{E,S}$ values of xylitol in ethanol + water co-solvent mixtures at several temperatures according to IKBI method.

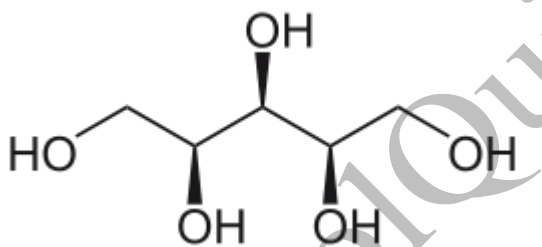
x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	0.00	0.00	0.00	0.00	0.00
0.10	0.48	0.46	0.40	0.35	0.30
0.20	0.24	0.20	0.19	0.17	0.14
0.30	-0.58	-0.50	-0.52	-0.49	-0.45
0.40	-2.35	-2.11	-2.13	-2.03	-1.93
0.50	-5.30	-4.98	-4.87	-4.65	-4.50
0.60	-9.18	-8.91	-8.58	-8.18	-8.00
0.70	-12.15	-12.25	-11.87	-11.46	-11.32
0.80	-10.16	-10.77	-10.77	-10.66	-10.64
0.90	-3.73	-4.10	-4.28	-4.29	-4.16
1.00	0.00	0.00	0.00	0.00	0.00

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463 **Table 13.** 100 $\delta x_{E,S}$ values of xylitol in ethanol + water co-solvent mixtures at several temperatures
464 according to QLQC method.

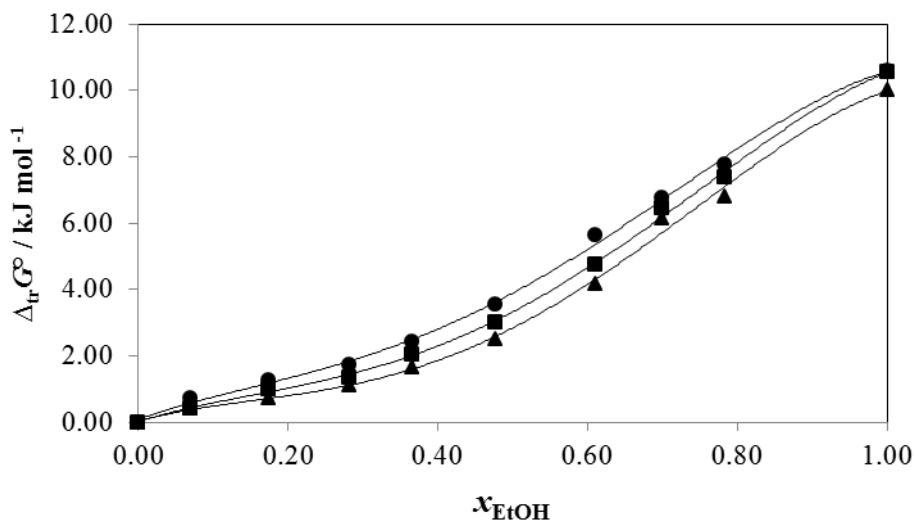
x_{EtOH}	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.00	0.00	0.00	0.00	0.00	0.00
0.10	-1.43	-1.40	-1.37	-1.30	-1.22
0.20	-2.76	-2.71	-2.64	-2.52	-2.38
0.30	-3.92	-3.85	-3.75	-3.59	-3.41
0.40	-4.83	-4.75	-4.64	-4.45	-4.24
0.50	-5.41	-5.33	-5.21	-5.01	-4.79
0.60	-5.60	-5.51	-5.40	-5.20	-4.98
0.70	-5.28	-5.20	-5.10	-4.92	-4.72
0.80	-4.34	-4.28	-4.20	-4.05	-3.89
0.90	-2.64	-2.61	-2.56	-2.47	-2.38
1.00	0.00	0.00	0.00	0.00	0.00

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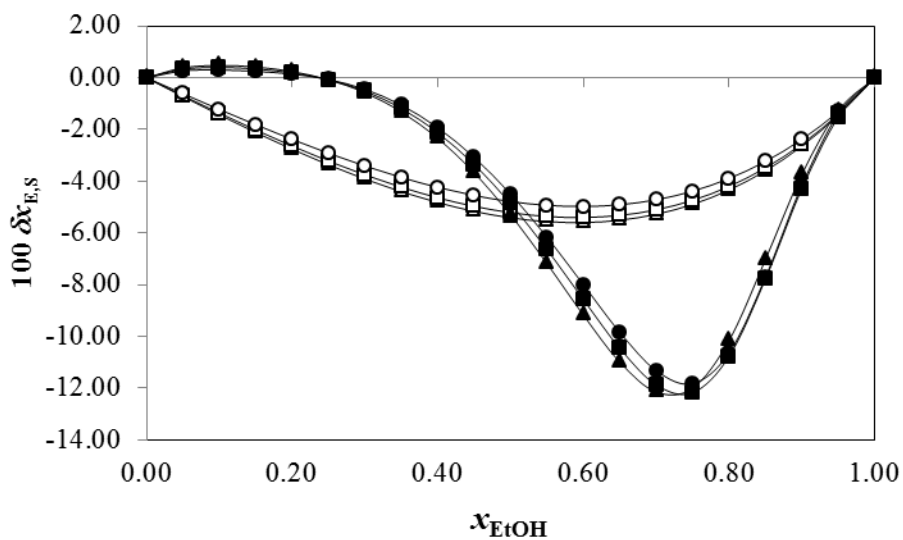


476 **Figure 1.** Molecular structure of xylitol.
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 488 **Figure 2.** Gibbs energy of transfer of xylitol from neat water to ethanol + water co-solvent mixtures at
 489 several temperatures. Triangles: 293.15 K; squares: 303.15 K; circles: 313.15 K.
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 497 **Figure 3.** $\delta x_{E,S}$ values ($\times 100$) for xylitol in ethanol + water co-solvent mixtures at several temperatures
 498 according to the IKBI (filled symbols) and QLQC (empty symbols) methods at several temperatures.
 499 Triangles: 293.15 K; squares: 303.15 K; circles: 313.15 K.
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