Design and characterization of sugar-based deep eutectic solvents using COSMO-RS

Liliana P. Silva,[a] Luis Fernandez,[b] João H. F. Conceição,[a] Mónia A. R. Martins,[a,c,d] Adriel Sosa,[b] Juan Ortega,[b] Simão P. Pinho,[c,d] João A. P. Coutinho[a*]

[a]CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal;

[b]Laboratorio de Termodinamica y Fisicoquímica de Fluidos, Universidad de Las Palmas de Gran Canaria, 35071 – Parque Científico-Tecnológico, Canary Islands, Spain;

[c]Associate Laboratory LSRE-LCM, Department of Chemical and Biological Technology, Polytechnic Institute of Bragança, 5300-253 Bragança, Portugal;

[d]Mountain Research Center – CIMO, Polytechnic Institute of Bragança, 5301-855 Bragança, Portugal.

*Corresponding author: jcoutinho@ua.pt. Phone: +351 234370200. Fax: +351 234370084.

Abstract

Inspired by the lack of characterization of natural eutectic and deep eutectic (DES) systems, we studied the solid-liquid equilibria (SLE) of binary and ternary mixtures involving choline chloride and sugars. The densities, viscosities and solvatochromic parameters for the binary systems containing choline chloride, [Ch]Cl, were measured at the eutectic composition, and the water impact on these properties was also investigated in order to address the tailoring of their properties using water. Mixtures of sugars are shown to present an ideal behavior, while their binary mixtures with choline chloride present negative deviations to the ideality, particularly in the sugar solubility curve. Aiming to develop a predictive model to design new sugar based DES, the [Ch]Cl + sugars phase diagrams were used to tune the COnductor-like Screening MOdel for Real Solvents (COSMO-RS) parameters, which was after applied in the estimation of the eutectic points of new ternary DES. The predictions quality was checked experimentally, proving that COSMO-RS can be a useful tool for the design of deep eutectic solvents.

Keywords: Sugars, choline chloride, SLE, COSMO-RS, solvatochromic parameters, densities, viscosities, eutectic solvents.

Introduction

The development of the chemical industries has led to an improvement in the quality of life, but it has also been deemed responsible for the generation of chemical pollutants and toxic wastes with worldwide impact in both human health and environment. Minimizing, or fully eliminating, the use of noxious solvents and contaminated effluents in industrial processes has been the target, under the head of "green chemistry", of much research in the last decades.[1] Nowadays, the search for green solvents to be used on chemical processes is being focused on bio-based compounds. In this context, the neoteric Deep Eutectic Solvents (DES) based on natural compounds are attracting a lot of interest.[2,3]

Natural based DES (NADES) are a particular group formed by biomolecules such as urea, choline chloride ([Ch]Cl) and organic acids, including amino acids. Some authors have also proposed sugar based DES.[3–8] These hold a lot of interest given its easy availability, low price, non-toxicity, and good biodegradability, that could lead to cheap environmental friendly solvents.

Given the recent interest for NADES and the number of articles reporting applications using sugars as DES precursors,[3,5,9,10] data on the solid-liquid equilibria (SLE) of their mixtures is surprisingly scarce, despite the information it provides on the range of compositions and temperatures to operate these systems. Moreover, a characterization of the physical properties of these systems is rarely presented.[4–6,11] Regarding mixtures of [Ch]Cl and sugars, only in a few cases[3,7,9] the authors report what they believe to be the eutectic composition. Even the information available on the SLE of mixtures of sugars is scarce with just 3 binaries and one ternary system published.[12,13] Kelly and Brown[12] evaluated the SLE of the ternary system sucrose+glucose+fructose and the correspondent binary subsystems. The thermal instability of the mixtures is mentioned as a limitation, as well as the need to implement fast measurements to minimize degradation. The limited experimental details reported inhibit a correct evaluation of the data. Later, Bhandari and Hartel[13] studied the effect of the presence of glucose, or fructose, on the co-precipitation of sucrose. This work includes experimental data on the SLE of the binary and ternary systems for high concentration of sucrose, measured by differential scanning calorimetry (DSC). The main reason for this dearth of data in sugar-based mixtures is related with their poor thermal stability. They are reactive

species with high melting points and their isomerization and polymerization may take place upon heating leading to the formation of brown chromophores characteristic of sugar degradation.[14] An interesting review on the decomposition of sugars is reported by Roos et al.[15]

Due to the lack of experimental data, and the poor characterization of the thermophysical properties of pure sugars and other NADES precursors, namely cholinium chloride,[16] it is not surprising that attempts to describe the SLE of DES by equations of state or activity coefficient models are scarce too. Moreover the complexity of the interactions between the DES constituents[17] are often not easily represented by conventional models. In previous works reporting experimental SLE phase diagrams of DES, PC-SAFT[17,18] and NRTL[17] were successfully used to model these systems.

Aiming at contributing to the characterization of systems containing sugars (sucrose, glucose, fructose, arabinose, mannose and xylose), in this work the SLE of sugar+sugar and choline chloride+sugar mixtures were studied, evaluating the nature of these systems and of their eutectic mixtures. The experimental phase diagrams for the binary systems composed by [Ch]Cl and sugars were described by two excess Gibbs energy (g^E) models, namely NRTL and a modified Redlich-Kister expansion, after used to develop tools for predicting the behavior of other sugar-based DES. The predictive ability of COSMO-RS[19] was tested, and a few parameters tuned with the knowledge gathered by the new binary experimental data and g^E modeling. The model was then used to predict novel systems that were experimentally validated. In a final stage of the work, densities, viscosities and solvatochromic parameters for the eutectic mixtures of systems containing choline chloride were measured. The water impact on these was also investigated in order to further discuss the tailoring of the properties by the presence of water.

Experimental

Chemicals

The properties of the compounds used in this work are presented in Table 1. Before use, choline chloride was dried under vacuum (0.1 Pa and 298.15 K) for at least 72 h, while the remaining compounds were stored at room temperature and used as received, due to

their reduced hygroscopicity. The water content was measured using a Metrohm 831 Karl-Fischer coulometer, with the analyte Hydranal®–Coulomat AG from Riedel-de Haën and found to be lower than 600 ppm for choline chloride and lower than 10 ppm for all the sugars. Distilled water was used in for properties measurements.

Table 1. Source, purity and melting properties of the substances used in this work.

Compound[a]	Supplier	Mass Purity %	T_m / K	$\Delta_m H$ / kJ·mol^{-1}
Choline Chloride	Acros Organics	98	597[16]	4.3[16]
D(-)-Fructose	Panreac	98	386.75[20]	33.0[21]
Sucrose	Himedia	99.5	462.05[20]	32.0[22]
D-Glucose	Analar	98	420[21]	32.0[21]
D(+)-Xylose	Sigma	99	423[23]	31.65[23]
D-Mannose	Aldrich	99	407[23]	24.69[23]
L(+)-Arabinose	Biochemicals	≥ 99	435[21]	35.78[21]

[a]The sugars stereochemistry is omitted in the rest of the manuscript.

Experimental methodology

Melting points determination

The mixtures were prepared weighing, inside a dry-argon glove-box, the desired amounts of each pure compound using an analytical balance model ALS 220-4N from Kern with an accuracy of ±0.002 g. The vials with the mixtures were heated under stirring until complete melting and then recrystallized. Depending on the physical state of the final mixture two different methods were employed: 1) For mixtures with a paste-like appearance a visual method using an oil bath was applied. The mixtures were gradually heated until complete melting and the temperature controlled with a PT100 probe with a precision of ±0.1 K. The probe was previously calibrated against a calibrated platinum resistance thermometer, SPRT100 (Fluke-Hart Scientific 1529 Chub-E4), traceable to the National Institute of Standards and Technology (NIST), with an uncertainty less than 2×10^{-2}; 2) For the remaining mixtures, the recrystallized solid was grounded inside the glove-box and the powder filled into a glass capillary. A melting point device model M-565 by Bucchi (100-240 V, 50-60 Hz, 150 W) with a temperature resolution of 0.1 K was used to determine the melting points, applying an

heating rate of 1 K·min^{-1}. Both procedures were repeated at least three times and the estimated reproducibility of the measurements is of ±1.8 K.

Density and viscosity

Densities and viscosities measurements of the mixtures [Ch]Cl+sugars at the eutectic composition, and of the [Ch]Cl+sugars+water mixtures were carried out at atmospheric pressure, in the temperature range (293.15 to 373.15) K using an automated SVM 3000 Anton Paar rotational Stabinger viscometer-densimeter. The uncertainty of temperature is ±0.02 K and the relative uncertainty of the dynamic viscosity is ±0.35%. The absolute uncertainty in density is ±5×10^{-4} g·cm^{-3}. The fixed water mass content in [Ch]Cl+sugars+water mixtures is presented in **Table S1** of Supporting Information (SI).

Kamlet Taft Solvatochromic Parameters

The Kamlet Taft solvatochromic parameters π*, β and α were measured at the eutectic composition for the mixtures [Ch]Cl+sugars, and also for the [Ch]Cl+sugars+water mixtures at 323.15 K. Small quantities of the probes *N,N*-diethyl-4-nitroaniline, 4-nitroaniline or pyridine-*N*-oxide were added to the mixtures and immediately stirred at 323.15 K using an Eppendorf Thermomixer Comfort (1400 rpm during 30 min) until complete dissolution. π* and β were obtained using the longest wavelength absorption band, determined by UV-Vis spectroscopy (BioTeck Synergy HT microplate reader) at 323.15 K. α was measured by ^{13}C nuclear magnetic resonance (NMR) spectra, using a Bruker Avance 300 apparatus at 75 MHz. Deuterium oxide (D$_2$O) and trimethylsilyl propanoic acid (TSP) were used as solvent and internal reference, respectively. The procedure was repeated at least three times for parameters π* and β. The water content used in the solvatochromic parameters was 9 wt%, the minimum amount of water required for all mixtures to become liquid at 298.15 K.

Modeling

Solid-liquid thermodynamics

The solid-liquid equilibrium of a compound *i* in a solution can be described using the following thermodynamic equation:[24]

$$\ln(x_i^L \gamma_i^L) = \frac{\Delta_m H_i}{R T_{m,i}}\left(1 - \frac{T_{m,i}}{T}\right) + \frac{\Delta_m C p_i}{R}\left(\frac{T_{m,i}}{T} - \ln\frac{T_{m,i}}{T} - 1\right) \tag{1}$$

where x_i^L is the mole fraction of the component i in the liquid phase and γ_i^L its activity coefficient, R is the ideal gas constant and T is the absolute temperature. $T_{m,i}$ and $\Delta_m H_i$ are the melting temperature and enthalpy of compound i, respectively, while $\Delta_m C p_i$ its the heat capacity change upon melting.

Data on $\Delta_m C p$ are seldom available, as is the case for most of the pure compounds studied here since they decompose upon heating. Magoń et al.[22] measured the sucrose $\Delta_m C p$ (around 250 J·mol^{-1}·K^{-1}) using fast scanning and temperature modulated calorimetry. This was the value used in this work for sucrose, while for all the other sugars that are monosaccharides a fixed $\Delta_m C p$=120 J·mol^{-1}·K^{-1}, roughly half of the value for the disaccharide, was adopted as proposed in the literature.[21,25] Choline chloride also degrades upon melting and so its melting properties cannot be measured directly. In this work, the estimated[16] set T_m = 597 K and $\Delta_m H$=4.3 kJ·mol^{-1} was applied and $\Delta_m C p$ was neglected. This last assumption has been checked in detail by us elsewhere.[26] The melting temperatures and enthalpies are summarized in **Table 1**.

Excess Gibbs energy models

To represent the non-ideality of the liquid phase, two excess Gibbs energy models were applied: the well-known Non-random Two-Liquid (NRTL) model[27] – a semi-empirical model based on the local composition concept; and an empirical model based on the Redlick-Kister (mRK) expansion models, where a dependence on the composition is achieved through the so-called active fraction.[28] Additional information about the models and their equations is available in the Supporting Information.

COSMO-RS model

The use of COSMO-RS[19] as a predictive model for DES have been explored by different authors.[29,30] In this work the geometry of all compounds was optimized at the B3LYP/6-31++G** computational level using the software Turbomole V7.2, which was also used to produce the COSMO files. Choline chloride was optimized as a neutral ion-paired structure. On a second step, the programme COSMOSthermX C30_1201

Results

The detailed experimental solid-liquid data for the systems composed of: sugar+sugar, sugar+sugar+sugar, [Ch]Cl+sugar, and [Ch]Cl+sugar+sugar are reported in **Tables S2 – S5** of the Supporting Information. All systems present a SLE phase diagram characterized by a single eutectic point. The consistency tests proposed by Kang et al.[31] and Cunico et al.[32] were used to evaluate the quality of the measured SLE data. Results are compiled in **Table S6,** revealing very satisfactory quality factors, even if invariably Q_2 is always much lower from the two others, which is related to the definition of that quality factor (equation 1 by Cunico et al.[32]). To the best of our knowledge there are no consistency tests to evaluate the data quality for ternary systems.

Thermodynamic behavior of mixtures of sugars

The phase diagrams for the binary mixtures of sugars are shown in **Figure 1** along with solubility curves calculated by equation 1 assuming ideality. Analyzing **Figure 1** it is possible to see that assuming ideality very satisfactory results are obtained, while the experimental eutectic temperature of each binary mixture (**Table S7**) is at least 10 K below to the lowest melting temperature of their constituents pure compounds.
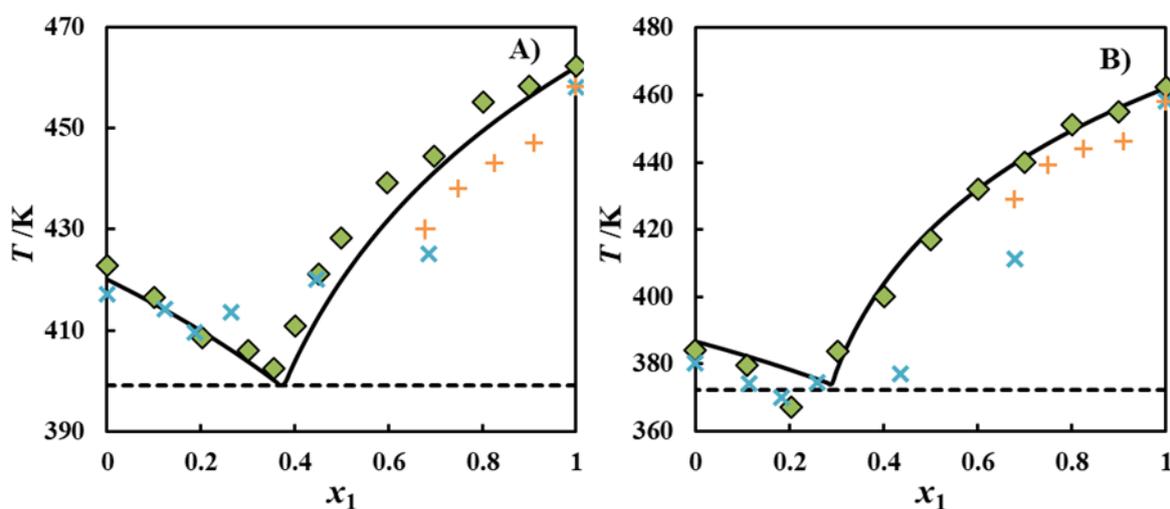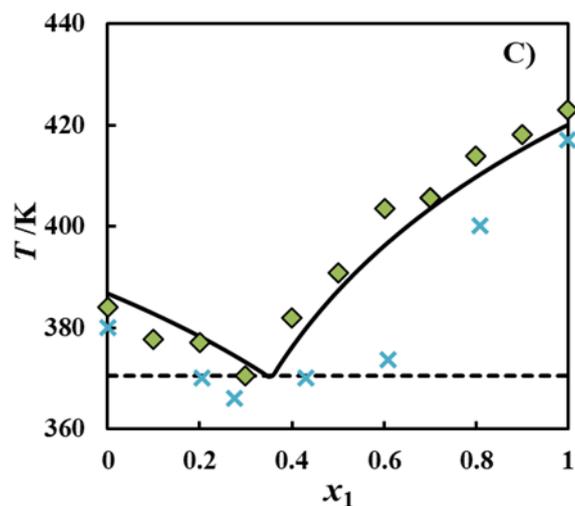
Figure 1. Phase diagrams of the binary systems composed of: A) sucrose (1)+glucose (2); B) sucrose (1)+fructose (2); C) glucose (1)+fructose (2). Legend: (♦) Data from this work; (×) Kelly and Brown[12]; (+) Bhandari and Hartel[13]; (—) Ideality curve; (---) Experimental eutectic temperature.

The data measured in this work is in Figure 1 compared with values previously reported in the literature.[12,13] The new data reported in this work show, in most cases, consistently higher melting temperatures than those previously reported. The data from Bhandari and Hartel[13], in the limited composition range studied, are close to the data from this work, while those from Kelly and Brown[13] show considerable differences particularly in the region rich in the compound with higher melting point.

The (x_1, T) projections of the ternary phase diagram sucrose+glucose+fructose are presented in **Figure 2**, where the solid black lines represent the SLE curve assuming ideality. The 3D surface is also represented in **Figure 2**, comparing the experimental data with ideality predictions. Other perspectives are presented in SI (**Figure S1**). **Figure S2** illustrates a plane projection of the 3D phase diagram with the respective eutectic compositions and the isothermal lines.

The eutectic temperatures of the ternary and binary mixtures of sugars are well above room temperature, in contradiction with some recent reports that claim these mixtures to be deep eutectic solvents and liquid at room temperature.[33] As shown before, the liquid phase of these mixtures behaves almost ideally, as the interactions between the different sugar molecules is similar to those of the pure compounds, forming simple eutectic

mixtures, not presenting a temperature depression to the ideal eutectic temperature of significant magnitude. Although theoretically these mixtures could potentially form DES, since they have both hydrogen-bond acceptors (HBA) and hydrogen-bond donors (HBD), the hydrogen bonds (HB) are present in both pure compounds, and in the liquid mixture the amount of HB formed or destroyed as result of the mixture is negligible.
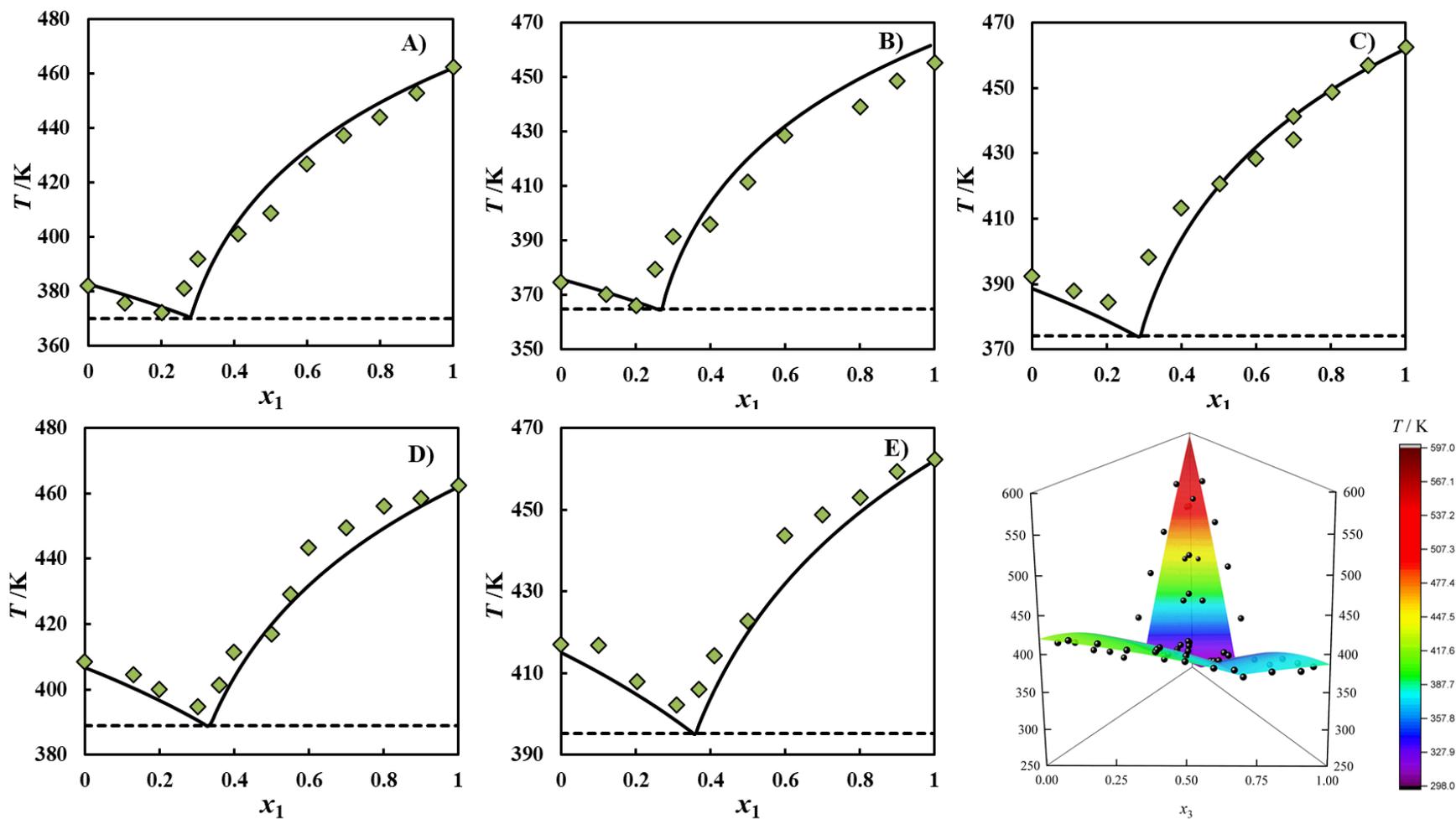
Figure 2. Representation of the solid-liquid equilibria of the ternary mixture sucrose+glucose+fructose, at constant glucose/fructose molar ratio, as a function of sucrose mole fraction (x_1): A) 0.10 glucose + 0.90 fructose; B) 0.25 glucose + 0.75 fructose; C) 0.50 glucose + 0.50 fructose; D) 0.75 glucose + 0.25 fructose; and E) 0.90 glucose + 0.10 fructose. The last figure represents the 3D phase diagram of the mixture. Legend: (●,♦) Data from this work; (—) Ideality curve; (---) Experimental eutectic temperature.

Thermodynamic behavior of [Ch]Cl + sugars systems

The experimental SLE data for the mixtures of [Ch]Cl with the six different sugars studied (sucrose, glucose, fructose, arabinose, mannose and xylose) are reported in **Table S4** and plotted in **Figure 3**. All systems present a eutectic point close to equimolar composition. The coordinates of the eutectic points are reported in **Table S8.** The activity coefficients of the ionic compound are always close to one, as shown in **Table S4** and **Figure S3,** indicating that [Ch]Cl presents a quasi-ideal behavior in the liquid phase. This behavior can be related to the stability of [Ch]Cl in solution as reported before.[34] However, the sugars activity coefficients show, in most of the cases, significant negative deviations to the ideality. These are particularly strong for the systems [Ch]Cl(1)+arabinose(2) and [Ch]Cl(1)+sucrose(2), where the values of the activity coefficient are very low in all the composition range, and for the binaries [Ch]Cl(1)+glucose(2) and [Ch]Cl(1)+xylose(2), with $\gamma(x_{[Ch]Cl}=0.6)<0.3$. These values suggest the formation of novel and favorable interactions between [Ch]Cl and the sugars, that are not present in the pure sugars. These interactions are related with the formation of HBs with the [Ch]Cl chloride anion and seem to be favored by some sugar configurations, as demonstrated by the difference in the values of the activity coefficient between the two isomers arabinose and xylose.

The estimated parameters for the two models during the correlation of the experimental data are reported in **Table S9.** The mRK model leads to a better description of the phase diagrams than NRTL, as shown in **Figure 3** and by the temperature deviation as defined in the SI (equation S6). Even using a temperature dependency the NRTL model cannot represent the data as well as the mRK, due to the asymmetry of the systems (Figure S3). As mentioned above while the activity coefficients of [Ch]Cl is very close to one the sugars present very low values for this property, where the mRK is quite suitable to represent such type of systems. Thus, this model was chosen as the basis to calculate the activity coefficients to be used in the COSMO-RS fine-tuning procedure as described below.
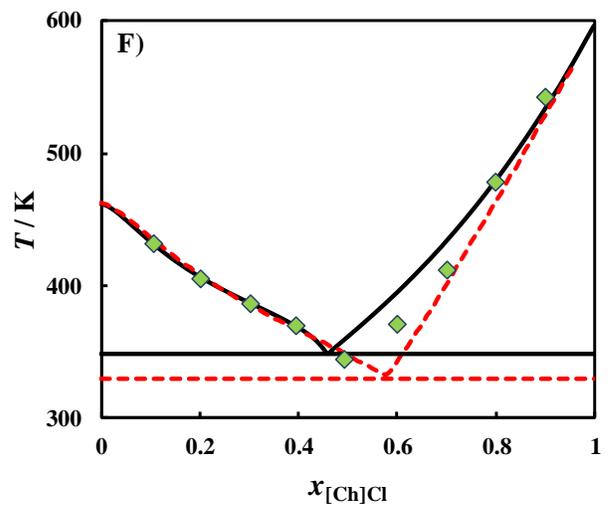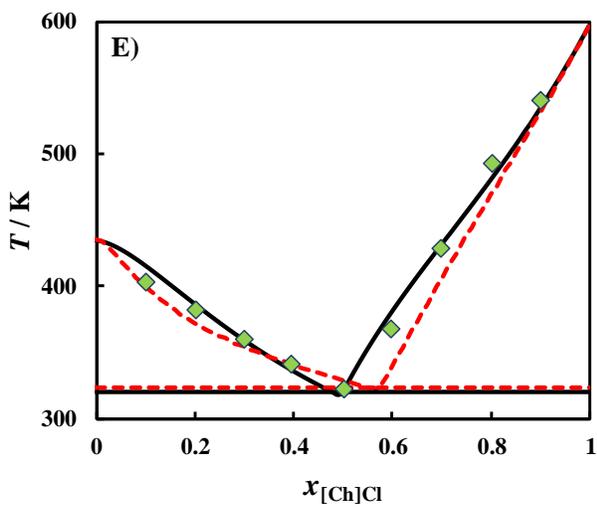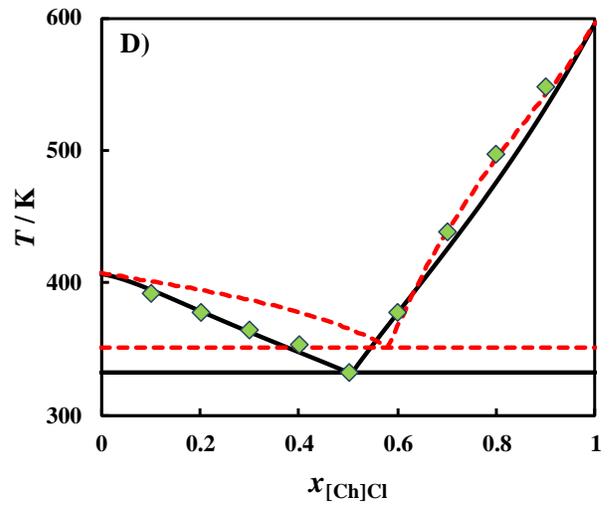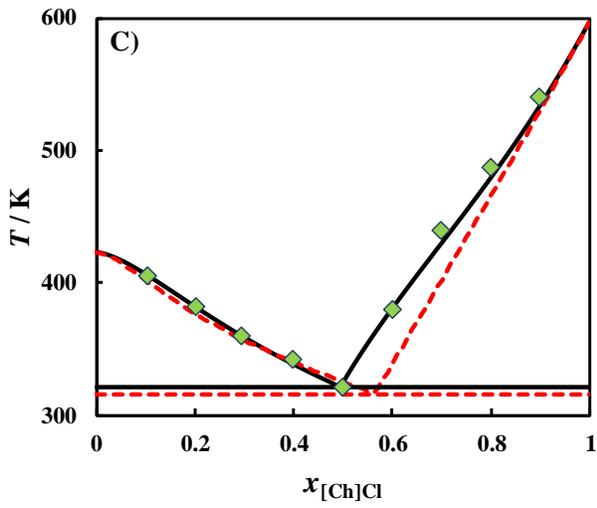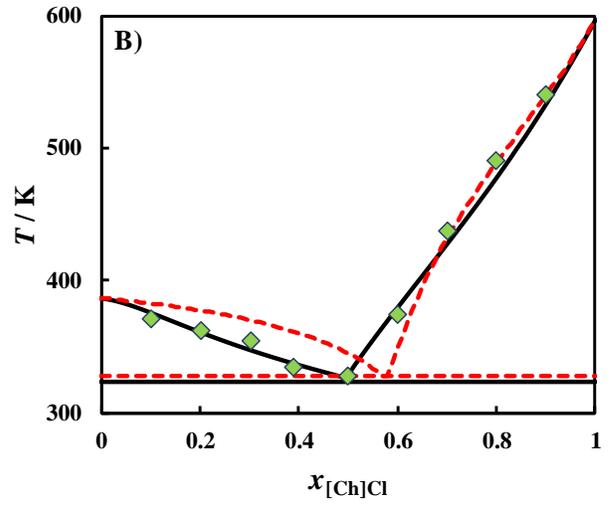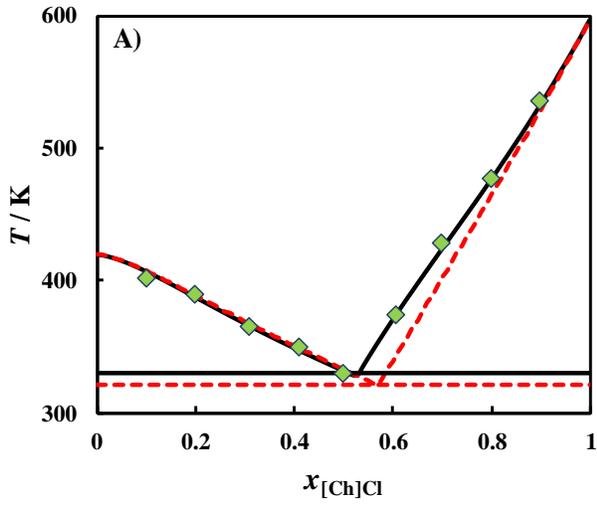
Figure 3. Solid-liquid phase diagrams for the binary mixtures composed of [Ch]Cl and: A) glucose, B) fructose, C) xylose, D) mannose, E) arabinose, and F) sucrose. Legend: (♦) experimental data from this work, (---) NRTL modeling, and (—) mRK modeling.

COSMO-RS description of the thermodynamic behavior of [Ch]Cl + sugars systems

Original COSMO-RS model was used to predict the phase diagrams of the [Ch]Cl + sugar systems. After, some sensitivity tests and analysis, when the values on heat capacity upon melting were used as given above, the COSMO-RS lead, generally, to eutectic temperatures well below the experimental values and, in some cases, as shown in the system containing sucrose, the solubility curves do not even intersect. As can be seen in **Figure 4**, even considering $\Delta_m Cp = 0$ J·mol^{-1}·K^{-1}, the descriptions obtained are not satisfactory particularly concerning the sugars solubility curve, what makes the predictions unreliable. Although the eutectic point for the systems with xylose and arabinose are estimated with a moderated error, the rest of the systems show predicted eutectic temperatures much lower than the experimental ones, and for the system [Ch]Cl+sucrose the two solubility curves never intersect at temperatures above the absolute zero.

The poor performance of COSMO-RS has already been shown by us[19] as in other systems containing [Ch]Cl, since COSMO-RS predicts very small values for the activity coefficients at lower temperatures. In order to improve the poor performance of COSMO-RS and aiming at improving the estimations of the [Ch]Cl+sugar SLE, a fine-tuning of the COSMO-RS parameters was attempted. The hydrogen bond contribution to the excess enthalpy was unusually high (>5000 J·mol^{-1}, as shown in **Figure S4**) and thus, the parameters corresponding to the hydrogen bond interaction were optimized. Additionally, the misfit parameters were also fitted to the experimental data. The optimized parameters are reported in **Table S10** and the procedure detailed in SI.
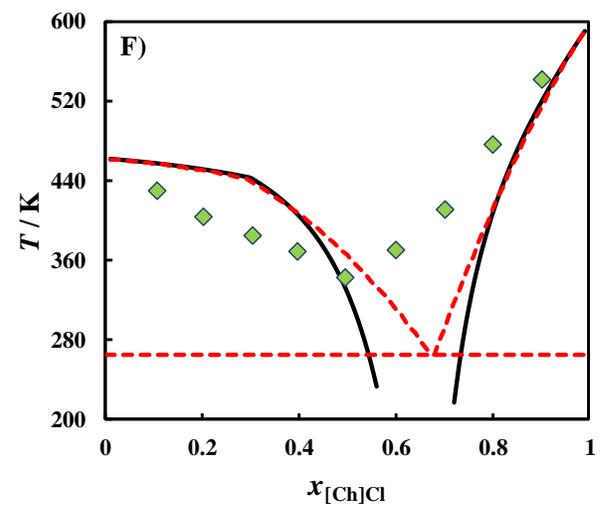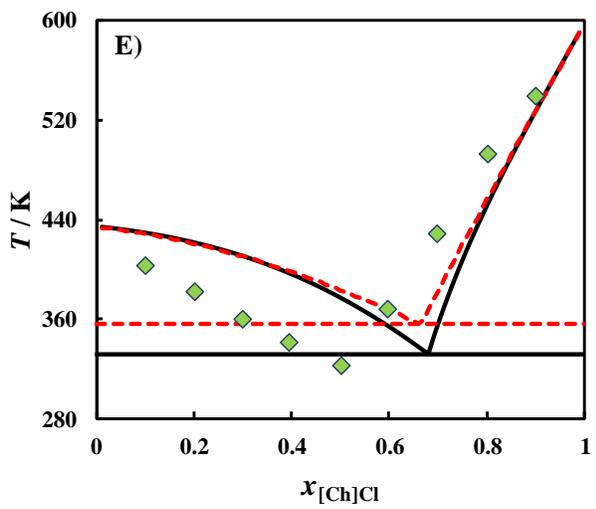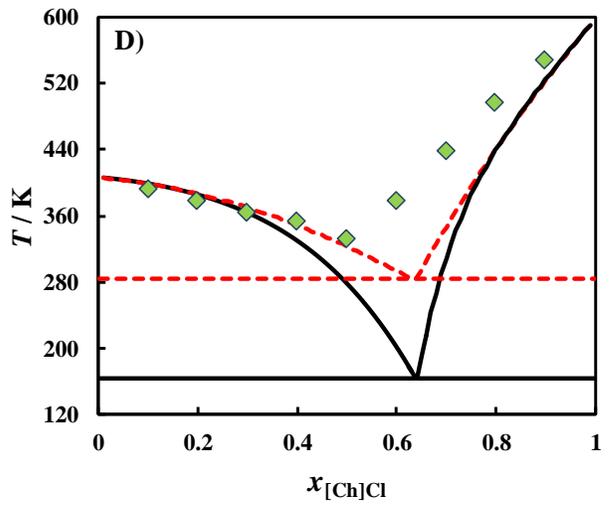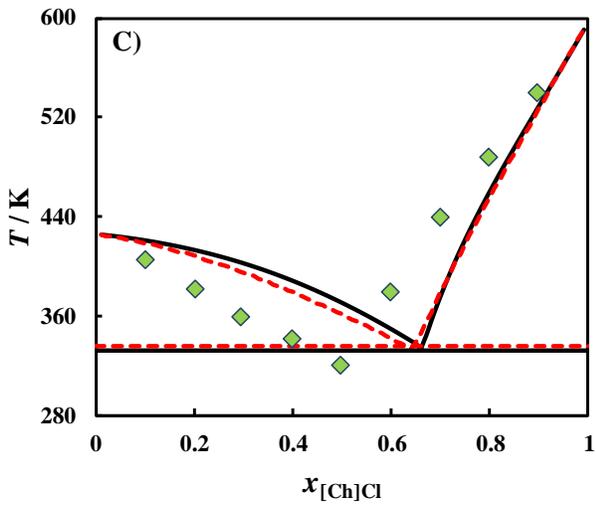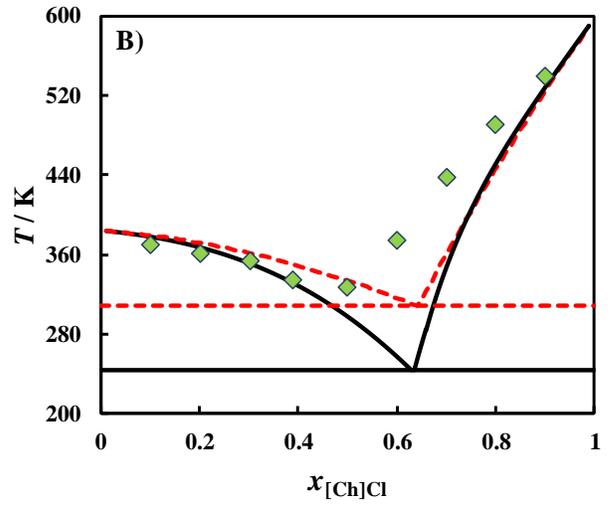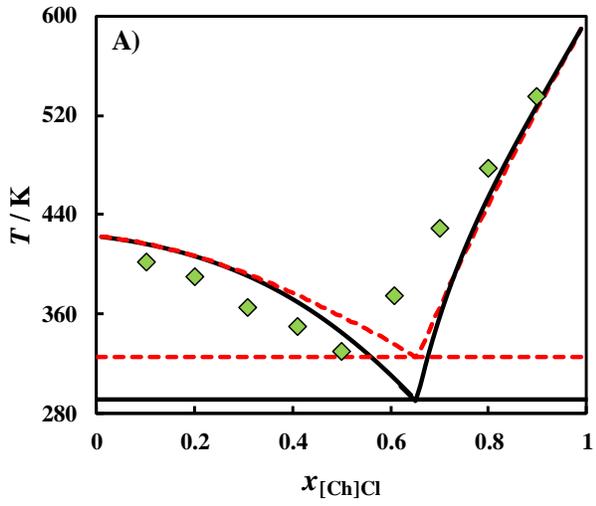
Figure 4. Solid-liquid phase diagrams for the binary mixtures composed of [Ch]Cl and sugars: A) glucose, B) fructose, C) xylose, D) mannose, E) arabinose, and F) sucrose. Symbols: (♦) experimental data from this work; (—) original COSMO-RS, and (- -) tuned COSMO-RS.

The SLE phase diagrams obtained using the modified parameters are plotted in **Figure 4**, showing a significant improvement on the calculation of the eutectic temperatures. Furthermore, the estimated excess enthalpy is now more reliable as shown in **Figure S4**. For the mixture [Ch]Cl+sucrose the problem observed before, concerning the inability to calculate the eutectic temperature, was overcome although the behavior is still not correctly reproduced (Figure 4F). In general COSMO-RS underestimates the non-ideality of the sugars and overestimates the non-ideality of choline chloride.

Prediction of new DES using COSMO-RS

The tuned COSMO-RS parameters were used to estimate the eutectic points of novel ternary DES, formed by [Ch]Cl and two different sugars (**Table S12**). Sucrose was not included in this study due to the poor results obtained in the previous section. Observing **Table S12** it is clear that in some cases results are somewhat unexpected. An evidence of that is the low content of one of the sugars in the estimated eutectic compositions of some mixtures {e.g. [Ch]Cl(1)+arabinose(2)+fructose(3) and [Ch]Cl(1)+arabinose(2)+mannose (3)}. In these cases we are dealing with a quasi-binary system, instead of a ternary, with the estimated values consistent to what can be found in Table S11.

Although the estimated values can be somehow influenced by the error of the model, some conclusions can be drawn in order to design novel ternary DES. The lower eutectic temperatures observed correspond to mixtures involving mannose, which present eutectic temperatures always inferior to 295.2 K. However only the mixture [Ch]Cl(1)+mannose(2) +xylose(3) presents what seems to be a more adequate proportion between the mole fractions of the two sugars. Another interesting eutectic system is formed by [Ch]Cl(1)+fructose(2)+glucose(3), which have an estimated eutectic temperature around 298 K.
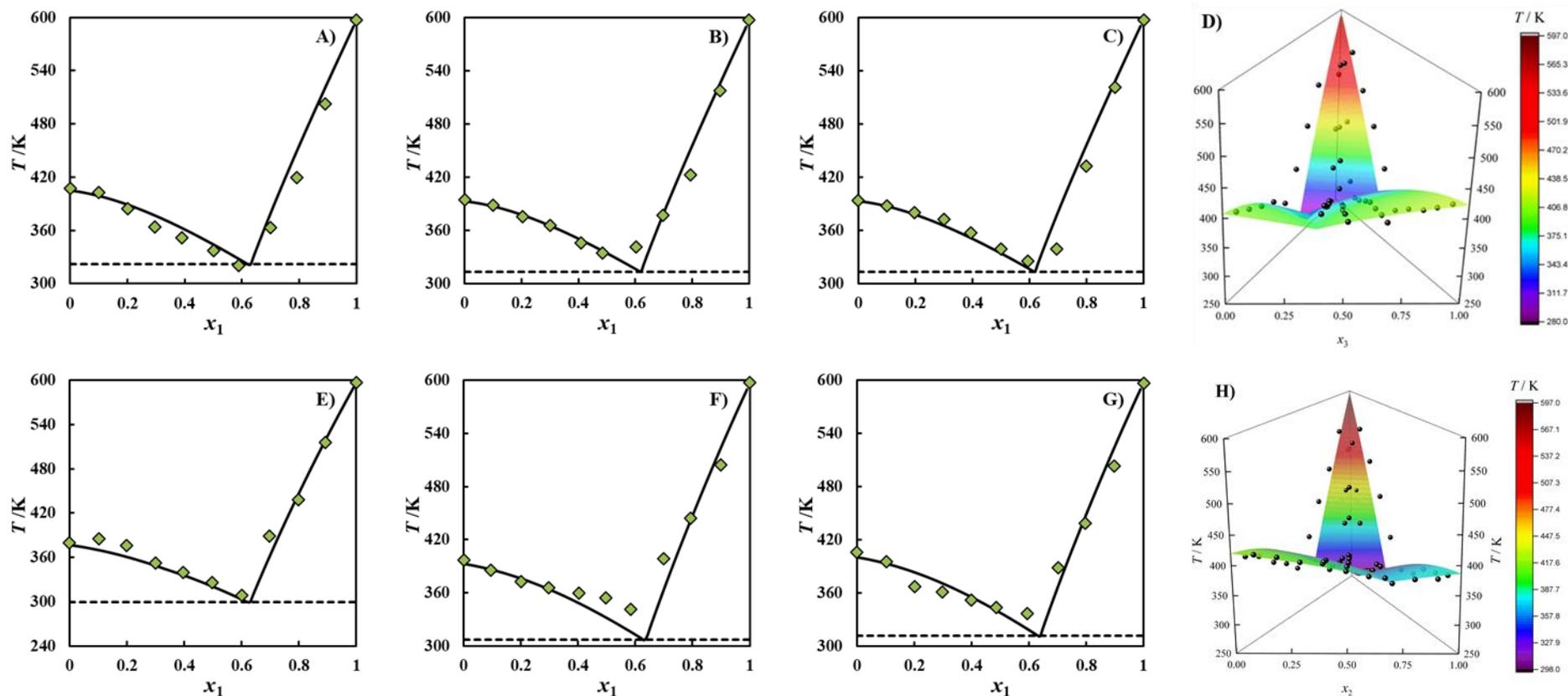
Figure 5. Solid-liquid behavior of the mixtures composed by: [Ch]Cl(1)+mannose(2)+xylose(3) as a function of [Ch]Cl (x_1): A) 0.33 mannose + 0.67 xylose; B) 0.50 mannose + 0.5 xylose; C) 0.67 mannose + 0.33 xylose; and [Ch]Cl(1)+fructose(2)+glucose(3), as a function of [Ch]Cl (x_1): E) 0.33 fructose + 0.67 glucose; F) 0.50 fructose + 0.50 glucose; G) 0.67 fructose + 0.33 glucose. Figure D) and H) represents the 3D phase diagram of [Ch]Cl(1)+mannose(2)+xylose(3) and [Ch]Cl(1)+fructose(2)+glucose(3), respectively. Legend: (●,♦) Experimental data from this work; (—) tuned COSMO-RS prediction.

The phase diagram of the two mentioned ternary systems {[Ch]Cl(1)+mannose(2)+xylose(3) and [Ch]Cl(1)+fructose(2)+glucose(3)} were experimentally measured at different sugar proportions. Results are reported in **Table S5** and presented in **Figure 5,** along with their respective binary systems.

The solubility curves were estimated by the tuned COSMO-RS and are also presented in **Figure 5**. The tuned COSMO-RS descriptions are in very good agreement with the experimental data measured in this work. However, the experimental temperatures in the eutectic point are slightly higher than the estimated by the tuned COSMO-RS, as observed above for the binaries (**Figure 4**). The estimated eutectic points coordinates are described in **Table S13** and the projections of the locus of the eutectic points depicted in **Figure S5**.

Since most of the studied systems present rather high melting eutectic points, in general well above room temperature, we decided to measure the amount of water required to bring the eutectic mixtures melting point down to 298.15 K. These values are reported in **Table S1**. To be a liquid at room temperature, the system [Ch]Cl+mannose needs just 3 wt% of water, while the system [Ch]Cl+xylose requires 9 wt% of water. In general, a water content lower than 10 wt% is enough to reduce the melting point of the [Ch]Cl+sugars mixtures to values close to the room temperature. Given the high hygroscopicity of [Ch]Cl this water can be easily absorbed from the atmosphere. However, it is important to state that 3 wt% of water corresponds to 35 mol% while, 10 wt% corresponds to 65 mol%. From a thermodynamic point of view, we are now dealing with aqueous solutions of sugar+[Ch]Cl. The addition of water to these systems leads to a higher number of potential hydrogen bonds between the solutes and water, decreasing their densities and viscosities, and turning the final mixtures into systems with enhanced transport properties for industrial applications as described below.

Densities

The experimental density data at the eutectic composition for the binary and ternary [Ch]Cl-sugar systems, and the same mixtures with water (water content present in **Table S1**) are presented in the SI (**Figures S6** and **S7**, **Tables S14** and **S15**). As expected, the

density decreases linearly with increasing temperature and with the addition of water. For the binary systems, in the studied temperature range, the density follows the rank; mannose > fructose > glucose > xylose, but systems containing the two last present very similar densities. This trend suggests that systems involving hexoses present higher densities than the ones involving pentoses. However, after the addition of water (8 and 9 wt% to the systems involving glucose and xylose, respectively) there is a much more evident difference between their densities. In general, the density of systems containing water is lower (reduction within the range 0.82 – 2.22%) than the density of the dry mixtures. Concerning the ternary systems, [Ch]Cl+fructose+glucose present a higher density than [Ch]Cl+mannose+xylose.

Viscosities

Viscosity measurements at the eutectic composition for the binary and ternary [Ch]Cl-sugar systems and of the same mixtures with water (water content **Table S1**) were carried out in the temperature range (293.15 to 373.15) K. Results are presented in **Figures 6** and **7**, and **Tables S16** and **S17 of SI**. The viscosity of the systems studied decrease with increasing temperature and with the addition of water. Similarly to the density, viscosity follows the rank; mannose > fructose > glucose > xylose, but systems containing the fructose and mannose are very close in terms of viscosity. In this way, the number and position of the functional groups strongly influence the behavior of these systems. The addition of water reduces by approximately half the viscosities of the dry mixtures. Concerning the ternary systems investigated, the mixture [Ch]Cl+fructose+glucose presents the highest viscosity, but again, with the addition of water this value decreases substantially (Figure 7). The high viscosities presented by the dry systems investigated here may be attributed to the strong hydrogen bonds between the components. Moreover, the large size of the components lead to a small void volume and, therefore, a lower mobility of the species contributing to the high viscosities observed.
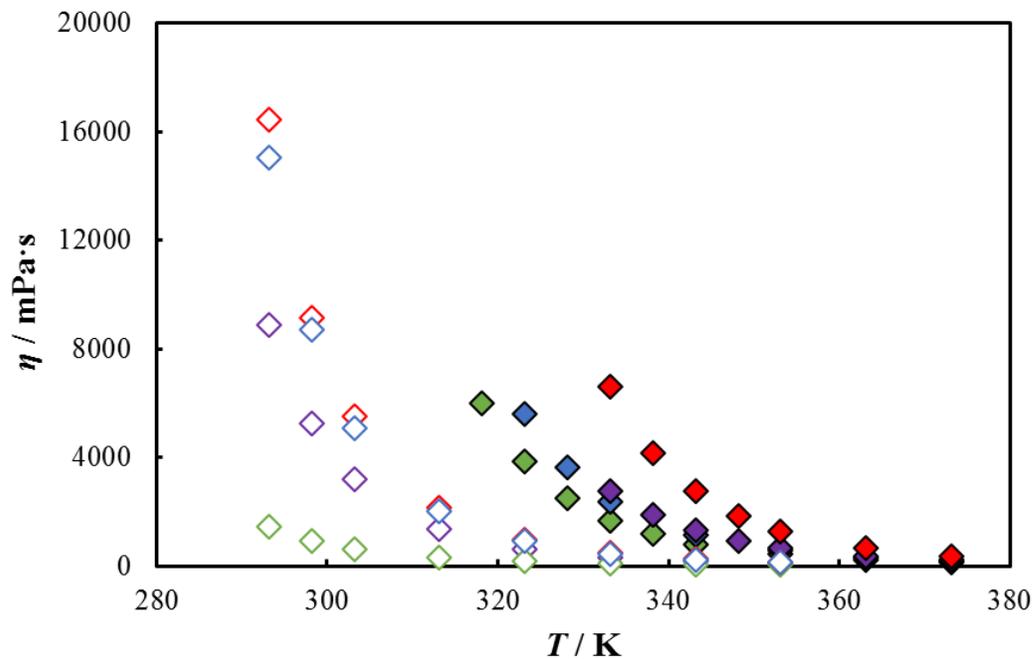
Figure 6. Viscosity of the binary systems [Ch]Cl+sugars at different temperatures. The full markers correspond to the dry systems while the empty markers to the same mixture with water: (♦) [Ch]Cl+mannose; (♦) [Ch]Cl+fructose; (♦) [Ch]Cl+glucose; (♦) [Ch]Cl+xylose.
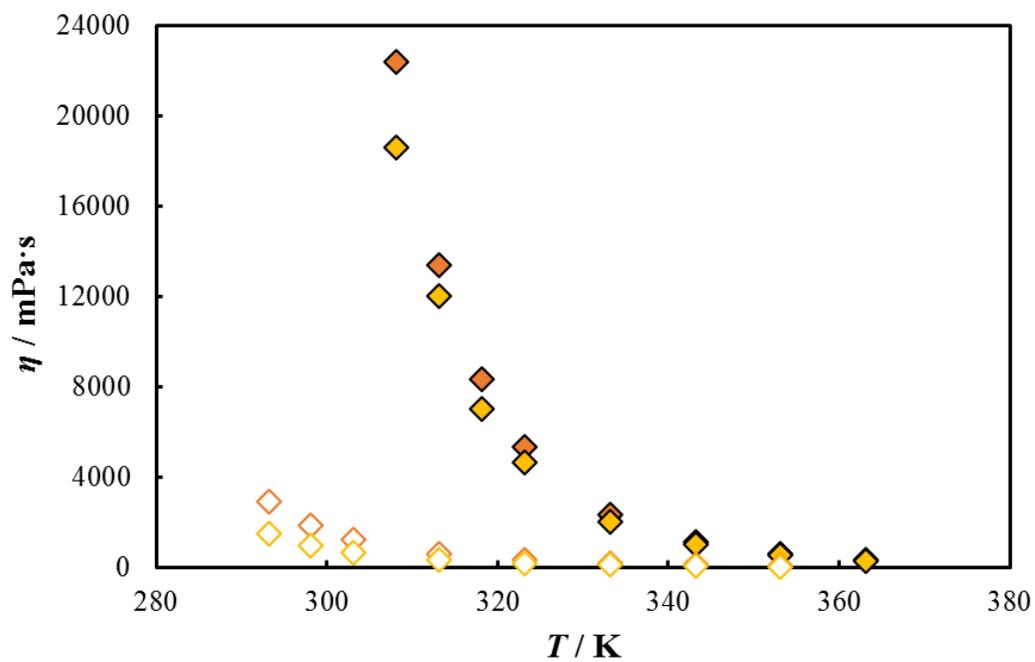
Figure 7. Viscosity of the ternary systems [Ch]Cl+sugar+sugar at different temperatures. The full markers correspond to the dried systems while the empty markers to the same mixture with water: (♦) [Ch]Cl+fructose+glucose; (♦) [Ch]Cl+mannose+xylose.

Solvatochromic Parameters

The Kamlet-Taft solvatochromic parameters of the [Ch]Cl-sugar were measured at 323.15 K and are presented in **Figure 8** and **Table S18** (an a brief description available in SI). Due to high viscosity of some mixtures, it was not possible to measure their solvatochromic parameters without the presence of water. To the best of our knowledge, no such experimental data is available in the literature.

Polarizablility, π*

The parameter π* provides a measure of the solvent polarizability. The π* values obtained here are between 1.1 and 1.3, considerably higher than those of conventional organic solvents (**Table S18**). However, they present values similar with other [Ch]Cl-based DES,[35] and are higher than those obtained for tetraalkylammonium-based DES.[35,36] This indicates that choline chloride plays an important role on the polarizability of the mixture. Moreover, the hydrophilic character of the mixtures investigated in this work contributes to higher values of π*. Hydrophobic mixtures of menthol with different HBD presented much lower values.[35] These differences are related with the fact that cholinium based DES are constituted by charged moieties with polar groups, more polar than the menthol-based mixtures formed by non-charged compounds. Among the sugars studied, the role of the HBD is not clear since they present very similar structures. However, the system [Ch]Cl+sucrose (+water) stands out. In general, ternary systems present lower values than binaries, showing that the addition of other HBD decreases the mixture polarizability. As expected, the addition of water increases the value of π*.

Hydrogen bonding acceptor ability, β

The parameter β describes the hydrogen bond acceptor capacity or hydrogen-bond basicity. When comparing the β values obtained in this work with other [Ch]Cl-based DES,[35] similar

values are obtained, while tetraalkylammonium-based DES[35,36] present higher values of β. This highlights the importance of the nature of the HBA and its interactions with the HBD. Among the systems containing water the different HBD used changes β from 0.36, ([Ch]Cl+sucrose) to 0.53 ([Ch]Cl+fructose). This considerable difference shows the important effect of the HBD on the basicity of the mixtures. The β values reported in the literature (**Table S18**) are much higher for the very strong HBDs like methanol and ethanol, but in some cases the values found in this work are close to the basicity of acetone.

Hydrogen bonding donor ability, α

The Kamlet-Taft parameter α describes the hydrogen bond acceptor capacity or the solvent acidity. The values obtained are in general higher than those obtained for tetraalkylammonium-based DES[36] and, as in the other parameters, similar to those obtained for [Ch]Cl-based DES.[35] All mixtures studied present α's higher than 1 and thus, higher than most of the organic solvents used nowadays (**Table S18**). Among the different HBD used, sucrose system with water stands, with α equal to 1.27, while the other binary systems (+water) present similar values. The system [Ch]Cl+mannose+xylose (+water) presents a value surprisingly low when comparing with the other ternary investigated here. The reported results suggest that the parameter α of the investigated mixtures is mainly driven by the HBA.
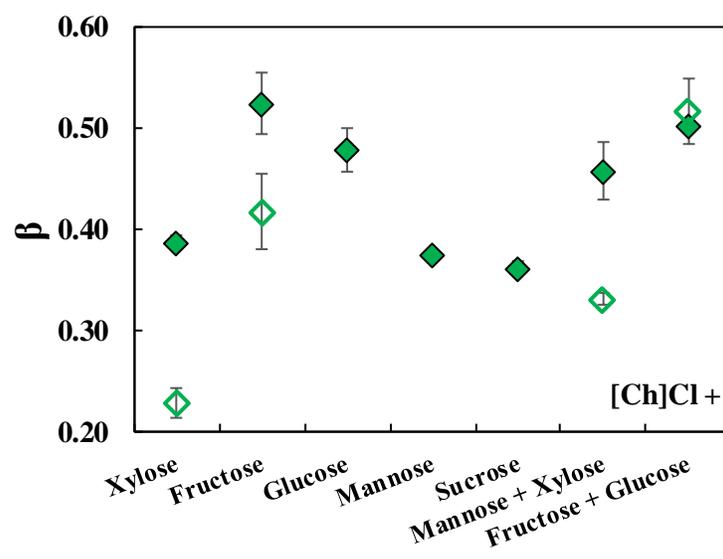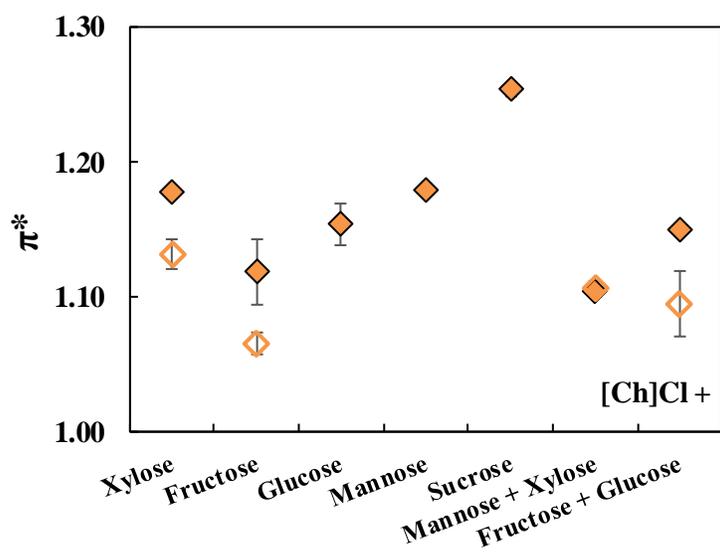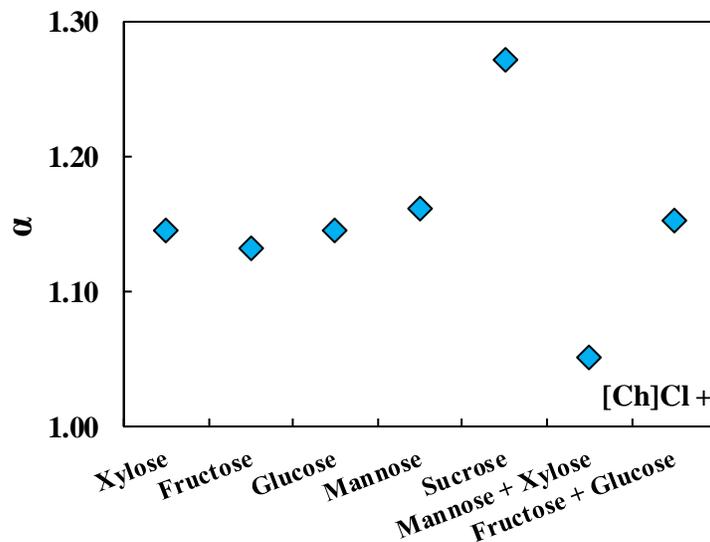
Figure 8. Kamlet-Taft solvatochromic parameters of the [Ch]Cl-based mixtures studied at 323.15 K. Full symbols correspond to [Ch]Cl+sugar+water (9 wt%) mixtures; empty symbols correspond to [Ch]Cl+sugar mixtures.

In summary, in this work the SLE phase diagrams of eutectic mixtures composed of sugar+sugar, sugar+sugar+sugar and [Ch]Cl+sugars were measured experimentally through visual techniques. For all the binary systems the quality of the data obtained was checked using consistency tests. While, mixtures of sugars present only slight deviations from ideal behavior, the binary mixtures of choline chloride with sugars present eutectic points with much lower temperatures than the sugar+sugar systems, and important negative deviations from the ideal behavior, especially in the sugar solubility curve, were observed. Despite being solids at room temperature, due to its deep temperature depression many of these systems can be considered deep eutectic mixtures. The non-ideal behavior observed for these mixtures was described using NRTL or a modified Redlich-Kister expansion, but due to the marked asymmetry of these systems only m-RK was able to correctly describe the SLE behavior of binary [Ch]Cl+sugar mixtures. Trying to develop a predictive tool to search for new multicomponent systems, a tuned version of COSMO-RS was proposed. Targeting liquid mixtures at room temperature, and in order to avoid an extensive number of experimental measurements, the tuned COSMO-RS was applied to estimate the eutectic points of possible novel ternary DES containing [Ch]Cl and two sugars. Results were

checked by measuring experimentally two ternary systems [Ch]Cl+mannose+xylose and [Ch]Cl+fructose+glucose showing that COSMO-RS can be a useful tool for screening and designing deep eutectic solvents of this kind. The amount of water required for the binary [Ch]Cl+sugar mixtures to be liquid at room temperature was found to vary between 3 and 9 wt%. The densities and viscosities of the dried and wet systems were measured in order to evaluate the potential of these systems to be used as solvents in industrial applications. The mixtures investigated were further characterized by the measurement of their solvatochromic parameters. While choline chloride plays the major role on the dipolarity/polarizability and acidity of the mixture, the parameter β is strongly influenced by both, the HBD and HBA used.

Acknowledgments

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

References

(1)   Anastas, P. T.; Kirchhoff, M. M. Origins, Current Status, and Future Challenges of Green Chemistry. *Acc. Chem. Res.* **2002**, *35* (9), 686–694, DOI 10.1021/ar010065m.

(2)   Francisco, M.; Van Den Bruinhorst, A.; Kroon, M. C. Low-Transition-Temperature Mixtures (LTTMs): A New Generation of Designer Solvents. *Angew. Chem. Int. Ed.* **2013**, *52* (11), 3074–3085, DOI 10.1002/anie.201207548.

(3)   Dai, Y.; van Spronsen, J.; Witkamp, G.-J. J.; Verpoorte, R.; Choi, Y. H. Natural Deep Eutectic Solvents as New Potential Media for Green Technology. *Anal. Chim. Acta* **2013**, *766*, 61–68, DOI 10.1016/j.aca.2012.12.019.

(4)   Hayyan, A.; Mjalli, F. S.; Alnashef, I. M.; Al-Wahaibi, T.; Al-Wahaibi, Y. M.; Hashim, M. A. Fruit Sugar-Based Deep Eutectic Solvents and Their Physical Properties. *Thermochim. Acta* **2012**, *541*, 70–75, DOI 10.1016/j.tca.2012.04.030.

(5)   Hayyan, A.; Mjalli, F. S.; Alnashef, I. M.; Al-Wahaibi, Y. M.; Al-Wahaibi, T.; Hashim, M. A. Glucose-Based Deep Eutectic Solvents: Physical Properties. *J. Mol. Liq.* **2013**, *178*, 137–141, DOI 10.1016/j.molliq.2012.11.025.

(6)   Maugeri, Z.; Domínguez de María, P. Novel Choline-Chloride-Based Deep-Eutectic-Solvents with Renewable Hydrogen Bond Donors: Levulinic Acid and Sugar-Based Polyols. *RSC Adv.* **2012**, *2* (2), 421–425, DOI 10.1039/C1RA00630D.

(7)   Paiva, A.; Craveiro, R.; Aroso, I.; Martins, M.; Reis, R. L.; Duarte, A. R. C. Natural Deep Eutectic Solvents – Solvents for the 21st Century. *ACS Sustain. Chem. Eng.* **2014**, *2* (5), 1063–1071, DOI 10.1021/sc500096j.

(8)   Carriazo, D.; Serrano, M. C.; Gutiérrez, M. C.; Ferrer, M. L.; del Monte, F. Deep-

Eutectic Solvents Playing Multiple Roles in the Synthesis of Polymers and Related Materials. *Chem. Soc. Rev.* **2012**, *41* (14), 4996–5014, DOI 10.1039/c2cs15353j.

(9)   Martins, M.; Aroso, I. M.; Reis, R. L.; Duarte, A. R. C.; Craveiro, R.; Paiva, A. Enhanced Performance of Supercritical Fluid Foaming of Natural-Based Polymers by Deep Eutectic Solvents. *AIChE J.* **2014**, *60* (504), 3701–3706, DOI 10.1002/aic.14607.

(10)   Larriba, M.; Ayuso, M.; Navarro, P.; Delgado-Mellado, N.; Gonzalez-Miquel, M.; García, J.; Rodríguez, F. Choline Chloride-Based Deep Eutectic Solvents in the Dearomatization of Gasolines. *ACS Sustain. Chem. Eng.* **2018**, *6* (1), 1039–1047, DOI 10.1021/acssuschemeng.7b03362.

(11)   Radošević, K.; Cvjetko Bubalo, M.; Gaurina Srček, V.; Grgas, D.; Landeka Dragičević, T.; Redovniković, R. I. Evaluation of Toxicity and Biodegradability of Choline Chloride Based Deep Eutectic Solvents. *Ecotoxicol. Environ. Saf.* **2015**, *112*, 46–53, DOI 10.1016/j.ecoenv.2014.09.034.

(12)   Kelly, F. H. C.; Brown, D. W. Phase Equilibria in the System Sucrose-Glucose-Fructose. *J. Chem. Technol. Biotechnol.* **1967**, *17* (5), 125–126, DOI https://doi.org/10.1002/jctb.5010170502.

(13)   Bhandari, B. R.; Hartel, R. W. Co-Crystallization of Sucrose at High Concentration in the Presence of Glucose and Fructose. *J. Food Sci.* **2002**, *67* (5), 1797–1802, DOI 10.1111/j.1365-2621.2002.tb08725.x.

(14)   Miller, E.; Hartel, R. W. Sucrose Crystallization in Caramel. *J. Food Eng.* **2015**, *153*, 28–38, DOI 10.1016/j.jfoodeng.2014.11.028.

(15)   Roos, Y. H.; Karel, M.; Labuza, T. P.; Levine, H.; Mathlouthi, M.; Reid, D.; Shalaev, E.; Slade, L. Melting and Crystallization of Sugars in High-Solids Systems. *J. Agric. Food Chem.* **2013**, *61* (13), 3167–3178, DOI 10.1021/jf305419y.

(16)   Fernandez, L.; Silva, L. P.; Martins, M. A. R.; Ferreira, O.; Ortega, J.; Pinho, S. P.; Coutinho, J. A. P. Indirect Assessment of the Fusion Properties of Choline Chloride from Solid-Liquid Equilibria Data. *Fluid Phase Equilib.* **2017**, *448*, 9–14, DOI 10.1016/j.fluid.2017.03.015.

(17) Crespo, E. A.; Silva, L. P.; Martins, M. A. R.; Fernandez, L.; Ortega, J.; Ferreira, O.; Sadowski, G.; Held, C.; Pinho, S. P.; Coutinho, J. A. P. Characterization and Modeling of the Liquid Phase of Deep Eutectic Solvents Based on Fatty Acids/Alcohols and Choline Chloride. *Ind. Eng. Chem. Res.* **2017**, *56* (42), 12192–12202, DOI 10.1021/acs.iecr.7b02382.

(18) Pontes, P. V. A.; Crespo, E. A.; Martins, M. A. R.; Silva, L. P.; Neves, C. M. S. S.; Maximo, G. J.; Hubinger, M. D.; Batista, E. A. C.; Pinho, S. P.; Coutinho, J. A. P.; et al. Measurement and PC-SAFT Modeling of Solid-Liquid Equilibrium of Deep Eutectic Solvents of Quaternary Ammonium Chlorides and Carboxylic Acids. *Fluid Phase Equilib.* **2017**, *448*, 69–80, DOI 10.1016/j.fluid.2017.04.007.

(19) Klamt, A. Conductor-like Screening Model for Real Solvents: A New Approach to the Quantitative Calculation of Solvation Phenomena. *J. Phys. Chem.* **1995**, *99* (7), 2224–2235, DOI 10.1021/j100007a062.

(20) Hurtta, M.; Pitkänen, I.; Knuutinen, J. Melting Behaviour of D-Sucrose, D-Glucose and D-Fructose. *Carbohydr. Res.* **2004**, *339* (13), 2267–2273, DOI 10.1016/j.carres.2004.06.022.

(21) Van Putten, R. J.; Winkelman, J. G. M.; Keihan, F.; Van Der Waal, J. C.; De Jong, E.; Heeres, H. J. Experimental and Modeling Studies on the Solubility of d -Arabinose, d -Fructose, d -Glucose, d -Mannose, Sucrose and d -Xylose in Methanol and Methanol-Water Mixtures. *Ind. Eng. Chem. Res.* **2014**, *53* (19), 8285–8290, DOI 10.1021/ie500576q.

(22) Magoń, A.; Wurm, A.; Schick, C.; Pangloli, P.; Zivanovic, S.; Skotnicki, M.; Pyda, M. Heat Capacity and Transition Behavior of Sucrose by Standard, Fast Scanning and Temperature-Modulated Calorimetry. *Thermochim. Acta* **2015**, *603*, 149–161, DOI 10.1016/j.tca.2014.12.013.

(23) Gong, X.; Wang, C.; Zhang, L.; Qu, H. Solubility of Xylose, Mannose, Maltose Monohydrate, and Trehalose Dihydrate in Ethanol-Water Solutions. *J. Chem. Eng. Data* **2012**, *57* (11), 3264–3269, DOI 10.1021/je300885g.

(24) Prausnitz, J. M.; Lichtenthaler, R. N.; Azevedo, E. G. *Molecular Thermodynamics Fluid Phase Equilibria*; Prentice-Hall, 1986.

(25) Ferreira, O.; Brignole, E. A.; Macedo, E. A. Phase Equilibria in Sugar Solutions Using the A-UNIFAC Model. *Ind. Eng. Chem. Res.* **2003**, *42* (24), 6212–6222, DOI 10.1021/ie030246n.

(26) Martins, M. A. R.; Pinho, S. P.; Coutinho, J. A. P. Insights into the Nature of Eutectic and Deep Eutectic Mixtures. *Accepted in Journal of Solution Chemistry* **2018**.

(27) Renon, H.; Prausnitz, J. M. Local Compositions in Thermodynamic Excess Functions for Liquid Mixtures. *AIChE J.* **1968**, *14* (1), 135–144, DOI 10.1002/aic.690140124.

(28) Ortega, J.; Espiau, F.; Wisniak, J. New Parametric Model to Correlate the Gibbs Excess Function and Other Thermodynamic Properties of Multicomponent Systems. Application to Binary Systems. *Ind. Eng. Chem. Res.* **2010**, *49* (1), 406–421, DOI 10.1021/ie900898t.

(29) Hizaddin, H. F.; Ramalingam, A.; Hashim, M. A.; Hadj-Kali, M. K. O. Evaluating the Performance of Deep Eutectic Solvents for Use in Extractive Denitrification of Liquid Fuels by the Conductor-like Screening Model for Real Solvents. *J. Chem. Eng. Data* **2014**, *59* (11), 3470–3487, DOI 10.1021/je5004302.

(30) Gouveia, A. S. L.; Oliveira, F. S.; Kurnia, K. A.; Marrucho, I. M. Deep Eutectic Solvents as Azeotrope Breakers: Liquid–Liquid Extraction and COSMO-RS Prediction. *ACS Sustain. Chem. Eng.* **2016**, *4* (10), 5640–5650, DOI 10.1021/acssuschemeng.6b01542.

(31) Kang, J. W.; Diky, V.; Chirico, R. D.; Magee, J. W.; Muzny, C. D.; Kazakov, A. F.; Kroenlein, K.; Frenkel, M. Algorithmic Framework for Quality Assessment of Phase Equilibrium Data. *J. Chem. Eng. Data* **2014**, *59* (7), 2283–2293, DOI 10.1021/je500327k.

(32) Cunico, L. P.; Ceriani, R.; Sarup, B.; O'Connell, J. P.; Gani, R. Data, Analysis and Modeling of Physical Properties for Process Design of Systems Involving Lipids. *Fluid Phase Equilib.* **2014**, *362*, 318–327, DOI 10.1016/j.fluid.2013.10.040.

(33)   Choi, Y. H.; van Spronsen, J.; Dai, Y.; Verberne, M.; Hollmann, F.; Arends, I. W. C. E.; Witkamp, G.-J.; Verpoorte, R. Are Natural Deep Eutectic Solvents the Missing Link in Understanding Cellular Metabolism and Physiology? *Plant Physiol.* **2011**, *156* (4), 1701–1705, DOI 10.1104/pp.111.178426.

(34)   López-Porfiri, P.; Brennecke, J. F.; Gonzalez-Miquel, M. Excess Molar Enthalpies of Deep Eutectic Solvents (DESs) Composed of Quaternary Ammonium Salts and Glycerol or Ethylene Glycol. *J. Chem. Eng. Data* **2016**, *61* (12), 4245–4251, DOI 10.1021/acs.jced.6b00608.

(35)   Florindo, C.; McIntosh, A. J. S.; Welton, T.; Branco, L. C.; Marrucho, I. M. A Closer Look into Deep Eutectic Solvents: Exploring Intermolecular Interactions Using Solvatochromic Probes. *Phys. Chem. Chem. Phys.* **2017**, *20* (1), 206–213, DOI 10.1039/C7CP06471C.

(36)   Teles, A. R. R.; Capela, E. V.; Carmo, R. S.; Coutinho, J. A. P.; Silvestre, A. J. D.; Freire, M. G. Solvatochromic Parameters of Deep Eutectic Solvents Formed by Ammonium-Based Salts and Carboxylic Acids. *Fluid Phase Equilib.* **2017**, *448*, 15–21, DOI 10.1016/j.fluid.2017.04.020.
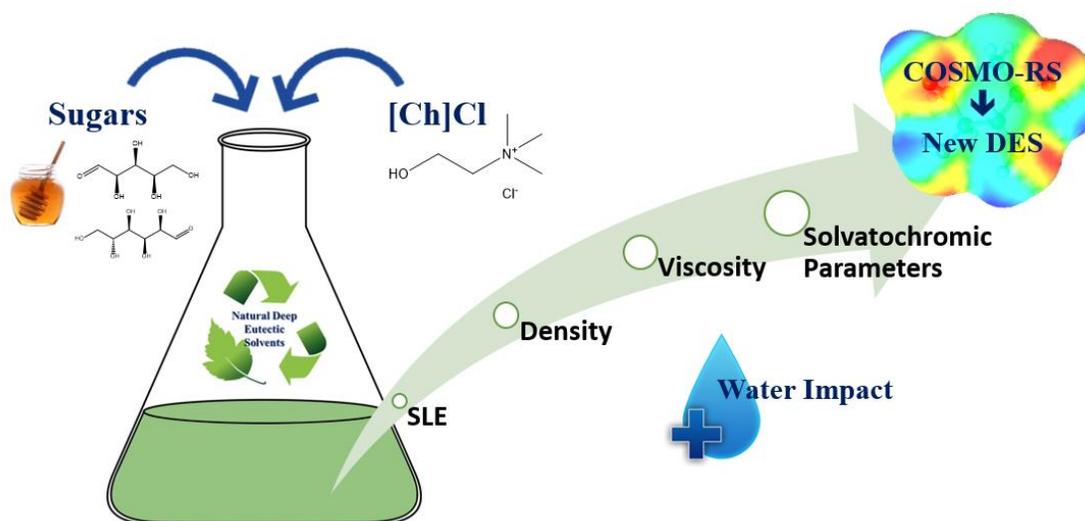
Synopsis: COSMO-RS as a useful tool for the design of natural deep eutectic solvents formed by sugars and choline chloride.