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Insights on the Cellulose Pretreatment at room Temperature by Choline-Chloride-based Deep Eutectic Solvents: An Atomistic Study.

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Abstract.

The pretreatment or disruption of a cellulose I β crystallite, was described from the atomistic interactions evaluated at room temperature within four deep eutectic solvents: choline-chloride ethylene glycol, choline-chloride oxalic acid, choline-chloride urea, and choline-chloride levulinic acid. The analysis was based on the obtained correlations for the Kamlet-Taft α and β parameters with a series of thermodynamic, structural, and energetic properties. The Kamlet-Taft parameters correlated with the thermodynamic properties of the solvent and their changes upon addition of the cellulose crystallite. Structural analysis revealed that the weaker the interactions within the molecules of solvent, the stronger the interactions between the hydroxyl group from cellulose with the chloride anion and with the hydrogen bond donor. Further analysis indicated that the $R - CO - R$ moieties in the hydrogen bond donor within the solvent, interacted better with the cellulose. The hydrogen bond occupancies within the cellulose crystallite, displayed that the main $O6 - H6 \cdots O2/O3$ and $O2 - H2 \cdots O6$ interchain hydrogen bonds in the glucan located at the edge of the solute were replaced by weak $O6 - H6 \cdots O4$ hydrogen bonds in all solvents. This effect was related to the $O - H \cdots Cl$, $C - H \cdots O$, and $O \cdots H - O$ HBs between cellulose and DES molecules and confirmed by the non-covalent interactions obtained through DFT calculations. Finally, the energetic interactions and the atomistic degree of disruption of the cellulose crystallite were not completely described by the Kamlet-Taft β or α parameters separately. Surprisingly, by using the net basicity ($\beta - \alpha$) definition, such correlations were improved suggesting that both parameters must be considered in order to develop new, green, and sustainable solvents for cellulose pretreatment process.

Keywords

Deep eutectic solvents / Cellulose pretreatment / Molecular dynamics simulations / Kamlet-Taft parameters correlations / Solvent net basicity

Introduction.

The global demand of energy is constantly increasing (Zhang et al. 2017), in consequence new efficient, ecological, and economic energy resources and processes are urgently needed (van Putten et al. 2013; Clarke et al. 2018; Körner et al. 2019). Lignocellulosic biomass (LCB) is the largest and greenest source of carbon on Earth (Tang et al. 2017; Körner et al. 2019). The use of the LCB as renewable source has been proposed to produce chemicals, materials, fuels, and energy, currently based on fossil oils (Gunny et al. 2015; Clarke et al. 2018; Tiong et al. 2018; Chen and Mu 2019; Zhou et al. 2020). The efficient use of LCB requires solvents capable to pretreating or dissolving its components (van Putten et al. 2013; Rocha et al. 2017; Tiong et al. 2018), namely, cellulose (40-80%), hemicellulose (15-30%), and lignin (10-25%) (van Osch et al. 2017; Kumar et al. 2020). These processes facilitate accessibility of either incoming third particles (such as reactants, catalysts, etc.) or enzymes (Procentese et al. 2015), to produce valuable products. Unfortunately, the common solvents used for these purposes are organic solvents, H_2SO_4 , H_3PO_4 , and NaOH , which are widely recognized by their potential environment concerns (Ren et al. 2016; Tang et al. 2017; Sert et al. 2018; Kumar et al. 2020).

A new class of solvents, including ionic liquids (ILs) and deep eutectic solvents (DESs) have been proposed for the LCB dissolution or its pretreatment (Swatloski et al. 2002; Pinkert et al. 2009; Francisco et al. 2012; Wang et al. 2012; Zhang et al. 2012; Sharma et al. 2013; Xia et al. 2014; Procentese et al. 2015; Ren et al. 2016; Tang et al. 2017; Clarke et al. 2018; Chen et al. 2019; Chen and Mu 2019; Kumar et al. 2020; Smirnov et al. 2020; Zhang et al. 2020). Despite their unique properties and the ability to dissolve LCB, the ILs (Swatloski et al. 2002; Pinkert et al. 2009; Wang et al. 2012; Kumar et al. 2020) have some drawbacks: high cost, complex synthesis, recycling problems, and toxicity issues (Rocha et al. 2017; Tang et al. 2017; Clarke et al. 2018) hindering their use at commercial or large scale. The DESs, also called low transition temperature mixtures (Rodríguez et al. 2015; Tang et al. 2017), are eutectic mixtures composed by a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD) in a specific HBA:HBD molar ratio. Due to the high number of hydrogen bond interactions, low lattice energy values, and the asymmetry of HBA and HBD, the DESs have much lower melting point than their constituting components, yielding the liquid state of the mixture (Smith et al. 2014; Chen and Mu 2019). Despite the fact that DESs and ILs present similar physicochemical properties (Smith et al. 2014; García et al. 2015; Kalhor and Ghandi 2019), the DESs are low cost (Gorke et al. 2008; Kalhor and Ghandi 2019) easy to synthesize (Brett 2018), non-toxic (Halder and Cordeiro 2019), and biodegradable solvents (Tang et al. 2017). These properties make the DESs an attractive, economical, and green alternative for several applications (Lawes et al. 2010; Abo-Hamad et al. 2015; García et al. 2015; Rodríguez et al. 2015; Faggian et al. 2016; Brett 2018; Körner et al. 2019; Ünlü et al. 2019), including the LCB pretreatment and its conversion (Procentese et al. 2015; Chen and Mu 2019; Körner et al. 2019).

The experimental ability of common DESs, which include the choline-chloride (ChCl) as HBA, to dissolve the LCB is far from that reached by ILs (Francisco et al. 2012; Zhang et al. 2012; Sharma et al. 2013; van Osch et al. 2017; Chen et al. 2019; Morais et al. 2020). However, it has been reported that DESs

are able to pretreat the LCB (Xia et al. 2014; Procentese et al. 2015; Kalhor and Ghandi 2019; Chen and Mu 2019), providing a green and novel way to synthesize valuable derivatives (Sirviö et al. 2015). Furthermore, DESs have been reported in studies to develop biomedical applications (Trache 2018), energy storage, food packaging, and catalysis (Trache et al. 2020). On this regard, the LCB pretreatment with DESs can enhance subsequent steps on the biomass valorization (Xia et al. 2014; Procentese et al. 2015), such as enzymatic hydrolysis (Xia et al. 2014), or acting as an effective media for the cellulose modification (Sirviö et al. 2015; Tang et al. 2017; Smirnov et al. 2020), even at low temperatures (Gunny et al. 2015; Lu et al. 2016).

The LCB dissolution capacity of DESs has been related to the disruption of the hydrogen bonds (HBs) present in the biomass structure by action of the both the HBD and the anion in the HBA (Sharma et al. 2013; Ren et al. 2016; Lu et al. 2016; Häkkinen and Abbott 2019). Ren et al. (2016), Xia et al. (2018), and Liang et al. (2021) found that the experimental solubility of the LCB can be correlated to the ability of the DESs to donating or accepting protons, measured by the Kamlet-Taft α and β parameters, respectively. Furthermore, Ren et al. (2016) also reported that the solubility of the cellulose can be associated with experimental thermodynamic properties of the pure DESs.

Nevertheless, there is a lack of fundamental knowledge regarding the basic interactions between DESs and biomass solutes, including carbohydrates (Mohan et al. 2017; van Osch et al. 2017). The development of new, green, sustainable, and efficient DESs in this field, needs to overcome these limitations. Molecular dynamics (MD) simulations have provided an efficient route to reveal, understand, and predict the microscopic interactions that drive the LCB dissolution (Wang et al. 2012; Mohan et al. 2017; van Osch et al. 2017; Xia et al. 2018; Fu et al. 2020; Smirnov et al. 2020; Zhou et al. 2020). Since the cellulose is the main component within the LCB (40-80%) (van Osch et al. 2017; Kumar et al. 2020), and the high molecular complexity of the LCB, most of the LCB-DES theoretical works reported in the literature, are focused on the cellulose-DES (Smirnov et al. 2020), or glucose-DES (Mohan et al. 2017; Fu et al. 2020) systems. Interestingly, the majority of these studies explored the cellulose dissolution and not its pretreatment.

Mohan et al. (2017) and Smirnov et al. (2020) have used classical MD simulations to reveal the glucose-DES and the cellulose surface-DES interactions, respectively. The authors found, by means of radial distribution functions (RDFs), that the anion from the HBA and the HBD are the main interactions towards the carbohydrates, and therefore responsible of the glucose dissolution and the surface deconstruction process.

Recently, Fu et al. (2020) performed quantum chemical calculations in order to evaluate the strength of the interactions between the cellobiose and DES molecules. The authors found that HBs between the HBA and the HBD are weakened when they interact with the cellobiose. This interaction reduces the cellobiose hydroxyl bond strength, consequently, the cellobiose HB network becomes weaker, favoring its dissolution.

The interaction mechanism between DESs and solutes such as cellulose and the relation with its dissolution or pretreatment process is still unclear (Chen et al. 2019). However, it seems that the HBs between solute and solvent might be the driving forces of such processes. These interactions can be revealed through MD simulations, and they can be further described in terms of the hydrogen bond basicity (Kamlet-Taft β parameter), hydrogen bond acidity (Kamlet-Taft α parameter), and pure thermodynamic properties of the DESs, providing valuable information in order to develop sustainable solvents from *in-silico* calculations.

In the present work, the choline-chloride (ChCl) was selected as HBA, due to its large biodegradability, high biocompatibility, low toxicity, low cost, and biomass-origin (Halder and Cordeiro 2019; Körner et al. 2019; Zhang et al. 2020). Consequently, we have selected the ChCl/ethylene glycol (molar ratio 1:2), ChCl/oxalic acid (1:1), ChCl/urea (1:2), and the ChCl/levulinic acid (1:2) DESs due to their broad range of both viscosity (which spans from 41 cP to ~7600 cP) (D'Agostino et al. 2011; Florindo et al. 2014; Xie et al. 2014; Yadav and Pandey 2014; Chemat et al. 2016; Harifi-Mood and Buchner 2017; Shekaari et al. 2017) and hydrogen bond basicity (from ~0.3 to ~0.6) (Florindo et al. 2018; Kundu et al. 2020). Furthermore, the observed properties have been related with the capability of DESs to dissolve cellulose (Ren et al. 2016).

The present study comprised two stages: (i) the DESs thermodynamic properties, their changes upon the addition of a cellulose $I\beta$ crystallite (cellulose-DES mixture), and their further relation with the Kamlet-Taft β and α parameters values of the DESs, i.e. the solvent behavior point of view. (ii) A description on the ability of DESs to disrupt the cellulose $I\beta$ crystallite and its relationship with the Kamlet-Taft β and α parameters of the DESs, i.e. the cellulose disruption from an atomistic perspective. For such purposes, density (ρ), molar volume (V_m), cohesive energy density (c), enthalpy of vaporization (ΔH_{vap}), Hildebrand parameter (δ), RDFs, cellulose-DES HBs (classical geometric and quantum electronic density definition), HB occupancies, cellulose diffusion coefficient ($D_{cellulose}$), non-bonded potential energy of cellulose ($E_{non-bonded, cellulose}$), and short-range non-bonded pair energies (E_{SR}) have been calculated for ChCl/ethylene glycol, ChCl/oxalic acid, ChCl/urea, and ChCl/levulinic acid DESs, as well as for their corresponding cellulose $I\beta$ crystallite-DES mixture. All the simulations were conducted at room temperature since desired green and sustainable applications require low energy consumptions (Welton 2015; Clarke et al. 2018; Körner et al. 2019). To the best of our knowledge, there is scarce literature information concerning the interactions between a cellulose crystallite $I\beta$ model and ChCl-based DESs regarding the cellulose pretreatment, as well as thermodynamic and structural properties of cellulose-DES mixtures.

Computational methods.

Force fields.

All the ChCl-based DESs were modeled with the force fields (FFs) developed by Doherty and Acevedo (2018), also-called OPLS-DES FF. These FFs use a $\pm 0.8e$ scaled charge for the cations and anions

present in the DES, providing a remarkable agreement between calculated and experimental properties including densities, viscosities, heat capacities, surface tensions, and diffusion coefficients (Doherty and Acevedo 2018). The corresponding HBA:HBD molar ratios for the evaluated ChCl/ethylene glycol, ChCl/oxalic acid, ChCl/urea, and ChCl/levulinic acid DESs in this work, were 1:2, 1:1, 1:2, and 1:2, respectively, as is also indicated in Table S1 in the Supplementary Information section and shown in Fig. 1a-d. On the other hand, the cellulose crystallite (Fig. 1e-f) was modeled with the OPLS 2005 FF (Banks et al. 2005), which has demonstrated to be a reliable FF for the modelling of carbohydrates, (Stortz et al. 2009; Rabideau et al. 2013, 2014; Rabideau and Ismail 2015; Velioglu et al. 2014; Kubicki et al. 2018; Stalker et al. 2019) and recently validated in our previous work (Sánchez-Badillo et al. 2021). The geometric combining rule was applied for all mixed ϵ_{ij} and σ_{ij} interactions along with a scaling factor of 0.5 for the 1-4 Lennard-Jones and the 1-4 electrostatic interactions.

Molecular dynamics simulations details.

All MD simulations were carried out with the GROMACS (2020.4) package (Abraham et al. 2015). The v-rescale (Bussi et al. 2007) thermostat and Berendsen (Berendsen et al. 1984) barostat were used to keep constant the temperature and the pressure at 300 K and 1 bar, respectively. The v-rescale and Berendsen algorithms have been successfully applied in the literature for the calculation of thermodynamic and transport properties of either DES or ILs through MD simulations (Doherty and Acevedo 2018; Doherty et al. 2018). A coupling time of 1 ps was used for both temperature and pressure. Newton's equations of motion were integrated with a time step (Δt) value of 1 fs by using the leap-frog algorithm. Periodic boundary conditions were used along with a cut-off value of 16 Å and 30 Å for the calculation of the non-bonded interactions for condensed and gas-phase systems, respectively. For the condensed systems, the long-range non-bonded interactions beyond the cut-off were calculated by using the Smooth Particle-Mesh-Ewald (Essmann et al. 1995). On the contrary, for the gas phase systems, the scheme *cut-off* was used instead. The LINCS algorithm (Hess et al. 1997) was employed to constraint all covalent hydrogen bonds. Equilibration and production runs were carried out for all the systems as indicated below.

Electronic density calculations were carried out in order to reveal the HBs between cellulose unit cell and DES molecules. The electronic wave function of each system was obtained through density functional theory (DFT) calculations conducted in the TeraChem (Ufimtsev and Martínez 2008) software at the PBE0 (Perdew et al. 1996, 1997; Adamo and Barone 1999)/6-311g** level of theory with empirical dispersion corrections (Grimme et al. 2010). Then, the non-covalent interactions were obtained by analyzing the bond critical points of the electronic density ($\rho(\mathbf{r})$) in the GPUAM (Hernández-Esparza et al. 2014, 2019; Cruz et al. 2019) package. Further details can be found in the Supplementary Information section.

Thermodynamic and structural properties for pure DES and cellulose-DES systems.

Cubic boxes containing the corresponding ChCl and HBD pairs as indicated in Table S1, were constructed using the Packmol package (Martínez et al. 2009). All DESs boxes were built in order to provide similar box length sizes after the production stage. A minimization stage was performed by using the steepest-descent method for 10000 steps in order to remove any possible steric clash. Then, the DESs systems were equilibrated for 10 ns in the *NPT* ensemble at 300 K and 1 bar, and a production run for 15 ns was carried out at the same conditions. The cellulose *I* β crystallite-DESs systems were constructed as follows: a cellulose *I* β crystallite of 39 glucan with a degree of polymerization (DP) of 12 each, see Fig. 1f, was built using the cellulose-builder toolkit (Gomes and Skaf 2012). The constructed model implies the current crystallographic standard for cellulose from Nishiyama et al. (2002). The cellulose crystallite was placed in the center of a cubic box and then surrounded by the same number of DES molecules as in their corresponding pure systems, see Table S1. A minimization stage of 10000 steps followed by 100 ns of equilibration, and by a production run of 50 ns were carried out for all cellulose-DES systems in the *NPT* ensemble at the same conditions as the pure state of DESs. Structural properties for both DES and cellulose-DES systems were calculated from the production stages by using the TRAVIS software (Brehm et al. 2020).

Fig. 1 Atomic labels and molecular structures for the deep eutectic solvents and cellulose crystallite modeled in this work. **a** Choline-chloride ethylene glycol (ChCl/ethylene glycol) with 1:2 HBA:HBD molar ratio. **b** Choline-chloride oxalic acid (ChCl/oxalic acid, 1:1). **c** Choline-chloride urea (ChCl/urea, 1:2). **d** Choline-chloride levulinic acid (ChCl/levulinic acid, 1:2). **e** Glucan atom labeling, including the commonly used atom numbering (in parenthesis); the OD atom label refers to the oxygen atom in the hydroxyl group, the OC atom label includes the oxygen atom within the six-member ring, and the HS atom label denotes the hydrogen atom attached to OD atom. **f** Cellulose crystallite composed by 39 glucan of 12 glucose units (GLU residues) each as indicated, arranged in seven layers; left: projection onto the a-b base plane, right: isometric projection. Glucan in these pictures have been green-scale colored for clarity. Color/atom code: blue/nitrogen, green/chlorine, grey/carbon, red/oxygen, and white/hydrogen. All images have been created with the visual molecular dynamics (VMD) software (Humphrey et al. 1996)

Enthalpy of vaporization (ΔH_{vap}).

The enthalpy of vaporization for both DES and cellulose-DES systems was calculated by using the following equation (Liu et al. 2006; Zhong et al. 2011):

$$\Delta H_{vap}(T, P) = \langle E_{pot,gas}(T) \rangle - \frac{\langle E_{pot,liq}(T, P) \rangle}{N} + RT \quad (1)$$

In Eq. (1) the $\langle E_{pot,gas}(T) \rangle$ and $\langle E_{pot,liq}(T, P) \rangle$ correspond to the average potential energy of gas and condensed phase, respectively; N , R , and T are the total number of molecules in the liquid phase, the universal gas constant, and the temperature, respectively. Despite there is a lack of evidence regarding the composition of the gas phase for the studied DESs in this work (Ferreira et al. 2016; Salehi et al. 2019), results from MD calculations (Ferreira et al. 2016; Salehi et al. 2019) suggest that DES gas phase could be composed mainly by HBDs or by both HBDs and HBA:HBD DES clusters. In this work, the $\langle E_{pot,gas}(T) \rangle$ for the pure DES systems was calculated by using one HBA:HBD DES cluster as indicated in Table S1 and depicted in Fig. 1a-d. The DES cluster was placed into a large enough cubic box in order to avoid interactions with its images. Then, a run of 1000 steps for a minimization stage was developed, followed by an NVT equilibration run of 10 ns at 300 K. The $\langle E_{pot,gas}(T) \rangle$ for cellulose-DES systems was calculated according to the literature (Liu et al. 2010), while the $\langle E_{pot,liq}(T, P) \rangle$ values for both DESs and cellulose-DES systems were obtained from their corresponding production runs.

Hildebrand solubility parameter (δ).

The solubility of one material in another is facilitated when their non-bond attractive forces are similar. Therefore, the dissolution capacity of a solvent regarding to a specific solute can be predicted if $\delta_{solvent} \sim \delta_{solute}$ (Rinaldi and Reece 2017). To explore this behavior in the pretreatment of cellulose by DESs, the δ parameters for the DESs were calculated through of the following equations (Liu et al. 2010):

$$c = \frac{\langle E_{pot,gas}(T) \rangle - \frac{\langle E_{pot,liq}(T, P) \rangle}{N}}{V_m} = \frac{\Delta H_{vap}(T, P) - RT}{V_m} \quad (2)$$

$$\delta = \sqrt{c} \quad (3)$$

Here c is the cohesive energy density and V_m the molar volume of the liquid phase.

Results and discussions.

DESs solvent behavior.

Density and molar volume. The calculated ρ and V_m for pure DES and cellulose-DES systems are shown in Table 1. It can be noticed that the calculated density of the DESs ($\rho_{sim,DES}$) agreed with the available experimental density values, presenting an overall average deviation of $\sim 2.0\%$. The addition of the cellulose crystallite (Fig. 1f and Fig. S2) into the DESs generated mixtures with an average mass cellulose composition of ~ 16 wt% and larger density values than those for pure DESs.

The effect of DES density in the cellulose pretreatment was explored through the relationship between calculated pure DES density and the β parameter, as is shown in Fig. 2a. It is important to note that, to our knowledge, it was not found a complete set of experimental data for the β and α parameters for the evaluated DESs in this work (Ren et al. 2016; Florindo et al. 2018). For this reason, the predicted Kamlet-Taft parameters values from *ab-initio* calculations by Kundu et al. (2020), were included. From Fig. 2a, a notable correlation emerged for the relationship between DESs density values and β values, with a squared correlation coefficient (R^2) of 0.91. Similarly, from Fig. S3a the relation between DESs density values and α values also showed an important correlation ($R^2 = 0.84$). Experimental evidence indicates that larger values of α and β parameters are related to larger LCB dissolution (Ren et al. 2016; Liang et al. 2021). The correlations observed in Fig. 2a and S3a suggest that low-density DESs such as ChCl/ethylene glycol and ChCl/levulinic acid could provide a favorable environment for cellulose dissolution than high-density DESs such as ChCl/oxalic acid.

Häkkinen and Abbott (2019) indicated that the dissolution of cellulose is favored in some ILs due to their crystalline structure, since the addition of cellulose produces an increase in the entropy of the system. Therefore, larger entropy changes could conduct to large changes in densities from solvent upon the addition of solute. On this basis, the calculated density variations from pure DES to cellulose-DES mixture ($\Delta\rho$) are indicated in Table 1, and their relationship with the Kamlet-Taft β parameter is shown in Fig. 2b. It can be observed that the larger $\Delta\rho$ values (~ 0.053 g/cm³) correspond to the low-density DESs, including the ChCl/ethylene glycol, the ChCl/urea, and the ChCl/levulinic acid, with β values of 0.57, 0.5, and 0.61, respectively. A similar behavior can be found for the $\Delta\rho$ vs Kamlet-Taft α parameter correlation, shown in Fig. S3b.

In the same way than the ρ and its change $\Delta\rho$ were studied, the molar volume and its change were also evaluated. As observed from Fig. 2c-d, the larger V_m values are associated to the larger ΔV_m ($V_{m,sim,cellulose-D} - V_{m,sim,DES}$) values, as indicated in Table 1. However, both V_m and ΔV_m displayed slight correlations with the Kamlet-Taft β values ($R^2 = 0.66$, $R^2 = 0.62$). Interestingly, the correlations between the V_m and ΔV_m and the Kamlet-Taft α values were slightly better correlated ($R^2 = 0.75$, $R^2 = 0.71$), as shown in Fig. S3c-d. The smallest ΔV_m (and V_m) values can be observed for the ChCl/oxalic acid DES for both cases. This behavior suggests that the small variations in the V_m could produce repulsive interactions between solute and solvent that hinder the cellulose pretreatment in the DES bulk. Thus, bulk properties such as density and molar volume can be used as reference properties to identify new and sustainable solvents for cellulose pretreatment, avoiding the exhaustive traditional experimental measurements.

291 **Table 1** Calculated density and molar volume for DES and cellulose-DES systems at 300 K and 1 bar

System	$x_{Cellulose}^a$ [wt%]	ρ_{sim} [g/cm ³]	ρ_{exp} [g/cm ³]	% <i>error</i> ^b	$V_{m,sim}$ [cm ³ /mol]	$\Delta\rho^c$ [g/cm ³]	ΔV_m^c [cm ³ /mol]	α (Kundu et al. 2020)	β
ChCl/ethylene glycol	1.1078 ± 0.0018	1.1131 (Yadav et al. 2015) 1.1146 (Shahbaz et al. 2012) ^d 1.116 (Leron et al. 2012) 1.115 (Lapeña et al. 2019)	-0.48	238.09	0.0569	33.37	1.4732	0.5694 (Kundu et al. 2020; Florindo et al. 2018)	
-0.61									
-0.73									
-0.65									
Cellulose-ChCl/ethylene glycol	16.64	1.1647 ± 0.0017		271.47					
ChCl/oxalic acid	1.2354 ± 0.0012	1.2575 (Florindo et al. 2014) 1.282 (Gontrani et al. 2018) ^e	-1.76	185.9	0.0383	26.2	1.1921	0.2707 (Kundu et al. 2020)	
-3.63									
Cellulose-ChCl/oxalic acid	15.03	1.2737 ± 0.0009		212.09					
ChCl/urea	1.1487 ± 0.001	1.1963 (Yadav and Pandey 2014) 1.1969 (Xie et al. 2014; Chemat et al. 2016; Leron and Li, 2012) 1.1964 (Shekaari et al. 2017)	-3.98	226.11	0.0501	30.64	1.4176	0.5 (Kundu et al. 2020; Florindo et al. 2018) 0.821 (Ren et al. 2016)	
-4.03									
-3.99									
Cellulose-ChCl/urea	15.67	1.1988 ± 0.001		256.76					
ChCl/levulinic acid	1.1342 ± 0.0013	1.1365 (Florindo et al. 2014)	-0.2	327.86	0.0516	46.77	1.5529	0.6102 (Kundu et al. 2020) 0.57 (Florindo et al. 2018)	
Cellulose-ChCl/levulinic acid	16.37	1.1858 ± 0.0014		374.63					

292 ^a Calculated as $x_{\text{cellulose}} = \frac{\text{cellulose mass}}{\text{total mass of solution}} \times 100$.

293 ^b Calculated as %error = $\frac{(\rho_{\text{sim}} - \rho_{\text{exp}})}{\rho_{\text{exp}}} \times 100$ for each experimental value.

294 ^c Change in the thermodynamic property (p), calculated as $\Delta p = p_{\text{sim,cellulose-DES}} - p_{\text{sim,DES}}$.

295 ^d At 303.15 K.

296 ^e At 298.15 K.

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305 **Table 2** Calculated enthalpy of vaporization, cohesive energy density, and Hildebrand parameter for DES and cellulose-DES systems at 300 K and 1 bar

System	$\Delta H_{vap,sim}$ [kcal/mol]	$\Delta H_{vap,sim,lit}^a$ [kcal/mol]	$\Delta H_{vap,exp}^b$ [kcal/mol]	c_{sim} [cal/cm ³]	δ_{sim} [MPa ^{0.5}]	$\delta_{sim,lit}^a$ [MPa ^{0.5}]	$\Delta \Delta H_{vap,sim}^c$ [kcal/mol]	Δc_{sim}^c [cal/cm ³]	$E_{pot,liq}$ [kcal/mol]
ChCl/ethylene glycol	49.00 ± 2.02	40.03 ± 0.07 (Ferreira et al. 2016) ^d 31.96 ± 0.05 (Ferreira et al. 2016) ^e 48.76 (Salehi et al. 2019) ^d 17.45 (Salehi et al. 2019) ^e	13.34 (Ravula et al. 2019)	203.3	29.17	29.3 (Salehi et al. 2019) ^d 24.5 (Salehi et al. 2019) ^e	5.53	-4.62	-81076 ± 227
Cellulose-ChCl/ethylene glycol	54.53 ± 1.92			198.68					-76741 ± 248
ChCl/oxalic acid	53.17 ± 1.45	51.86 (Salehi et al. 2019) ^d		282.81	34.4		4.03	-15.69	-142880 ± 120
Cellulose-ChCl/oxalic acid	57.25 ± 1.47			267.12					-138304 ± 105
ChCl/urea	54.72 ± 3.07	54.49 (Salehi et al. 2019) ^d 19.60 (Salehi et al. 2019) ^e 48.04 (Salehi et al. 2019) ^d 25.57 (Salehi et al. 2019) ^e	18.88 (Ravula et al. 2019) 11.2 (Shahbaz et al. 2016)	239.37	31.65	31.6 (Salehi et al. 2019) ^d 26.5 (Salehi et al. 2019) ^e 30.5 (Salehi et al. 2019) ^d 31.2 (Salehi et al. 2019) ^e	4.94	-9.33	-51357 ± 130
Cellulose-ChCl/urea	59.66 ± 2.94			230.04					-47012 ± 140
ChCl/levulinic acid	53.59 ± 2.46			161.64	26.01		7.29	-0.72	-147303 ± 163
Cellulose-ChCl/levulinic acid	60.88 ± 2.39			160.92					-142843 ± 151

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^a At 298.15 K.

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^b Calculated from Clausius-Clapeyron equation by using the vapor pressure data from the indicated reference.

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^c Change in the thermodynamic property (p), calculated as $\Delta p = p_{sim,cellulose-DES} - p_{sim,DES}$.

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^d Reported values in the literature by means of MD simulations, suggesting the DES cluster as the gas phase composition.

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^e Reported values in the literature by means of MD simulations, suggesting the HBD as the gas phase composition.

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Fig. 2 Linear correlations observed between the Kamlet-Taft β parameter and: **a** Density ($\rho_{sim,solvent}$, $R^2 = 0.91$), **b** Density change ($\Delta\rho$, $R^2 = 0.86$), **c** Molar volume ($V_{m,sim}$, $R^2 = 0.66$), **d** Molar volume change (ΔV_m , $R^2 = 0.61$), **e** Enthalpy of vaporization ($\Delta H_{vap,sim}$, $R^2 = 0.06$), **f** Enthalpy of vaporization change ($\Delta\Delta H_{vap}$, $R^2 = 0.72$), **g** Cohesive energy density (c_{sim} , $R^2 = 0.87$), **h** Cohesive energy density change (Δc , $R^2 = 0.93$), and **i** Hildebrand parameter (δ , $R^2 = 0.84$)

Enthalpy of vaporization. Results for the energetic thermodynamic properties of the bulk, including ΔH_{vap} , c , and δ obtained for both DES and cellulose-DES systems through eq 1-3, are displayed in Table 2. The calculated enthalpy of vaporization ($\Delta H_{vap,sim}$) values agreed with MD estimated values reported in the literature ($\Delta H_{vap,sim,lit}$) which also assumed the same composition of the gas phase (Salehi et al. 2019). However, the $\Delta H_{vap,sim}$ values displayed a significant deviation respect to those calculated from experimental properties (Shahbaz et al. 2016; Ravula et al. 2019). This was to be expected, since more information is needed regarding the composition of the DESs in gas phase (Ferreira et al. 2016; Salehi et al. 2019).

The relationship between the $\Delta H_{vap,sim}$ and the β and α parameters revealed no correlation, due to $R^2 = 0.06$, and $R^2 = 0.03$ as displayed in Fig. 2e and Fig. S3e, respectively. Interestingly, the addition of the cellulose crystallite into the bulk of the DESs produced positive enthalpy of vaporization changes ($\Delta\Delta H_{vap} \sim 5.5$ kcal/mol), as consequence of the $E_{pot,liq}$ reduction (repulsion interactions) of the mixture compared with the pure system, as it can be noticed in the Table 2. Surprisingly, after the cellulose crystallite addition, the correlation between the $\Delta\Delta H_{vap}$ and the Kamlet-Taft β values increased up to $R^2 = 0.72$ (Fig. 2f), and $R^2 = 0.80$ for the Kamlet-Taft α parameter (Fig. S3f). This was probably related to the absence of strong attractive interactions between cellulose crystallite and DES molecules, thus favoring the repulsion interactions with the bulk of the DES and the gas phase formation. Accordingly, the energy required to achieve the gas phase upon the addition of the cellulose crystallite could be smaller than those in pure DESs where attractive interactions are larger. In other words, the larger Kamlet-Taft β and α values the larger $\Delta\Delta H_{vap}$ for the evaluated DESs.

Cohesive energy density. Tang et al. (2017) indicated that, despite both 1-butyl-3-methylimidazolium chloride ([C₄mim][Cl]) IL and ChCl-based DESs are composed by chloride anions, the largely reduced activity of the Cl^- ion within the DESs was probably related to the restricted HB network. The above despite that the Kamlet-Taft β parameter (proton accepting) of the [C₄mim][Cl] IL is larger ($\beta=0.94$ (Lungwitz and Spange 2008)) than, for example, the ChCl/levulinic acid DES ($\beta=0.61$ (Kundu et al. 2020)). Thus, it seems reasonable that low c values might provide a favorable media to dissolve or pretreat the cellulose.

The calculated values for the c of both DESs and cellulose-DES systems are indicated in Table 2, and the corresponding relationships between calculated c of the pure DES ($c_{sim,DES}$) and the Kamlet-Taft β and α values are shown in Fig. 2g and Fig. S3g, respectively. As it can be observed, there was a suitable correlation between cohesiveness and the Kamlet-Taft parameters ($R^2 = 0.87$ and 0.91 for β and α , respectively). This could be explained since the c is a direct measure of the strength of the intermolecular forces. Thus as c becomes larger, the favorable solute-solvent interactions are hindering due to the strength of the solvent-solvent interactions. Similar highlights have suggested from García et al. (2015) comparing DESs compressibility experimental values.

Interestingly, the relationship between Δc values and Kamlet-Taft (β or α) parameters correlated better ($R^2 = 0.93$ for β in Fig. 2h and $R^2 = 0.95$ for α in Fig. S3h), than the relationship c values vs Kamlet-Taft parameters ($R^2 = 0.87$ for β and $R^2 = 0.91$ for α). This was to be expected since Δc involved the reduction of the $E_{pot,liq}$ (shown in Table 2) in the cellulose-DES mixture, as reported for the $\Delta\Delta H_{vap,sim,DES}$. From Fig. 2h and Fig. S3h, it can be noted that the (absolute) small Δc values corresponded to the DESs with larger both Kamlet-Taft β and α values. This suggest the formation of attractive interactions between solute and solvent at same time the solvent maintains its own interactions. This is in accordance with the findings of Häkkinen and Abbott (2019) who evaluated the interactions between glucose and ChCl/ethylene glycol DES. They found that DES was able to maintain its interactions with itself as the same time the ChCl and ethylene glycol HBD were able to form new HBs with glucose.

Hildebrand parameter. The Hildebrand parameter (δ) is a key property to select solvents for separation process (Salehi et al. 2019). As it can be noted from Table 2, the calculated Hildebrand parameter ($\delta_{sim,DES}$) values agreed with those reported by Salehi et al. (2019) by using the HBA:HBD DES cluster as the component of the gas phase. Furthermore, by analyzing the $\delta_{sim,lit}$ set, it can be observed that the average of the $\delta_{ChC/ethylene\ glycol}$ is larger than the average of the $\delta_{ChCl/urea}$ value, in qualitative agreement with the $\delta_{sim,DES}$ calculated in this work. Despite the δ values can be estimated through the reported vapor pressure (p_{vap}) data from Shahbaz et al. (2016), Salehi et al. (2019) indicated that the units of the enthalpies of vaporization (and thus δ) remained unclear from experiments.

Rinaldi and Reece (2017) have summarized the available data regarding the experimental δ for cellulose ($\delta_{cellulose}$). Unfortunately, the $\delta_{cellulose}$ experimental values presented large variation between them, since they range from 25.7 up to 39.9 MPa^{0.5}, therefore a direct comparison with $\delta_{sim,DES}$ could provide unclear conclusions. Despite the DESs were not able to dissolve the cellulose crystallite under the evaluated conditions, it seems reasonable to suggest a possible relationship between δ_{sim} and Kamlet-Taft parameters for cellulose pretreatment for the tested DESs. The relationship between the $\delta_{sim,DES}$ with Kamlet-Taft parameters is shown in Fig. 2i for β parameter and in Fig. S3i for α parameter. Interestingly, both Kamlet-Taft values for the β and α parameters, and the $\delta_{sim,DES}$ presented meaningful correlations ($R^2 = 0.84$ and $R^2 = 0.89$, respectively), suggesting that DESs with small δ values are suitable to disrupt the cellulose crystallite.

It seems that the cellulose pretreatment ability of the DESs, described by the Kamlet-Taft parameters, can be correlated with a series of thermodynamic properties of the DESs (Fig. 2 and Fig. S3), as suggested Ren et al. (2016). However, the evaluation of the atomistic structure and energetics involving in the disruption of the cellulose crystallite might provide a more detailed description of the cellulose pretreatment or its disruption with DESs, as well as towards the Kamlet-Taft parameter values. The following section was focused to provide valuable atomistic information regarding the use of DESs as possible sustainable solvents for the cellulose pretreatment.

Cellulose crystallite disruption.

Cellulose-DES radial distribution functions. Briefly, the RDF indicates the probability $g(r)$ that one particle finds another particle as a function of distance, r . The calculated cellulose-DES RDFs involved the interactions between OD, OC, and HS atoms from cellulose crystallite and the corresponding: HA, HW, HS_D, HY, HO, HG, HC, HT, Cl, OY, OG, OH, OD_D, O, OB, and OC_D atoms from DES. The RDF plots are displayed in Fig. 3, Fig. S4, Fig. S5, and Fig. S6 for the cellulose-ChCl/ethylene glycol, cellulose-ChCl/oxalic acid, cellulose-ChCl/urea, and cellulose-ChCl/levulinic acid systems, respectively. On the other hand, the HBA-HBD RDFs involving the interactions between the Cl atom from HBA and the corresponding: HY, HO, HC, and HT atoms from HBD, are displayed in Fig. S7 for the same cellulose-DES systems. For all the interactions, the first peak position and its corresponding coordination number (N_{coord}), calculated by integrating the $g(r)$ until the first minimum, have also been summarized in Table 3. Additionally, the final configuration of the cellulose crystallite and a close view to the deformed chains surrounded by DES molecules are displayed in Fig. S8 to Fig. S11 for all the cellulose-DES systems.

Fig. 3 RDFs for searching possible HBs between cellulose crystallite (OD, OC, and HS atoms) and ChCl/ethylene glycol (HA, HW, HS_D, HY, HO, HG, Cl, OY, and OG atoms) in the cellulose-ChCl/ethylene glycol system. The interactions involved: **a** OD oxygen atoms from glucose units and hydrogen atoms from choline cation. **b** OC oxygen atoms from glucose units and hydrogen atoms from choline cation. **c** HS hydrogen atoms from glucose units and OY oxygen atom from choline cation and chloride anion. **d** OD oxygen atoms from glucose units and hydrogen atoms from ethylene glycol HBD. **e** OC oxygen atoms from glucose units and hydrogen atoms from ethylene glycol HBD. **f** HS hydrogen atoms from glucose units and oxygen atoms from ethylene glycol HBD. Atomic labels are also shown in Fig. 1

Table 3 First peak distance position ($\text{\AA}$) and corresponding N_{coord} (in parenthesis) for pair interactions between cellulose and DESs,^a and between HBA and HBD in pure DESs and cellulose-DES systems

Interactions between cellulose and DES.								
Interaction	cellulose-ChCl/ethylene glycol	cellulose-ChCl/oxalic acid	cellulose-ChCl/urea	cellulose-ChCl/levulinic acid				
<i>OD – HA</i>	2.75(0.682)	2.73(0.632)	2.77(0.482)	2.73(0.451)				
<i>OD – HW</i>	2.71(0.120)	2.65(0.154)	2.67(0.100)	2.67(0.087)				
<i>OD – HS_D</i>	2.73(0.111)	2.69(0.105)	2.71(0.074)	2.71(0.088)				
<i>OD – HY</i>	2.01(0.023)	1.99(0.030)	2.01(0.030)	2.03(0.021)				
<i>OC – HA</i>	2.77(0.109)	---	---	2.69(0.036)				
<i>OC – HW</i>	---	2.61(0.039)	2.49(0.006)	---				
<i>OC – HS_D</i>	2.71(0.014)	2.99(0.028)	---	---				
<i>OC – HY</i>	1.97(0.007)	2.11(0.021)	1.95(0.007)	2.09(0.008)				
<i>HS – Cl</i>	2.01(0.125)	2.03(0.123)	2.01(0.122)	2.03(0.103)				
<i>HS – OY</i>	2.01(0.006)	1.97(0.009)	2.11(0.006)	2.05(0.004)				
<i>OD – HO</i>	1.85(0.078)	1.85(0.055)	2.29(0.222)	1.81(0.044)				
<i>OD – HG</i>	3.01(0.531)							
<i>OD – HC, HT</i>								
<i>OD – HT</i>				2.89(0.292)				
<i>OC – HO</i>	1.95(0.022)	2.01(0.015)	2.29(0.087)	1.89(0.006)				
<i>OC – HG</i>	2.95(0.233)							
<i>OC – HC, HT</i>								
<i>OC – HT</i>				---				
<i>HS – OG</i>	1.83(0.060)		1.97(0.057)					
<i>HS – OH</i>		3.35(0.833)		---				
<i>HS – OD_D</i>		2.11(0.034)						
<i>HS – O</i>								
<i>HS – OB</i>				2.07(0.019)				
<i>HS – OC_D</i>				1.97(0.032)				
Interactions between HBA and HBD in pure DES and cellulose-DES.								
Interaction	ChCl/ethylene glycol	Cellulose-ChCl/ethylene glycol	ChCl/oxalic acid	Cellulose-ChCl/oxalic acid	ChCl/urea	Cellulose-ChCl/urea	ChCl/levulinic acid	Cellulose-ChCl/levulinic acid
<i>Cl – HY</i>	2.183(0.479)	2.17(0.461)	2.15(0.734)	2.15(0.705)	2.15(0.694)	2.15(0.694)	2.183(0.587)	2.15(0.598)
<i>Cl – HO</i>	2.05(0.745)	2.05(0.72)	2.017(0.831)	2.02(0.859)			2.017(0.969)	2.01(0.936)
<i>Cl – HC, HT</i>					2.417(0.513)	2.43(0.489)		

^a In **bold** the shortest interaction distance for each of the general interactions between cellulose and DES molecules. The “---” indicates that no defined peaks were found for such interaction.

It can be noted from Table 3, that all the interactions between cellulose and DES were comprised within six general relations: (a) the OD and (b) OC oxygen atoms from cellulose towards the HA, HW, HS_D, and HY hydrogen atoms from choline; (c) the HS hydrogen atom from cellulose paired with Cl or OY from HBA; (d) OD and (e) OC towards the HO, HG, HC, and HT hydrogen atoms from HBD; and finally, (f) the HS hydrogen atom towards the OG, OH, OD_D, O, OB, and OC_D oxygen atoms from HBD. These general relations are also displayed in the Fig. 3, Fig. S4, Fig. S5, and Fig. S6.

The $OD - HA, HW, HS_D$ interactions were located at similar distances ($\sim 2.7 \text{ \AA}$), whereas the $OD - HY$ interaction was positioned at $\sim 2.01 \text{ \AA}$, as it is observed in Fig. 3a, S4a, S5a, and S6a. In a RDF analysis, a strong HB is generally related to a short interaction distance with a large and well-defined $g(r)$ peak (Doherty et al. 2018). Accordingly, not only the strongest $OD - HY$ HBs were found in the cellulose-ChCl/oxalic acid system ($1.99 \text{ \AA}$), but also all the remaining HBs involving the $OD - HA, HW, HS_D$ atoms, were stronger or more frequent than in the other DESs (see also Fig. S9). This might suggest that the cellulose crystallite presented favorable interactions towards the choline cation through HBs in the ChCl/oxalic acid DES, which is also indicated by the larger N_{coord} shown in Table 3 (note that the small N_{coord} values are due to absence of cellulose dissolution). This behavior could hinder other relevant and stronger cellulose-DES interactions such as those involving Cl^- and the HBD. Interestingly, the remaining cellulose-DES systems (which have larger Kamlet-Taft β values) showed weaker $OD - HY, HA, HW, HS_D$ interactions. These results may explain the smallest $\Delta\Delta H_{vap}$ and the largest change in the cohesiveness of the cellulose-DES mixture reported in Table 2 for the ChCl/oxalic acid DES.

Interactions involving the $OC - HA, HW, HS_D$ were less frequent than those involving the OD oxygen atom, as is shown in Fig. 3b and in Fig. S4b, S5b, S6b. This is probably caused by a steric effect surrounded the OC atom within the glucose unit. Despite the $OC - HA, HW, HS_D, HY$ interactions play a minor role due to the larger position and non-well-defined of their initial peaks, the shortest interaction distances corresponded to the $OC - HY$ HBs.

From Fig. 3c, S4c, S5c, and S6c, the $HS - Cl$ interaction was located at around of $2.02 \text{ \AA}$ for all cellulose-DES systems (see also Fig. S8b, S9b, S10b, and S10b). This HB was the most prominent and thus frequent interaction due to its large $g(r)$ value, in agreement with the findings of Häkkinen and Abbott (2019). However, other interactions involving the HS hydrogen atom are positioned at shorter distances. For example, the $HS - OG$ in the cellulose-ChCl/ethylene glycol system (Fig. 3f), is located at $1.83 \text{ \AA}$, and the $HS - O$ in the cellulose-ChCl/urea system at $1.97 \text{ \AA}$ (Fig. S5f), as it was reported in the literature (Smirnov et al. 2020). It can be noted from Table 3, that shorter $HS - Cl$ distances occurred in DESs with relatively large Kamlet-Taft β and α values ($2.01 \text{ \AA}$ in the ChCl/ethylene glycol and ChCl/urea DESs), however the distances were slightly larger for ChCl/oxalic acid and ChCl/levulinic acid DESs. Recently, some authors (Chen et al. 2019; Zhang et al. 2020) have suggested that the presence of strong HB network within the solvent hinders its interaction with cellulose, making difficult either its pretreatment or dissolution. On this regard, the main interactions between HBA and HBD within the DES were also calculated and shown in Table 3. It can be noticed that the smallest $Cl - HY$ distances for pure DESs (displayed also in Fig. S7a, S7c, S7e, and S7g) are present in ChCl/oxalic acid and ChCl/urea. Furthermore, the $Cl - HY$ in the ChCl/oxalic acid DES also displayed the largest N_{coord} (0.734). The small $Cl - HY$ distance in conjunction with the largest N_{coord} could be an indicative of the HB network strength within the DES.

It was observed in Table 3 that the first peak for the $Cl - HY$ interaction, decreases its height for the most of the evaluated DESs upon the addition of the cellulose crystallite, contrary to what was found in the ChCl/oxalic acid DES, which remained constant. This reduction of the $Cl - HY$ HB distance might explain the small Δc values calculated for the ChCl/ethylene glycol, ChCl/urea, and ChCl/levulinic acid DESs. Meanwhile, the largest Δc value for the ChCl/oxalic acid DES can be associated to the null change in the $Cl - HY$ distance.

The $HS - OY$ interactions in Fig. 3c, S4c, S5c, and S6c seems to be correlated with the $OD - HY$ interactions, due to small $OD - HY$ distances promote a closer interaction between their bonded atoms: HS and OY, respectively. For example, the smallest $OD - HY$ distance was found in the cellulose-ChCl/oxalic acid system, consequently, the smallest $HS - OY$ distance was also found in such DES. These findings and those related for the $OD - HA, HW, HS_D, HY$, suggest that DESs with smaller Kamlet-Taft α and β values presented larger interactions between cellulose and choline cation.

Interactions involving the OD and hydrogen atoms from HBD are displayed in Fig. 3d, Fig. S4d, S5d, and S6d. These figures display the distances between the OD and the hydrogen atoms from the hydroxyl moieties in the HBD (HO). As it can be noted, these interactions show higher $g(r)$ peaks than those related to the HA, HW, HS_D, HY hydrogen atoms in the choline cation (Fig. 3a, S4a, S5a, S6a). Accordingly, the $OD - HO$ HBs play a more relevant role towards the cellulose crystallite disruption than the $OD - HA, HW, HS_D, HY$ HBs. This ability to form stronger hydrogen bonds of the HBD towards the OD atoms, i.e. the hydrogen bond acidity capacity, measured through the Kamlet-Taft α parameter (Dwamena and Raynie 2020; Kundu et al. 2020), could be explained from the interactions between Cl^- and the HO atoms (Fig. S7b, S7d, S7f, and S7h). On this line, large $Cl - HO$ interaction distances (weak HBs) within the DES might enhance the formation of HBs with solute, such as in the ChCl/ethylene glycol DES, contrary to the stronger $Cl - HO$ HBs present in ChCl/oxalic acid and ChCl/levulinic acid DESs. Interestingly, the larger interaction distance between Cl^- anion and hydrogen atoms from HBD was found for the $Cl - HC, HT$ HB present in ChCl/urea DES (Table 4 and Fig. S7f). The shortest $OD - HO$ distance was found for the cellulose-ChCl/levulinic acid system, in agreement with its larger Kamlet-Taft α parameter (1.55 (Kundu et al. 2020)). Finally, from the RDFs analysis, the HBs involving the OD and the HG atoms in ChCl/ethylene glycol (Fig. 3d) and the HT atom in ChCl/levulinic acid (Fig. S6d) DESs, presented the largest interactions distances and displayed the smallest $g(r)$ values.

The $OC - HO$ interactions (including the $OC - HC, HT$ in the cellulose-ChCl/urea) are shown in Fig. 3e, Fig. S4e, S5e, and S6e. The $OC - HO$ interactions showed similar behavior than the $OC - HA, HW, HS_D, HY$ HBs. From Table 3, the behavior of the $OC - HO$ HB becomes stronger in the following order: ChCl/oxalic acid < ChCl/ethylene glycol < ChCl/levulinic acid, because its corresponding distance decreases as $2.01 > 1.95 > 1.81 \text{ \AA}$. These behavior agrees with the corresponding Kamlet-Taft β values (0.27, 0.57, and 0.61, respectively), and Kamlet-Taft α values (1.19, 1.47, and 1.55) (Kundu et al. 2020). Regarding to the cellulose-ChCl/urea system, due to the absence of OH hydrogen atoms in the urea HBD, the $OC - HC, HT$ interactions in Fig. S5e presented the largest distances ($2.29 \text{ \AA}$).

Finally, the interactions between HS and oxygen atoms from HBD are displayed in Fig. 3f, S4f, S5f, and S6f. As it can be observed, the stronger interactions were $HS - OG$, $HS - O$, and $HS - OC_D$, in cellulose-ChCl/ethylene glycol (Fig. 3f), cellulose-ChCl/urea (Fig. S5f), and cellulose-ChCl/levulinic (Fig. S6f) systems, respectively. Interestingly, the OH atom in the $-COOH$ moiety present in ChCl/oxalic acid (Fig. S4f) and ChCl/levulinic acid (Fig. S6f) DESs, formed the weaker interactions with the HS atom. The peaks of these interactions were located at larger distances or showed less occurrences, compared with the $HS - OG$ HB in the cellulose-ChCl/ethylene glycol system (Fig. 3f), or even with the $HS - OC_D$ in the cellulose-ChCl/levulinic acid system. This suggests that stronger HS-oxygen interactions between cellulose and HBD, might be enhanced for R-CO-R structures within the HBD. However, in order to validate such an assumption, a larger number of HBD must be evaluated.

The largest $g(r)$ values present in the interactions between $HS - Cl$ (hydrogen bond basicity) and the relevant $OD - HO$ (hydrogen bond acidity), indicated that such HBs might play a significant role in the deformation or disruption of the cellulose crystallite. These processes are related with the weakening or the breaking of the inter- and intrachain HBs within the solute (Procentese et al. 2015) (van Osch et al. 2017; Chen et al. 2019). In order to explore this effect, the total (inter- and intrachain) HBs have been analyzed for all cellulose-DES systems.

HBs within the cellulose crystallite. The disruption of the inter- and intrachain HBs must be a key step towards the understanding of the cellulose pretreatment with DESs (Procentese et al. 2015). The total interchain and intrachain number of HBs within the cellulose crystallite has been plotted as function of the last 50 ns of simulation (production time) and displayed in Fig. S12. The number of HBs formed between the cellulose crystallite and choline cation ($HBs_{cellulose-ch}$), chloride anion ($HBs_{cellulose-chloride}$), and HBD ($HBs_{cellulose-HBD}$), was also obtained and indicated in Table 4. All the HBs in this analysis have been calculated through the Hydrogen Bonds plugin available in the VMD program (Humphrey et al. 1996), which involves a donor-acceptor (D-A) distance less than 3.5 Å and an acceptor-donor-hydrogen (A-D-H) angle less than 30° (Li et al. 2015).

Table 4 Calculated number of HBs and molecular properties of the cellulose crystallite in DES at 300 K and 1 bar

System	intrachain	interchain	cellulose-choline	cellulose-chloride	cellulose-HBD	$r_{intrachain\ HBs}$ [HBs/ns]	$D_{sim, cellulose-DES} \times 10^{10}$ [cm ² /s]	$E_{non-bonded, cellulose}$ [kcal/mol]
cellulose-ChCl/ethylene glycol	518 ± 13	476 ± 16	46 ± 6	161 ± 8	176 ± 12	-0.403	8.380	-6447.83
cellulose-ChCl/oxalic acid	540 ± 12	468 ± 16	59 ± 7	151 ± 5	92 ± 7	-0.216	0.444	-6660.10
cellulose-ChCl/urea	555 ± 12	454 ± 16	43 ± 6	155 ± 5	198 ± 12	-0.277	0.369	-6530.86
cellulose-ChCl/levulinic acid	561 ± 14	468 ± 16	35 ± 6	126 ± 6	98 ± 8	-0.514	1.543	-6735.63

From Fig. S12a and Fig. S12d, a reduction of the intrachain HBs can be observed for the ChCl/ethylene glycol and ChCl/levulinic acid DESs, contrary to the behavior shown in ChCl/oxalic acid and even ChCl/urea DESs (Fig. S12b and Fig. S12c). On the other hand, the number of the interchain HBs remained almost constant for all cellulose-DES systems along the production time. Furthermore, the interchain HBs were all similar to each other as indicated in the Table 4. From such observations, it can be suggested that the cellulose pretreatment process starts by reducing the intrachain HBs. This effect was further explored by extracting the cellulose unit cell (composed by five units of cellobiose) from the top and the edge of the cellulose crystallite (Fig. S8a, S9b, S10a, and S11a) along with the closest DES molecules. Then, the strength of the HBs was evaluated through the density functional theory (DFT) calculations (see Supplementary Information for details).

The HBs present in the cellulose unit cell and DES molecules systems were directionally optimized, to calculate the strength of the solute-solvent HBs (in terms of the electronic density, $\rho(\mathbf{r})$) (Johnson et al. 2010). The results are displayed in Table S2 and Table S3 in the Supplementary Information. The optimized HBs corresponding to the unit cell at the edge of the cellulose crystallite (Table S3), showed largest $\rho(\mathbf{r})$ values compared to those related to the unit cell at the top of the cellulose crystallite (Table S2). Furthermore, results from Tables S2 and S3 suggest a synergetic role of the DES molecules towards the cellulose disruption. This is because the $D-H \cdots Cl$ HBs are largely present at the edge of the cellulose crystallite as well as those related with the HBD or the choline cation, whereas the $D-H \cdots Cl$ HBs are not present at the top of the cellulose crystallite for most of the cellulose-DES systems. This synergetic effect at the edge of the cellulose crystallite, probably enhances the breaking of the both intra- and interchain HBs in the solute.

Unfortunately, there was no linear correlation between intra- or interchain HBs and the Kamlet-Taft parameters of DESs, Fig. 4a-b and Fig. S13a-b. However, the slight decrease in the number of intrachain HBs in ChCl/ethylene glycol and ChCl/levulinic acid DESs, suggested that the rate of change (or the slope in Fig. S12) could provide useful information. We calculated this slope ($r_{intrachain\ HBs}$), obtaining -0.403, -0.216, -0.277, and -0.514 intrachain HBs/ns for cellulose-ChCl/ethylene glycol, cellulose-ChCl/oxalic acid, cellulose-ChCl/urea, and cellulose-ChCl/levulinic acid systems, respectively.

Surprisingly, a meaningful correlation between these values and the Kamlet-Taft β and α values is displayed in Fig. 4c and Fig. S13c.

The lack of correlation between the intra- or the interchain HBs with the Kamlet-Taft β parameter of the DESs and the correlation with $r_{intrachain\ HBs}$, might suggest that mass transfer play a relevant role in the cellulose pretreatment with DESs (Ren et al. 2016; Körner et al.; Zhang et al. 2020). Consequently, the diffusion coefficient of the cellulose crystallite in the ChCl-based DESs ($D_{sim,cellulose-DE}$) was also evaluated through its mean squared displacement and the Einstein relation (Batista et al. 2015). Results are indicated in Table 4 and shown in Fig. 4d and Fig. S13d. Even though it was not found a linear correlation with the Kamlet-Taft β and α values ($R^2 = 0.20$ and $R^2 = 0.14$, respectively), the larger $D_{sim,cellulose-D}$ value was found in the ChCl/ethylene glycol DES (8.38×10^{-11} cm²/s) which also presented the smallest experimental viscosity (~ 40 cP) (D'Agostino et al. 2011).

Fig. 4 Linear correlations observed between the Kamlet-Taft β parameter and: **a** Intrachain HBs ($R^2 = 0.011$), **b** Interchain HBs ($R^2 = 0.013$), **c** Rate of change of intrachain HBs ($r_{intrachain\ HBs}$, $R^2 = 0.76$), **d** Cellulose diffusion coefficient in DES ($D_{sim,cellulose-DE}$, $R^2 = 0.20$), **e** HBs between cellulose crystallite and choline cation ($HBs_{cellulose-choli}$, $R^2 = 0.86$), **f** HBs between cellulose crystallite and chloride anion ($HBs_{cellulose-chlori}$, $R^2 = 0.10$), **g** HBs between cellulose crystallite and HBD ($HBs_{cellulose-HBD}$, $R^2 = 0.13$), and **h** Non-bonded potential energy of the cellulose crystallite ($E_{non-bonded,cellulose}$, $R^2 = 0.03$)

The HBs between the cellulose crystallite and the choline cation may inhibit the disruption of the cellulose crystallite, since the lower the Kamlet-Taft β (or α) parameter the larger the number of $HBs_{cellulose-choli}$, as is displayed in the Fig. 4e and Fig. S13e. The large number of $HBs_{cellulose-choline}$ was found in the ChCl/oxalic acid DES ($\beta = 0.27, \alpha = 1.19$), and could be related to the large OD -, and OC - HA, HS, HS, HD_D correlations indicated in the RDF analysis, Table 4. These RDF results indicate that the interaction between cellulose and the oxalic acid HBD, is limited. On the other hand, the

small number of $HBs_{cellulose-cho}$ in the remaining solvents might be a consequence of the largest $Cl - HY$ and the $Cl - HO, HC, HT$ distances, limiting the role of the choline cation and thus improving other interactions with cellulose crystallite, such as the larger number of $HBs_{cellulose-HBD}$. However, based on our results, there was no correlation between $HBs_{cellulose-H}$ and the Kamlet-Taft parameters of the evaluated ChCl-based DESs ($R^2 = 0.13$ in Fig. 4g for β parameter and $R^2 = 0.08$ in Fig. S13g for α parameter) as would be expected.

Finally, for the $HBs_{cellulose-ch}$, shown in Fig. 4f and Fig. S13f, the largest number of HBs was found for the cellulose-ChCl/ethylene glycol system (161 ± 8), in concordance with the large distance found for the $Cl - HY$ HB in pure DES (i.e., a small interaction between anion and cation). The smallest number of $HBs_{cellulose-chl}$ (and small number of $HBs_{cellulose-HBD}$) was found in the cellulose-ChCl/levulinic acid system. This is in agreement with the stronger $Cl - HO$ HBs reported in the pure DES as indicated in Table 3 (and the total $D - H \cdots Cl$ HBs shown in Tables S2 and S3), which might hinder better interactions from the levulinic acid HBD towards the cellulose crystallite. It is interesting to note that, from the observations indicated above, the ChCl/levulinic acid DES seems to be limited by the interactions present between its HBA and HBD.

It was found in our previous work (Sánchez-Badillo et al. 2021) that the energetics related to HBs (as suggested the number of stronger HBs reported in Table S2 and S3), their stability, and quality might play a significant role in order to understand better the cellulose pretreatment. For this reasons, HB occupancies were also calculated.

HB occupancies. The HB occupancy indicates the percentage of occurrence (or fraction, and thus the stability) of a particular HB along the simulation. Intrachain and interchain HB occupancies in two different sections of the cellulose crystallite: chain 0 (located at the edge of the cellulose crystallite) and chain 17 (located at the middle of the cellulose crystallite), see the top of Fig. S14, were calculated for all systems (Fig. S14 to S17).

As it can be noted from Fig. S14a-b, S15a-b, S16a-b and S17a-b, the intrachain HB occupancies present in both the chain 17 and chain 0 were related to the typical $O2 - H2 \cdots O6$, $O3 - H3 \cdots O5$, $O6 - H6 \cdots O3$, and $O6 - H6 \cdots O2$ HBs found in cellulose I β (Shen and Gnanakaran 2009). Despite the chain 0 was surrounded by only two glucan chains, larger intrachain HB occupancies were absent or less frequent than in the chain 17. This suggests also that the cellulose disruption process in DESs started by weakening (or diminishing the HB occupancies of) the chains located at the edge of the cellulose crystallite, in agreement with the stronger unit cell-DES HBs presented in Table S3. On the other hand, the interchain HB occupancies are displayed in Fig. S14c-d, S15c-d, S16c-d, and S17c-d. As observed, the most of the interchain HBs corresponded to the $O6 - H6 \cdots O2$, $O6 - H6 \cdots O3$, and $O2 - H2 \cdots O6$ HBs. The interchain HB occupancies in chain 17 (Fig. S14c, S15c, S16c, and S17c) presented minor variation than those in chain 0 (Fig. S14d, S15d, S16d, and S17d). By comparing such figures, it can be noted that the strong interchain HBs for the glucan at chain 0 in contact with the solvent, were replaced by the $O6 -$

$H6 \cdots O4$ HBs. This effect was probably caused by a synergetic effect between the $O - H \cdots Cl$, the $C - H \cdots O$, and the $O \cdots H - O$ HBs between cellulose and DES molecules, as suggested the results from DFT calculations shown in Table S2 and Table S3. Detailed discussion regarding the HB occupancies for each cellulose-DES system can be found in the Supplementary Information. The emerging occurrence of the $O6 - H6 \cdots O4$ HB by action of the DESs, promotes the releasing of the O2 and O3 oxygen atoms, favoring the functionalization of the hydroxyl group and thus the synthesis of cellulose derivatives, required for example, in the acetylation of wood (Sun et al. 2019). This effect suggest the use of the DES as potential sustainable media to synthesize cellulose derivatives due to promotion of the interactions between cellulose and third incoming particles.

The overall effect on the cellulose crystallite disruption caused by DESs from the potential energy of the cellulose crystallite ($E_{non-bonded, cellulose}$), was evaluated by computing the single point (molecular mechanics) energy of the final configuration of the cellulose crystallite (shown in Fig. S8a, S9a, S10a, and S11a). The results of $E_{non-bonded, cellulose}$ are displayed in Table 4. Unfortunately, there was no correlation between $E_{non-bonded, cellulose}$ and Kamlet-Taft parameters as shown in Fig. 4h and Fig. S13h. Hauru et al. (2012) suggested an effective dissolution window, defined as $\beta - \alpha$ in order to correlate the “net basicity” with the dissolution/regeneration of cellulose in water-IL mixtures. Surprisingly, by evaluating this net basicity of the evaluated DESs, a notable correlation with the $E_{non-bonded, cellulose}$ arises as shown in Fig. S18. Furthermore, other relevant properties including intrachain HBs (Fig. S18a, $R^2 = 0.71$), $D_{sim, cellulose-D}$ (Fig. S18b, $R^2 = 0.39$, partially improved), $HBs_{cellulose-chloride}$ (Fig. S18c, $R^2 = 0.95$), and $HBs_{cellulose-HB}$ (Fig. S18d, $R^2 = 0.45$, partially improved) are better correlated towards the net basicity $\beta - \alpha$ definition than with the Kamlet-Taft β or α parameters separately. This highlight suggests that both Kamlet-Taft parameters are important in order to understand the role of the DESs in the cellulose pretreatment. However, in order to validate such a hypothesis, a large number of DESs is required. To explore deeper the origin of the observations regarding $E_{non-bonded, cellulose}$ and Kamlet-Taft β and α parameters, the short range (SR) van der Waals and coulombic non-bonded pair energies (E_{SR}) were evaluated for the all cellulose-DES systems.

Non-bonded pair energies. The E_{SR} were evaluated among the molecules belonging to the groups CEL (i.e. the cellulose crystallite), CHOL (choline cations), Cl (chloride anions), and HBD in an additional *NPT* MD simulation of 25 ns for all cellulose-DES systems. Remaining MD simulation details corresponded to those used in the *NPT* condensed phase production stage, as indicated in the methodology section. It is important to indicate that the E_{SR} corresponded only to the *LJ*(SR) (van der Waals) and *Coul*(SR) (electrostatic) terms from the GROMACS energy output file.

The pair energy interactions between cellulose crystallite and DES molecules (cellulose crystallite ($E_{SR, CEL-CEL}$), cellulose-choline ($E_{SR, CEL-CHOL}$), cellulose-chloride ($E_{SR, CEL-Cl}$), and cellulose-HBD ($E_{SR, CEL-H}$)) are displayed in Fig. S19. The largest $E_{SR, CEL-CEL}$ value (more stable cellulose

crystallite) was found within the ChCl/levulinic acid DES (-47035 kcal/mol in Fig. S19a) in agreement with the large intra- and inter HBs, presented in Table 4. This behavior is probably caused by the small energy contributions from $E_{SR,CEL-CHOL}$, $E_{SR,CEL-}$, and $E_{SR,CEL-HBD}$ within the ChCl/levulinic acid DES, indicated by the small number of HBs reported in Table S2 and Table S3. On the other hand, the largest interactions towards cellulose crystallite were found in the ChCl/ethylene glycol and ChCl/urea DESs (Fig. S19 b-d). This behavior was probably caused by the smallest $HS - Cl$ distance (Table 3) as is also suggested by the stronger $O - H \cdots Cl$ HBs from Table S3 in the case of ChCl/ethylene glycol (Fig. S19c); and with both the small $HS - O$ (Table 3, Fig. S19d, and Table S3) and the larger $OD - HA, HW, HS_D, HY$ and $Cl - HC, HT$ distances (Table 3, Fig. S5, Fig. S19b-d) in the case of ChCl/urea. Finally, from Fig. S19b, it can be observed that the $E_{SR,CEL-CHOL}$ was more stable in ChCl/oxalic acid DES, in agreement with the short distance of the $OD - HA, HW, HS_D, HY$ first peak in the RDFs and the large N_{coord} shown in Table 3, as well as the stronger $O - H \cdots O$ HBs reported in Table S3. These large interactions do not seem to reduce the interactions with Cl^- anion (Fig. S19c) when compared with the remaining cellulose-DES systems (see also Table S3); however, a largest reduction in the $E_{SR,CEL-HBD}$ can be noticed. Interestingly, by combining these interaction energy contributions regarding the cellulose crystallite (i.e. $E_{SR,CEL-CHOL} + E_{SR,CEL-Cl} + E_{SR,CEL-HBD}$) from the DESs with net basicity ($\beta - \alpha$) definition, a notable correlation is obtained, as shown in Fig. S18f ($R^2 = 0.73$), unlike the correlation with the Kamlet-Taft parameters β and α separately.

It is important to note that, despite the ChCl/levulinic acid DES had the largest Kamlet-Taft β parameter it was not able to disrupt further the cellulose crystallite as indicated by the $E_{SR,CEL-C}$ in Fig. S19a. Additionally, as it was found in the previous section, the cellulose pretreatment with this DES produced the small number of $O6 - H6 \cdots O4$ HB occupancies compared with the remaining solvents. On this line, it seems that there is a limited role of this DES towards the cellulose crystallite, which it cannot be explained directly by its Kamlet-Taft β parameter. In order to explore this point, the $Cl - CHOL$, $Cl - HBD$, $CHOL - HBD$, $CHOL - CHOL$ and $HBD - HBD$ E_{SR} were also calculated and displayed in Fig. 5.

Fig. 5 Calculated non-bonded pair energies (E_{SR}) for: **a** Chloride anion and choline cation ($E_{SR,Cl-CHOL}$), **b** Chloride anion and hydrogen bond donor ($E_{SR,Cl-H}$), **c** Choline cation and hydrogen bond donor ($E_{SR,CHOL-HBD}$), **d** Choline cations ($E_{SR,CHOL-CHOL}$), **e** Hydrogen bond donors ($E_{SR,HBD-HBD}$) in cellulose-ChCl/ethylene glycol system (black bar), cellulose-ChCl/oxalic acid (blue bar), cellulose-ChCl/urea (yellow bar), and cellulose-ChCl/levulinic acid (green bar). It should be indicated that, since the number of clusters were different for all cellulose-DES systems, these interactions were scaled by the number of the corresponding DES clusters present in each system (as indicated in Table S1)

Rapidly, from Fig. 5d-e the interactions between the choline cation and HBD and between HBDs in ChCl/levulinic acid DES showed the largest negative values (-16.15 and -63.67 kcal/mol, respectively) among all the cellulose-DES systems. These interactions within the DES might be the origin of the low cellulose disruption performance as is reported in Table 4 and Fig. S19a, as well as the low correlation displayed in Fig. 4b, 4f, and 4g. This finding suggested that both choline cation and the levulinic acid HBD are both interacting strongly, limiting the role of the DES molecules in the cellulose pretreatment. This effect is also correlated with its smallest net basicity value ($\beta - \alpha = -0.9427$) among the evaluated DESs.

This competing effect has been reported by Zgrzeba et al. (2015) and by Crowhurst et al. (2003) in ILs, indicating the importance of both Kamlet-Taft parameters.

From Fig. 5a, it can be noted that the largest $E_{SR,Cl-CHOL}$ was found for the ChCl/oxalic acid DES, in agreement with the observations reported in Table 3 for the small $Cl-HY$ interaction distance. Regarding to the $E_{SR,Cl-HB}$ in Fig. 5b, the ChCl/oxalic acid DES shows the most positive value (-14.95 kcal/mol); this potential advantage over the Cl^- anion to interact better with cellulose crystallite, turned also into a large $E_{SR,Cl-CH}$ interaction. On the contrary, despite the large value obtained for the $E_{SR,Cl-HBD}$ in the ChCl/ethylene glycol DES (-25.58 kcal/mol in Fig. 5b), seems that did not limit the performance of the chloride anion towards the cellulose disruption as reported in Fig. S19a, Fig. S19c, and in Table 4. This is probably related to the small energy value of the $E_{SR,Cl-CHOL}$ interaction, which releases the chloride anion, in agreement with the large $Cl-HY$ distance shown in Table 3. Interestingly, the ChCl/urea and ChCl/ethylene glycol DESs showed similar $E_{SR,Cl-H}$ values (probably related to their similar net basicity values), however, the ChCl/urea DES also showed the most positive $E_{SR,HBD-H}$ value (52.82 kcal/mol in Fig. 5e). Accordingly, there was not competing between urea HBDs to interact with the cellulose crystallite, as is indicated by the large cellulose crystallite disruption shown in Fig. S19a and Table 4.

Regarding the role of the interactions between choline cations ($E_{SR,CHOL-CH}$, Fig. 5c), it can be noticed that all of them were similar and showed a repulsive nature.

Finally, from Fig. 5e, the largest repulsion between HBDs molecules within the DES could promotes a better performance of HBD towards the cellulose crystallite. This is the case of ChCl/ethylene glycol and ChCl/urea DESs, which also presented the largest $E_{SR,CEL-H}$ as indicated in Fig. S19d, and similar net basicity. In further agreement with the $E_{non-bonde,cellulose}$ values presented in Table 4. Thus, potential new, green, and sustainable DESs can be selected from their net basicity values not only for an effective cellulose pretreatment but also for lignocellulosic biomass valorization applications.

Conclusions.

It was found by means of molecular dynamics simulations that density, molar volume, cohesive energy density, and Hildebrand parameter of a series of choline-chloride deep eutectic solvents displayed meaningful correlations towards the Kamlet-Taft β and α parameters. These results suggest that thermodynamic properties can be used as a qualitative measure of the cellulose pretreatment process at low temperature. Further insights indicated that $Cl-HY$ interactions in conjunction with its corresponding N_{coord} within the solvent, could be an indicative of the hydrogen bond network strength. The last impacts the interaction of the Cl^- anion towards the hydrogen atoms in the hydroxyl groups from glucose units as occurred in the choline-chloride ethylene glycol deep eutectic solvent.

Analysis regarding the cellulose crystallite and DESs suggested that the $HS-Cl$ and the $OD-HO$ hydrogen bonds play a relevant role in the deformation or disruption of the cellulose crystallite.

Interestingly, the $OD - HO$ interactions between glucose units and hydrogen bond donor presented shorter distances than the $HS - Cl$ interaction. Furthermore, it was found that substantial $HS - oxygen$ interactions between cellulose and hydrogen bond donor were obtained for $R - CO - R$ structures within the hydrogen bond donor.

Analysis of the hydrogen bonds within the cellulose crystallite indicated that the intrachain hydrogen bonds were reduced first compared to the interchain hydrogen bonds. Additionally, the hydrogen bond occupancies indicated that the stronger $O6 - H6 \cdots O2/O3$ and $O2 - H2 \cdots O6$ interchain hydrogen bonds are present in the inner chains. Interestingly, the same analysis revealed that such hydrogen bonds are slightly reduced and replaced by weak $O6 - H6 \cdots O4$ hydrogen bonds in the glucan located at the edge, i.e., chains in direct contact with the solvent.

The analysis of the atomistic properties of the cellulose crystallite did not show a complete correlation with the Kamlet-Taft β or α parameters separately. Interestingly, both parameters need to be considered to achieve correlations with such properties, by means of the net basicity ($\beta - \alpha$) for each DES.

Energetic analysis from the pair energies contributions suggested that even though the choline-chloride levulinic acid has the largest Kamlet-Taft β parameter (0.61) among the evaluated solvents, it also presented a larger hydrogen bond donor-hydrogen bond donor pair energy interaction, which strongly limited the role of the levulinic acid towards cellulose crystallite.

Summarizing, for the evaluated choline-chloride-based deep eutectic solvents, effective solvents for the cellulose pretreatment could be related (but not limited) with the following: low density, low cohesive energy density, Hildebrand parameter around 30 MPa^{0.5}, large molar volume, $R - CO - R$ moieties within the HBD, a large net basicity value, and small HBD-HBD interaction. Fortunately, all these properties can be obtained through *in-silico* evaluations, providing relevant insights for the development of new, sustainable, and more efficient DESs solvents for the cellulose pretreatment.

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Declaration.

Conflict of interest.

The authors declare that they have no conflict of interest.

Ethical approval.

This article does not contain any studies with human beings or animals.

Supplementary information.

The number of molecules for each system modeled in this work is indicated in Table S1. Atomic labels and molecular structures are shown in Fig. S1 for the reader convenience. The final configuration of the cellulose-DES systems is shown in Fig. S2. Linear correlations observed between Kamlet-Taft α parameter and the same thermodynamic properties shown in Fig. 2, are displayed in Fig. S3. RDFs for searching possible HBs between cellulose crystallite and DESs are shown in Fig. S4 to Fig. S6, respectively. RDFs for searching possible HBs within choline-chloride and between choline-chloride and HBD are displayed in Fig. S7. The final molecular configuration of the cellulose crystallite along with a closed view to the disrupted chains within the DESs are shown in Fig. S8 to Fig. S11. The calculated number of (total, interchain, intrachain, cellulose crystallite-choline cation, cellulose crystallite-choline-chloride anion, and cellulose crystallite-choline HBD) HBs is shown in Fig. S12. Electronic density of the HBs between cellulose unit cell extracted from top and edge of the cellulose crystallite and DES molecules, obtained by DFT calculations, are displayed in Table S2 and Table S3. Linear correlations observed between Kamlet-Taft α parameter and the same atomistic properties shown in Fig. 4, are displayed in Fig. S13. Intrachain and interchain HB occupancies for chain 17 and chain 0 within DESs are shown in Fig. S14 to S17. Linear correlations observed between net basicity ($\beta - \alpha$) and atomistic properties of the cellulose crystallite are shown in Fig. S18. Finally, the calculated non-bonded pair energies within the cellulose crystallite and between cellulose crystallite and DES molecules are shown in Fig. S19.

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