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A perspective on cellulose dissolution with deep eutectic solvents

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Currently, membrane manufacturing relies heavily on fossil-based solvents and polymers, resulting in significant negative impacts on human health and the environment. Thus, there is an urgent need for eco-friendly, low-toxicity, and sustainable solvents and polymers to comply with the United Nations' sustainable development goals. Cellulose, as a green, natural, and abundant polymer, offers a sustainable source for membrane manufacturing. However, a significant challenge exists in dissolving cellulose due to strong intermolecular and intramolecular hydrogen bonds within cellulose molecules. Deep eutectic solvents (DESs), which contain both hydrogen bond donor and acceptor groups, have received significant attention as alternative solvents for cellulose dissolution owing to their low cost, low toxicity, environmentally friendly nature, ease of synthesis, and versatility. This review examines experimental studies, and theoretical approaches, highlighting key findings and factors influencing cellulose dissolution in deep eutectic solvents.

KEYWORDS

deep eutectic solvents, cellulose, polymer membranes, COSMO-RS aided deep eutectic solvent design, green solvent, basic deep eutectic solvent

1 Introduction

Membrane technology has been considered a green technology. However, the green membrane manufacturing process has just recently become a concern. Membrane production requires a large amount of fossil-based solvents and polymers. Polyethylene, polypropylene, polysulfone, poly(vinylidene fluoride), polyimide, and poly(benzimidazole) are commonly used petroleum derived polymers to fabricate membranes. Conventional solvents used for dissolving these polymers, such as N-methyl pyrrolidone (NMP), N, N-dimethylformamide (DMF), and dimethylacetamide (DMAc) (Heinze and Koschella, 2005), are also derived from fossil raw materials causing negative impact on the environment and human health. Bio-solvents have been alternatively produced from bio-based feedstock such as carbohydrates, carbohydrate polymers, proteins, alkaloids, plant oils, and animal fats. However, purification of these solvents, usually with extraction, requires toxic chemicals and high-energy input and generates a waste stream (Jin et al., 2017). Therefore, the adoption of greener membrane fabrication methods is currently being considered to align with the United Nations Sustainable Development Goals. In this regard, transitioning from fossil-based polymers to natural polymers is crucial, with cellulose emerging as a significant and abundant renewable biopolymer among them. Composed of repeating D-glucose monomers, each with three hydroxyl groups, cellulose offers a favorable structure for chemical modification. However, its strong intermolecular hydrogen bonds make this semicrystalline polymer insoluble in most organic solvents (Chen et al., 2019), thus, presenting a challenge for cellulose membrane

fabrication using conventional methods like phase inversion. Traditional solvents like N-methylmorpholine-N-oxide (Rosenau et al., 2002), lithium chloride/N,N-dimethylacetamide (DMAc) (Zhang et al., 2014), alkali/urea, or alkali/thiourea aqueous solutions (Xiong et al., 2014), used for dissolving cellulose, are not considered environmentally friendly due to their negative impact on the environment. High-temperature pretreatment or solvent exchange is necessary before dissolving cellulose in DMAc (Raus et al., 2012), while the alkali-urea aqueous system can only dissolve low molecular weight cellulose below -12°C (Egal et al., 2008). Newer, more popular ionic liquids (ILs) have been suggested as sustainable alternatives for cellulose dissolution (Swatloski et al., 2002; Zhao et al., 2009; Velioglu et al., 2014; Zhang et al., 2017). The low vapor pressure of ILs is an appealing feature for reducing air pollution. However, their relatively high solubilities in water and poor biodegradability (Jordana and Gathergood, 2015) cause toxicity in water (Flieger and Flieger, 2020), and their dissolution requires high energy consumption (Chundawat et al., 2020). Additionally, their synthesis is not environmentally friendly.

Deep eutectic solvents (DESs) are also recognized as green solvents and can be easily prepared by combining hydrogen bond donors (HBD) and acceptors (HBA) in a stoichiometric ratio (Cardellini et al., 2015). Similar to ILs, DESs exhibit low vapor pressure but with lower toxicity profiles, particularly when derived from natural compounds such as amino acids, sugars, and carboxylic acids (Hayyan et al., 2016). Furthermore, their synthesis does not require any solvent or extensive purification, making it a more cost-effective option. Like ILs, DESs have the potential to dissolve cellulose due to the hydrogen bonding interaction of hydrogen bond donor (HBD) and hydrogen bond acceptor (HBA). DESs are considered “designer” solvents of a new generation; changing the type and molar ratio of HBA and HBDs can finely adjust their physicochemical properties. This adaptability presents a challenge in selecting the appropriate DES for cellulose dissolution. The multitude of HBA and HBD combinations in various molar ratios increase the potential number of DES candidates for exploration. Consequently, developing predictive tools for designing DESs to enhance cellulose solubility is crucial for greener membrane fabrication. This mini-review aims to offer insights into cellulose dissolution in DESs and investigate the synergies between experimental and theoretical approaches to advance our current understanding of cellulose dissolution in designer DESs.

2 Recent progress in cellulose dissolution using deep eutectic solvents

The research on cellulose dissolution with DESs started in 2012 by testing 26 different DESs to evaluate their capability to dissolve lignin, starch, and cellulose (Francisco et al., 2012). Even though the tested DESs dissolved up to 14.9 wt% of lignin, they demonstrated a limited dissolution capacity for cellulose. The highest cellulose solubility (0.78 wt%) was observed with the DES composed of malic acid and proline in a 1:3 ratio, while the DES consisting of malic acid (HBD) and alanine (HBA) in a 1:1 ratio showed the lowest solubility (0.11 wt%). Sharma et al. (2013) tried

different cellulose dissolution methods, including heating at 100°C for 10 h, ultrasonication followed by heating at 80°C for 1 h, and microwave irradiation at 80°C for 2 h. They achieved an 8 wt% cellulose solubility using the choline chloride and urea (1:2 ratio) combination by keeping the dissolution temperature at 100°C . Surprisingly, microwave irradiation did not significantly enhance cellulose solubility.

Pan et al. (2017) observed that while choline chloride/urea effectively dissolved amorphous cellulose in rice straw, it was not efficient for the solubility of α -cellulose. Tenhunen et al. (2017) similarly reported that choline chloride/urea (molar ratio 1:2) failed to modify cellulose fibers. Hertel et al. (2012) noted the importance of temperature on cellulose dissolution. They found that microcrystalline cellulose (MCC) did not dissolve in DESs containing urea/choline chloride (2:1), oxalic acid/choline chloride, malonic acid/choline chloride (1:1), and formamide/ammonium formate (2:1) at 45°C . Increasing the temperature to 80°C slightly improved the dissolution in malonic acid/choline chloride and formamide/ammonium formate. While the acidic environment for urea/choline chloride and oxalic acid/choline chloride did not enhance cellulose dissolution, a basic medium (pH 14) did enhance it. Ren et al. (2016a) first activated the cellulose using ultrasound-assisted saturated calcium chloride solution. Their data demonstrated that cellulose solubility increased from 1.43 wt% in a choline chloride and urea mixture to 2.48 wt% when imidazole replaced urea. Malaek et al. (2018) reported a maximum solubility of 6.1 wt% in choline chloride and resorcinol through the use of ultrasound irradiation. Zhong et al. (2022) claimed that in contrast to the data reported in the literature, most choline chloride-based DESs cannot effectively dissolve cellulose. They introduced a novel DES by combining urea (Ur) with choline hydroxide (ChOH), which dissolved 9.5 wt% cellulose with a degree of polymerization (DP) of 926 (from cotton litter pulp). The ChOH/Ur system contained approximately 11 wt% water, and complete dissolution was achieved within 30 min at 70°C . The highest reported cellulose solubility in deep eutectic solvents (DESs) thus far is 15%, as documented by Sirvio and Heiskanen (2020), Sharma et al. (2021), and Tong et al. (2021; 2022). Sirvio and Heiskanen (2020) formulated DESs using tetraethylammonium hydroxide (TEAOH) combined with urea, N-methylurea, N-ethylurea, and 1,3-dimethylurea, achieving the best dissolution performance (15%) with the TEAOH:Water:Urea DES in a ratio of 1:15:2. Sharma and colleagues synthesized 22 zwitterion-based DESs by mixing four types of zwitterions with four saccharides at varying ratios. Two DES formulations, involving zwitterion C15 and 5 wt% sucrose and fructose, respectively, dissolved 15% and 10% cellulose at 120°C . Tong et al. (2021) combined zinc chloride (ZnCl_2), water, and phosphoric acid, achieving 15 wt% cellulose dissolution at room temperature in this DES with a molar ratio of 1:3:0.6. In a subsequent study, Tong et al. (2022) developed DESs using ZnCl_2 , water, and formic acid combinations, achieving the highest solubility of 15% for microcrystalline cellulose in a molar ratio of 1:1:4. The dissolution process occurred under relatively mild conditions with minimal heat energy usage, effectively dissolving various cellulose types, including cotton with high crystallinity and degree of polymerization (DP). Table 1 provides a summary of cellulose solubility in different DESs as reported in the literature.

TABLE 1 Solubilities of the cellulose in different DESs.

Hydrogen bond acceptor (HBA)	Hydrogen bond donor (HBD)	Molar ratio (HBA:HBD)	Dissolution Technique	Dissolution time	Solubility (wt%)	References
Alanine	Malic acid	1:1	Heating at 100°C		0.11	Francisco et al. (2012)
Proline	Malic acid	3:1	Heating at 100°C		0.78	Francisco et al. (2012)
Choline Chloride	Urea	1:2	Heating at 100°C	10 h	8	Sharma et al. (2013)
Choline Chloride	Urea	1:2	Ultrasonication and heating at 80°C	1 h	6	Sharma et al. (2013)
Choline Chloride	Urea	1:2	Microwave irradiation at 80°C	2 h	1.5	Sharma et al. (2013)
Choline Bromide	Urea	1:2	Heating at 100°C	10 h	5	Sharma et al. (2013)
Choline Bromide	Urea	1:2	Ultrasonication and heating at 80°C	1 h	6	Sharma et al. (2013)
Choline Bromide	Urea	1:2	Microwave irradiation at 80°C	2 h	6	Sharma et al. (2013)
Choline Chloride	Urea	1:2	Heating at 100°C	10 h	5	Sharma et al. (2013)
Choline Chloride	Urea	1:2	Ultrasonication and heating at 80°C	1 h	5	Sharma et al. (2013)
Choline Chloride Bromide	Urea	1:2	Microwave irradiation at 80°C	2 h	3	Sharma et al. (2013)
Betaine Hydrochloride	Urea	1:4	Heating at 100°C	10 h	2.5	Sharma et al. (2013)
Betaine Hydrochloride	Urea	1:4	Ultrasonication and heating at 80°C	1 h	2.5	Sharma et al. (2013)
Choline Chloride	Ethylene Glycol	1:2	Heating at 100°C	10 h	Non	Sharma et al. (2013)
Choline Chloride	Ethylene Glycol	1:2	Ultrasonication and heating at 80°C	1 h	Non	Sharma et al. (2013)
Choline Chloride	Ethylene Glycol	1:2	Microwave irradiation at 80°C	2 h	Non	Sharma et al. (2013)
Choline Chloride	Glycerol	1:2	Heating at 100°C	10 h	3	Sharma et al. (2013)
Choline Chloride	Glycerol	1:2	Ultrasonication and heating at 80°C	1 h	2.5	Sharma et al. (2013)
Choline Chloride	Glycerol	1:2	Microwave irradiation at 80°C	2 h	3.5	Sharma et al. (2013)
Choline Chloride	Imidazole	3:7	Heating from 20 to 120°C at a rate of 10°C intervals	1.5 h	2.48	Ren et al. (2016a)
Choline Chloride	Urea	1:2	Heating from 20 to 120°C at a rate of 10°C intervals	2 h	1.43	Ren et al. (2016a)
Choline Chloride	Ammonium thiocyanate	1:1	Heating from 20 to 120°C at a rate of 10°C intervals	3 h	0.85	Ren et al. (2016a)
Choline Chloride	Caprolactam	1:1	Heating from 20 to 120°C at a rate of 10°C intervals	4 h	0.16	Ren et al. (2016a)
Choline Chloride	Acetamide	1:2	Heating from 20 to 120°C at a rate of 10°C intervals	24 h	0.22	Ren et al. (2016a)
Allyl triethyl ammonium Chloride	Oxalic acid	1:1	Heating at 110°C		6.48	Ren et al. (2016b)
Choline Chloride	Oxalic acid	2:1	Heating at 110°C		0.8	Ren et al. (2016b)

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TABLE 1 (Continued) Solubilities of the cellulose in different DESs.

Hydrogen bond acceptor (HBA)	Hydrogen bond donor (HBD)	Molar ratio (HBA:HBD)	Dissolution Technique	Dissolution time	Solubility (wt%)	References
Choline Chloride	Phenol	2:1	Heating at 75°C and 20 min ultrasonic irradiation	24 h	4.7	Malaek et al. (2018)
Choline Chloride	α-naphthol	1:1	Heating at 75°C and 20 min ultrasonic irradiation	24 h	3.39	Malaek et al. (2018)
Choline Chloride	Resorcinol	1:1	Heating at 75°C and 20 min ultrasonic irradiation	24 h	6.1	Malaek et al. (2018)
Choline Chloride	Maleic acid	1:1	Heating at 75°C and 20 min ultrasonic irradiation	24 h	2.57	Malaek et al. (2018)
Choline Chloride	Ethylene Glycol	1:2	Stirring (500 rpm) at 25°C	1 week	1.3×10^{-4} *	Hakkinen and Abbott (2019)
Choline Chloride	1,5-pentanediol	1:3.5	Stirring (500 rpm) at 25°C	1 week	2.3×10^{-5} *	Hakkinen and Abbott (2019)
Choline Chloride	Glycerol	1:2	Stirring (500 rpm) at 25°C	1 week	1.9×10^{-5} *	Hakkinen and Abbott (2019)
Choline Chloride	Urea	1:2	Stirring (500 rpm) at 25°C	1 week	1.7×10^{-5} *	Hakkinen and Abbott (2019)
Choline Chloride	Oxalic acid dihydrate	1:1	Stirring (500 rpm) at 25°C	1 week	6.8×10^{-5} *	Hakkinen and Abbott (2019)
Choline Chloride	Formic acid	2:1	Heating at 60°C		<1	Lynam et al. (2017)
Choline Chloride	Lactic acid	10:1	Heating at 60°C		<3	Lynam et al. (2017)
Choline Chloride	Acetic acid	2:1	Heating at 60°C		<1	Lynam et al. (2017)
Choline Chloride	Lactic acid	2:1	Heating at 60°C		<1	Lynam et al. (2017)
Choline Chloride	Lactic acid	3.3:1	Heating at 60°C		<1	Lynam et al. (2017)
Tetraethylammonium hydroxide/water	Urea	1:15:2	Room temperature		15	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Urea	1:16:3	Room temperature		10	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Urea	1:15:4	Room temperature		10	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Urea	1:16:5	Room temperature		7.5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Urea	1:15:6	Room temperature		7.5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Methylurea	1:15:2	Room temperature		12.5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Methylurea	1:16:3	Room temperature		5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Methylurea	1:15:4	Room temperature		5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Methylurea	1:16:5	Room temperature		5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Methylurea	1:15:6	Room temperature		5	Sirvio and Heiskanen (2020)

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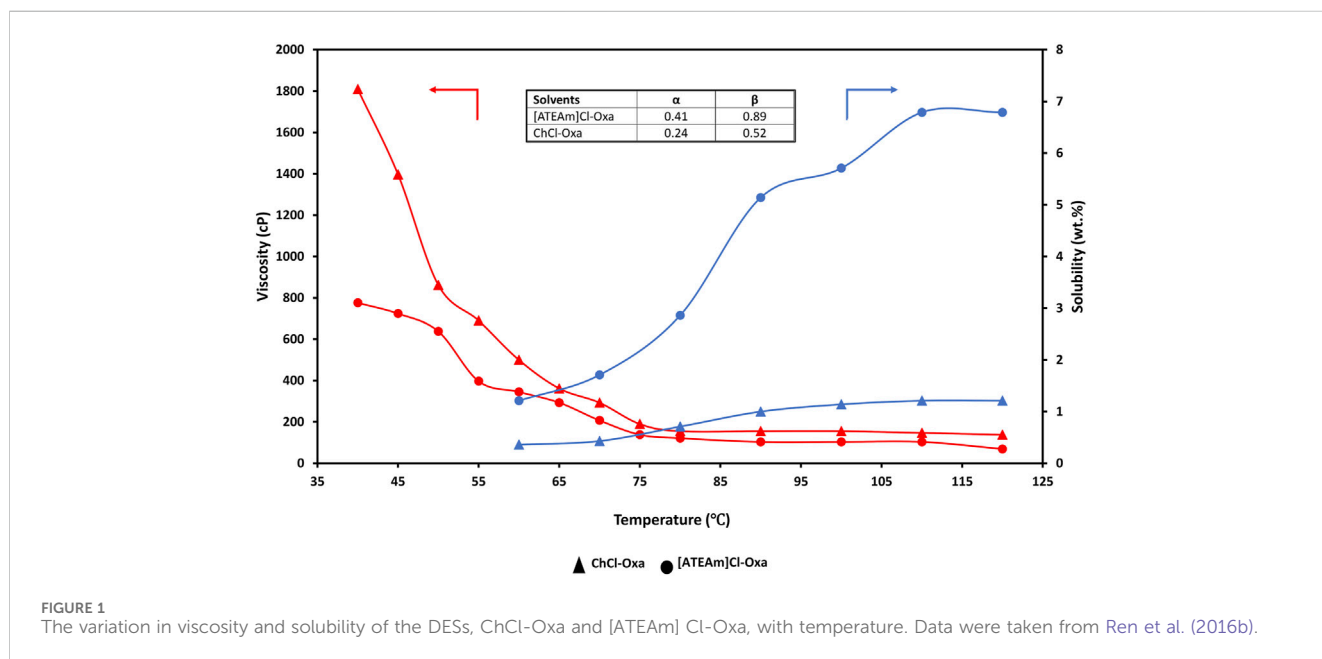
TABLE 1 (Continued) Solubilities of the cellulose in different DESs.

Hydrogen bond acceptor (HBA)	Hydrogen bond donor (HBD)	Molar ratio (HBA:HBD)	Dissolution Technique	Dissolution time	Solubility (wt%)	References
Tetraethylammonium hydroxide/water	Methylurea	1:15:7	Room temperature		5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Ethylurea	1:16:2	Room temperature		12.5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Ethylurea	1:16:3	Room temperature		Non	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Ethylurea	1:15:4	Room temperature		Non	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	Ethylurea	1:15:5	Room temperature		Non	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	1,3 Dimethylurea	1:16:2	Room temperature		7.5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	1,3 Dimethylurea	1:16:3	Room temperature		5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	1,3 Dimethylurea	1:15:4	Room temperature		5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	1,3 Dimethylurea	1:15:5	Room temperature		5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	1,3 Dimethylurea	1:16:6	Room temperature		5	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	1,3 Dimethylurea	1:14:7	Room temperature		Non	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	1,3 Dimethylurea	1:15:2	Room temperature		10	Sirvio and Heiskanen (2020)
Tetraethylammonium hydroxide/water	1,3 Dimethylurea	1:15:3	Room temperature		Non	Sirvio and Heiskanen (2020)
Zinc Chloride/Water	Phosphoric acid	1:3:0.6	Room temperature		15	Tong et al. (2021)
Zinc Chloride/Water	Formic acid	1:1:4	Room temperature	1.6 h	15	Tong et al. (2022)
Zinc Chloride/Water	Formic acid	1:2:4	Room temperature	6 h	12.5	Tong et al. (2022)
Zinc Chloride/Water	Formic acid	1:3:4	Room temperature	7 h	9	Tong et al. (2022)
Zinc Chloride/Water	Formic acid	1:4:4	Room temperature	13.5 h	8	Tong et al. (2022)
Choline Chloride	Urea	2:1	Heating at 100°C	3 h	1.03	Zhang et al. (2020)
Choline Chloride	Citric acid	2:1	Heating at 100°C	2 h	1.94	Zhang et al. (2020)
Choline Chloride	Oxalic acid	2:1	Heating at 100°C	1.5 h	2.54	Zhang et al. (2020)
Choline Chloride	Glycerol	2:1	Heating at 100°C	12 h	0.6	Zhang et al. (2020)
Choline	L-lysine	1:2	Ultrasound (600 W) 40 min and heating at 90°C	24 h	~5	Wang et al. (2020)
Choline Chloride	Urea	1:2	Heating at 100°C	24 h	Non	Zhong et al. (2022)
Choline Chloride	Thiourea	1:2	Heating at 100°C	24 h	Non	Zhong et al. (2022)
Choline Chloride	Resorcinol	1:1	Heating at 100°C	24 h	Non	Zhong et al. (2022)
Choline Chloride	Imidazole	3:7	Heating at 100°C	24 h	Non	Zhong et al. (2022)
Choline Chloride	Acetic acid	1:1	Heating at 60°C	24 h	Non	Zhong et al. (2022)
Choline Hydroxide	Urea	1:2	Heating at 70°C	20 min	9.51	Zhong et al. (2022)

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TABLE 1 (Continued) Solubilities of the cellulose in different DESs.

Hydrogen bond acceptor (HBA)	Hydrogen bond donor (HBD)	Molar ratio (HBA:HBD)	Dissolution Technique	Dissolution time	Solubility (wt%)	References
Choline Hydroxide	Thiourea	1:2	Heating at 70°C	2 h	Non	Zhong et al. (2022)
Choline Hydroxide	Resorcinol	1:1	Heating at 100°C	2 h	Non	Zhong et al. (2022)
Choline Hydroxide	Imidazole	3:7	Heating at 100°C	2 h	Non	Zhong et al. (2022)
Choline Hydroxide	L-Histidine	1:1	Heating at 100°C	2 h	Non	Zhong et al. (2022)
Choline Hydroxide	Serine	1:1	Heating at 100°C	2 h	Non	Zhong et al. (2022)
Tetramethylammonium Chloride	Formic acid	1:3	Heating at 90°C	2 h	<0.49	Zhang et al. (2023)
Tetramethylammonium Chloride	Glycolic acid	1:2	Heating at 90°C	2 h	<0.54	Zhang et al. (2023)
Tetramethylammonium Chloride	Ethylene glycol	1:2	Heating at 90°C	2 h	<0.66	Zhang et al. (2023)
Choline Chloride	Oxalic acid	1:2	Heating at 90°C	2 h	<0.58	Zhang et al. (2023)
Choline Chloride	Oxalic acid	1:1	Heating at 90°C	2 h	<0.62	Zhang et al. (2023)



3 Exploration of key factors for cellulose dissolution in deep eutectic solvents

Literature studies indicate that the hydrogen bond acceptor strength (β) of a deep eutectic solvent (DES) is the primary factor influencing its ability to dissolve cellulose. Ren et al (2016a) reported the highest cellulose solubility of 2.48% for the DES, choline chloride/imidazole, with the highest basicity ($\beta = 0.864$). The order of solubility of DES correlated with the order of basicity values: Choline chloride/imidazole (2.48 wt%, $\beta = 0.864$) > choline chloride/urease (1.45 wt%, $\beta = 0.821$) > choline

chloride/ammonium thiocyanate (0.83 wt%, $\beta = 0.81$). Similarly, the data reported by Zhong et al. (2022) show that the higher cellulose solubility in choline hydroxide/urea ($\beta = 1.88$) than in choline chloride/urea ($\beta = 0.49$) is directly related to the basicities of the DESs.

Viscosity of the DES is another important parameter controlling its dissolution power. The solvents with lower viscosity penetrate the polymer matrix more readily, enhancing polymer chain mobility, leading to faster dissolution rates. Ren et al. (2016b) noted that the DES composed of allyl triethyl ammonium chloride ([ATEAm]Cl) and oxalic acid (Oxa) demonstrated greater cellulose dissolution compared to choline chloride (ChCl) and Oxa. This difference was

attributed to its lower viscosity, as illustrated in Figure 1. A lower activation energy for [ATEAm]Cl-Oxa (44.56 kJ mol⁻¹), compared to ChCl-Oxa (57.82 kJ mol⁻¹) suggests weaker hydrogen bonding between chloride and Oxa in [ATEAm]Cl-Oxa, leading to increased interaction with cellulose molecules and a higher cellulose dissolution capacity. In another study, the same research group reported the highest cellulose solubility at 2.48% in choline chloride/imidazole, which exhibited the lowest viscosity among the investigated DESs (Ren et al., 2016a). Fan et al. (2021) found that the viscosity of the natural deep eutectic solvents (NADES) correlates with the hydrogen-bond number and lifetime. Among five terpene-based natural deep eutectic solvents (NADES) including camphor/formic acid, menthol/acetic acid, menthol/ β -citronellol, menthol/lactic acid, and thymol/ β -citronellol, terpene-acid-based NADES with single sites exhibited the lowest viscosity due to their weak and unstable hydrogen bonding. Conversely, NADES based on multi-site terpene acids had comparatively higher viscosity. Based on their results, the DES with the lowest binding energy also demonstrated the lowest viscosity. Ghaedi et al. (2017) reported that the higher molecular weight of the DES resulted in the higher viscosity and surface tension.

The intrinsic viscosity (η_{sp}) of a DES/cellulose solution serves as another reference standard for solvation capacity of the DESs and can be calculated by Eqs 1, 2.

$$\eta = \left(\frac{\eta_{sp}}{C}\right)_{C \rightarrow 0} \quad (1)$$

$$\eta_{sp} = C[\eta] + K_H(C[\eta])^2 + A(C[\eta])^n \quad (2)$$

where K_H represents the Huggins constant, and solutes are considered dissolved in solvents when K_H is less than 0.5 (Kulicic and Kniewsker, 1984). Tong et al. (2022) reported that the K_H values, and consequently the viscosity of the cellulose solution increased with the degree of polymerization of cellulose, leading to a lower level of cellulose dissolution.

Theoretically, cellulose dissolution takes place when Gibbs free energy change ($\Delta G < 0$) is negative. Considering that $\Delta G = \Delta H - T\Delta S$, then, if the dissolution is endothermic ($\Delta H > 0$), the entropic contribution, $T\Delta S$, may not be sufficient to counterbalance the ΔH , thus the dissolution process will not be spontaneous. Tong et al. (2022) observed enhanced cellulose solubility with the increased exothermic heat of mixing for DESs formulated using combinations of ZnCl₂, water, and formic acid. Additionally, they noted that the DESs that induce more exothermic dissolution, leading to lower ΔG values, consequently, an exponential increase in the equilibrium constant shortened the dissolution time. Conversely, DESs that exhibited increased cellulose solubility with temperature, suggesting endothermic dissolution, dissolved cellulose at lower levels (Figure 1).

The presence of excessive water molecules is another factor affecting the dissolution power of DES. An increased water content in the DES formulation resulted in a reduction of the dissolved cellulose amount. (Tong et al., 2022; Zhong et al., 2022). Furthermore, the addition of the hydrophilic compound PEG in the DES formulation played a crucial role in disrupting the strong intermolecular hydrogen bonds between cellulose molecules. Ren et al. (2016a) reported improved cellulose solubility in choline chloride/imidazole-coupled PEG.

4 Computational tools for predicting the cellulose solubility in deep eutectic solvents

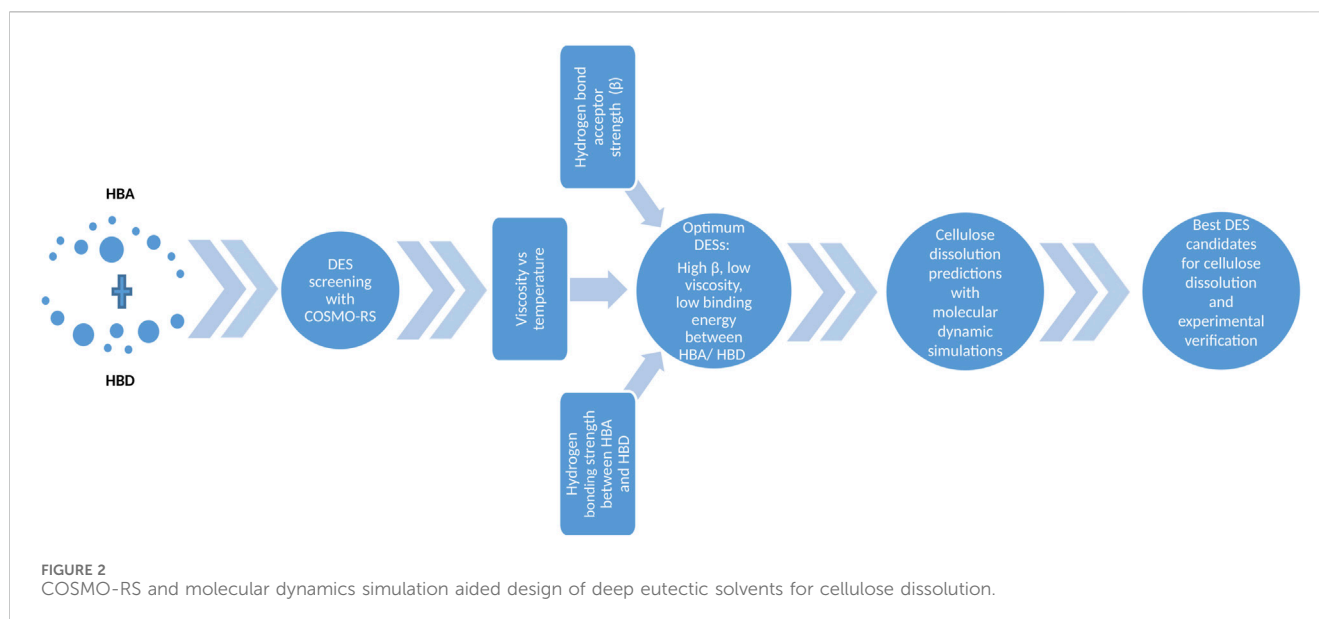
Generally, the solubility parameter (or Hildebrand parameter) is the most commonly used criterion in choosing a suitable solvent for dissolving a polymer based on the principle of “like dissolves like” (Hildebrand et al., 1962; Hansen et al., 2007). The small value of Flory-Huggins interaction parameter, ($\chi < 0.5$), which is proportional to polymer (δ_p) and solvent (δ_s) Hildebrand solubility parameters, $\chi \approx \frac{(\delta_p - \delta_s)^2}{RT}$ indicates complete dissolution of polymer by the selected solvent (Miller-Chou and Koenig, 2003). However, recent reports showed that solubility parameters cannot be a guideline for predicting polymer solubilities in DES and ILs (Winterton et al., 2006; Ueki and Watanabe, 2012; Ismail et al., 2022). For example, Ismail et al. (2022) calculated the solubility parameters from the group contribution method for three types of non-ionic DES and polyvinylidene fluoride (PVDF). According to their results, PVDF was not expected to be soluble in any of the DES, but indeed, PVDF was dissolved in all three DES.

Recent experimental studies have shown that the HBA strength, β values, can be a valuable indicator for evaluating the DES's cellulose dissolving power. β values and the other 2 Kamlet-Taft (KAT) polarity parameters can be experimentally measured using solvatochromic dyes (Zhong et al., 2022). However, considering the large number of HBA and HBD combinations for DES formulation, experimental screening of all formulations is expensive and impractical. A quantum chemical (QC) based conductor-like screening model real solvent (COSMO-RS) approach is a practical tool for predicting the KAT parameters of the DESs. In this method, the COSMO file is generated through independent optimization of the geometries of the HBAs and HBDs by QC calculation. Next, hydrogen bonding energy (EHB), misfit energy (EMF), van der Waals energy, and non-bonded interactions of DES are estimated using the COSMO-RS model. The H-bond acidity and basicity values are then calculated using the three specific interactions by Eqs 3, 4.

$$\alpha = A_\alpha \frac{E_{HB}}{\sum_n E_{HB}} + B_\alpha \frac{E_{MF}}{\sum_n E_{MF}} + C_\alpha \frac{E_{vDW}}{\sum_n E_{vDW}} + D_\alpha \quad (3)$$

$$\beta = A_\beta \frac{E_{HB}}{\sum_n E_{HB}} + B_\beta \frac{E_{MF}}{\sum_n E_{MF}} + C_\beta \frac{E_{vDW}}{\sum_n E_{vDW}} + D_\beta \quad (4)$$

The constants A_α , B_α , C_α , and D_α , as well as A_β , B_β , C_β , and D_β , are determined by fitting the interaction energies of a specific subclass of DES to the experimentally determined KAT parameters. The subclasses are constructed based on the hydrophilicity/hydrophobicity of the DESs. Within each hydrophilic or hydrophobic group, the subgroups are then generated based on HBA and HBD types. Kundu et al. (2020) analyzed experimental data on 88 types of DESs. Among these, 26 fall into the hydrophilic class while the remaining belong to the hydrophobic class. The hydrophilic class comprises 19 ChCl-based DESs, 3 other choline cation-based DESs, 3 betaine DESs, and 1 ethyl (2-hydroxyethyl) dimethylammonium DES. The hydrophobic class is further divided into 34 tetraalkylammonium salt-based DESs (including chloride and bromide anions), 11 menthol-based DESs, and 17 thymol-based DESs. They predicted α and β parameters for these 88 DESs, yielding deviations of less than 2.25% and 3.14%, respectively. Subsequently, these models were applied to predict α and β values for novel hydrophilic and hydrophobic DESs formulated with new HBA and HBD. Based on



their predictions, tetraalkylammonium-based hydrophobic deep eutectic solvents (DESs) containing tetraheptylammonium chloride octanoic acid ([N7777]Cl/OctA) and tetraoctylammonium chloride octanoic acid ([N8888]Cl/OctA) show potential for high cellulose dissolution capacity, attributed to their relatively high β values. These estimations align with the experimental data reported by *Sirvio and Heiskanen (2020)* for tetraethylammonium hydroxide/water, which dissolved 15% cellulose at room temperature.

The KAT parameters were also predicted with the molecular dynamics (MD) and Monte Carlo (MC) approaches based on interactions with solvatochromic dye. However, developing reliable force fields for the DESs is still challenging. Consequently, the accuracy of predicted datasets remains questionable when employing the MD approach. Moreover, both approaches are computationally expensive, and given the ever-growing number of DES, constructing a comprehensive database using these approaches would be time consuming. Therefore, these methods are not suitable for a fast priori prediction.

5 Future directions and conclusion

Knowing the hydrogen bond acceptor strength (β) and viscosity of the DESs can provide insight into their capacity for dissolving cellulose. However, the experimental measurement of these quantities is a significant challenge and practically unfeasible task due to numerous alternative HBA and HBD couples that can be used in DES formulation. At this stage, computational tools can serve as a valuable resource for fast screening alternative DES formulations (*Figure 2*).

The COSMO-RS-aided design proves helpful in attaining this objective, as it can predict KAT parameters, viscosity, and hydrogen bonding strength between HBA and HBD groups in DES. Screening numerous DES formulations to identify those with high hydrogen bond basicity (β), low viscosity, low activation energy, and weak hydrogen-bonding strength saves time and resources. As a result, this approach enhances the chances of discovering promising DESs. The subsequent step involves implementing molecular dynamic

simulations to predict cellulose dissolution with optimal DES formulations, followed by experimental verification of the predictions. Utilizing computational power and experimental tools is believed to advance our current understanding of cellulose dissolution in DESs. The accuracy of COSMO-RS predictions is significantly dependent on the precise theoretical representation of interaction energies within the framework. As a result, further improvement of the predicted and extended scale database should be achieved by incorporating various interaction parameters available in the literature. Moreover, the emergence of artificial intelligence (AI)-based methodologies provides a novel avenue for establishing correlations between structure and material properties.

Cellulose dissolution occurs only when the dissolved state has lower energy compared to the solid state, indicating a balance between the enthalpy of mixing and the entropy term. From this perspective, designing DESs with excellent interaction with cellulose, thereby overcoming the low entropy gain, and providing an exothermic heat of mixing will enhance cellulose dissolution. Given that cellulose has both hydrophilic (equatorial OH-groups) and hydrophobic (axial CH groups) features, DES formulations should incorporate both a hydrogen bonding component and a hydrophobic segment to achieve high dissolution capacity for cellulose. Additionally, the experimental findings suggest that the HBA and HBD couples for DES design should feature short chains and single sites for binding. This design choice leads to DESs with lower molecular weights, resulting in reduced viscosity and weaker hydrogen bonding.

The exploration of industrial applications for DESs is still in its early stages of development. Future research in this area should focus on developing tailored DESs with low viscosity, high thermal stability, long lifetime, and the ability to provide efficient dissolution at room temperature within a short timeframe.

Author contributions

SA: Conceptualization, Data curation, Formal Analysis, Investigation, Writing—original draft, Writing—review and editing.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

- Cardellini, F., Germani, R., Cardinali, G., Corte, L., Roscini, L., Spreti, N., et al. (2015). Room temperature deep eutectic solvents of (1S)-(+)-10-camphorsulfonic acid and sulfobetaines: hydrogen bond-based mixtures with low ionicity and structure-dependent toxicity. *RSC Adv.* 5, 31772–31786. doi:10.1039/c5ra03932k
- Chen, Y.-L., Zhang, X., You, T.-T., and Xu, F. (2019). Deep eutectic solvents (DESs) for cellulose dissolution: a mini-review. *Cellulose* 26, 205–213. doi:10.1007/s10570-018-2130-7
- Chundawat, S. P. S., Sousa, L. D., Roy, S., Yang, Z., Gupta, S., Pal, R., et al. (2020). Ammonia-salt solvent promotes cellulosic biomass deconstruction under ambient pretreatment conditions to enable rapid soluble sugar production at ultra-low enzyme loadings. *Green Chem.* 22, 204–218. doi:10.1039/c9gc03524a
- Egal, M., Budtova, T., and Navard, P. (2008). The dissolution of microcrystalline cellulose in sodium hydroxide-urea aqueous solutions. *Cellulose* 15, 361–370. doi:10.1007/s10570-007-9185-1
- Fan, C., Liu, Y., Sebbah, T., and Cao, X. L. (2021). A theoretical study on terpene-based natural deep eutectic solvent: relationship between viscosity and hydrogen-bonding interactions. *Glob. Challenges* 5, 2000103. doi:10.1002/gch2.202000103
- Flieger, J., and Flieger, M. (2020). Ionic liquids toxicity—benefits and threats. *Int. J. Mol. Sci.* 21, 6267. doi:10.3390/ijms21176267
- Francisco, M., van den Bruinhorst, A., and Kroon, M. C. (2012). New natural and renewable low transition temperature mixtures (LTTMs): screening as solvents for lignocellulosic biomass processing. *Green Chem.* 14, 2153–2157. doi:10.1039/c2gc35660k
- Ghaedi, H., Ayoub, M., Sufian, S., Shariff, A. M., and Lal, B. (2017). The study on temperature dependence of viscosity and surface tension of several Phosphonium-based deep eutectic solvents. *J. Mol. Liq.* 241, 500–510. doi:10.1016/j.molliq.2017.06.024
- Hakkinen, R., and Abbott, A. (2019). Solvation of carbohydrates in five choline chloride-based deep eutectic solvents and the implication for cellulose solubility. *Green Chem.* 21, 4673–4682. doi:10.1039/c9gc00559e
- Hansen, C. M. (2007). *Hansen solubility parameters: a user's handbook*. Boca Raton, FL: CRC Press.
- Hayyan, M., Mboous, Y. P., Looi, C. Y., Wong, W. F., Hayyan, A., Salleh, Z., et al. (2016). Natural deep eutectic solvents: cytotoxic profile. *SpringerPlus* 5, 913. doi:10.1186/s40064-016-2575-9
- Heinze, T., and Koschella, A. (2005). Solvents applied in the field of cellulose chemistry: a mini review. *Polimeros* 15, 84–90. doi:10.1590/s0104-14282005000200005
- Hertel, M., Bommarium, A., Realf, M., and Kang, Y. (2012). Deep eutectic solvent systems and methods. *Patent*. WO2012/145522.
- Hildebrand, J. H., and Scott, R. L. (1962). *Regular solutions*. Prentice Hall. Englewood Cliffs, N. J.
- Ismail, N., Pan, J., Rahmati, M., Wang, Q., Bouyer, D., Khayet, M., et al. (2022). Non-ionic deep eutectic solvents for membrane formation. *J. Membr. Sci.* 646, 120238. doi:10.1016/j.memsci.2021.120238
- Jin, S., Byrne, F., McElroy, C. R., Sherwood, J., Clark, J. H., and Hun, A. J. (2017). Challenges in the development of bio-based solvents: a case study on methyl(2,2-dimethyl-1,3-dioxolan-4-yl)methyl carbonate as an alternative aprotic solvent. *Faraday Discuss.* 202, 157–173. doi:10.1039/c7fd00049a
- Jordana, A., and Gathergood, N. (2015). Biodegradation of ionic liquids – a critical review. *Chem. Soc. Rev.* 44, 8200–8237. doi:10.1039/c5cs00444f
- Kulicke, M., and Kniewsker, R. (1984). The shear viscosity dependence on concentration, molecular weight, and shear rate of polystyrene solutions. *Rheol. Acta* 23, 75–83. doi:10.1007/bf01333878
- Kundu, D., Rao, P. S., and Banerjee, T. (2020). First-principles prediction of Kamlet–Taft solvatochromic parameters of deep eutectic solvent using the COSMO-RS model. *Industrial Eng. Chem. Res.* 59, 11329–11339. doi:10.1021/acs.iecr.0c00574
- Lynam, J. G., Kumar, N., and Wong, M. J. (2017). Deep eutectic solvents' ability to solubilize lignin, cellulose, and hemicellulose; thermal stability; and density. *Bioresour. Technol.* 238, 684–689. doi:10.1016/j.biortech.2017.04.079
- Malaek, H., Housaindokht, M. R., Monhemi, H., and Izadyar, M. (2018). Deep eutectic solvent as an efficient molecular liquid for lignin solubilization and wood delignification. *J. Mol. Liq.* 263, 193–199. doi:10.1016/j.molliq.2018.05.001
- Miller-Chou, B. A., and Koenig, J. L. (2003). A review of polymer dissolution. *Prog. Polym. Sci.* 28, 1223–1270. doi:10.1016/s0079-6700(03)00045-5
- Pan, M., Zhao, G., Ding, C., Wu, B., Lian, Z., and Lian, H. (2017). Physicochemical transformation of rice straw after pretreatment with a deep eutectic solvent of choline chloride/urea. *Carbohydr. Polym.* 176, 307–314. doi:10.1016/j.carbpol.2017.08.088
- Raus, V., Sturcova, A., Dybal, J., Slouf, M., Vackova, T., Salek, P., et al. (2012). Activation of cellulose by 1,4-dioxane for dissolution in N,N-dimethylacetamide/LiCl. *Cellulose* 19, 1893–1906. doi:10.1007/s10570-012-9779-0
- Ren, H., Chen, C., Guo, S., Zhao, D., and Wang, Q. (2016b). Synthesis of a novel allyl-functionalized deep eutectic solvent to promote dissolution of cellulose. *BioResources* 11 (4), 8457–8469. doi:10.15376/biores.11.4.8457-8469
- Ren, H. W., Chen, C. M., Wang, Q. H., Zhao, D. S., and Guo, S. H. (2016a). The properties of choline chloride-based deep eutectic solvents and their performance in the dissolution of cellulose. *BioResources* 11, 5435–5451. doi:10.15376/biores.11.2.5435-5451
- Rosenau, T., Potthast, A., Adorjan, I., Hofinger, A., Sixta, H., Firgo, H., et al. (2002). Cellulose solutions in N-methylmorpholine-N-oxide (NMMO)–degradation processes and stabilizers. *Cellulose* 9, 283–291. doi:10.1023/a:1021127423041
- Sharma, G., Takahashi, K., and Kuroda, K. (2021). Polar zwitterion/saccharide-based deep eutectic solvents for cellulose processing. *Carbohydr. Polym.* 267, 118171. doi:10.1016/j.carbpol.2021.118171
- Sharma, M., Mukesh, C., Mondal, D., and Prasad, K. (2013). Dissolution of α -chitin in deep eutectic solvents. *RSC Adv.* 3, 18149–18155. doi:10.1039/c3ra43404d
- Sirvio, J. A., and Heiskanen, J. P. (2020). Room-temperature dissolution and chemical modification of cellulose in aqueous tetraethylammonium hydroxide–carbamide solutions. *Cellulose* 27, 1933–1950. doi:10.1007/s10570-019-02907-x
- Swatloski, R. P., Spear, S. K., Holbrey, J. D., and Rogers, R. D. (2002). Dissolution of cellulose [correction of cellose] with ionic liquids. *J. Am. Chem. Soc.* 124 (18), 4974–4975. doi:10.1021/ja025790m
- Tenhunen, T.-M., Lewandowska, A. E., Orelma, H., Johansson, L.-S., Virtanen, T., Harlin, A., et al. (2017). Understanding the interactions of cellulose fibres and deep eutectic solvent of choline chloride and urea. *Cellulose* 25, 137–150. doi:10.1007/s10570-017-1587-0
- Tong, Z., Meng, J., Liu, S., Liu, Y., Zeng, S., Wang, L., et al. (2021). Room temperature dissolving cellulose with a metal salt hydrate-based deep eutectic solvent. *Carbohydr. Polym.* 272, 118473. doi:10.1016/j.carbpol.2021.118473
- Tong, Z., Wang, W., Zeng, S., Sun, Y., Meng, J., Liu, Y., et al. (2022). Hydrogen bond reconstruction strategy for eutectic solvents that realizes room-temperature dissolution of cellulose. *Green Chem.* 24, 8760–8769. doi:10.1039/d2gc03372k
- Ueki, T., and Watanabe, M. (2012). Polymers in ionic liquids: dawn of neoteric solvents and innovative materials. *Bull. Chem. Soc. Jpn.* 85, 33–50. doi:10.1246/bcsj.20110225
- Velioglu, S., Yao, X., Devémy, J., Ahunbay, M. G., Tantekin-Ersolmaz, S. B., Dequidt, A., et al. (2014). Solvation of a cellulose microfibril in imidazolium acetate ionic liquids: effect of a cosolvent. *J. Phys. Chem. B* 118, 14860–14869. doi:10.1021/jp508113a
- Wang, J., Wang, Y., Ma, Z., and Yan, L. (2020). Dissolution of highly molecular weight cellulose isolated from wheat straw in deep eutectic solvent of Choline/L-lysine hydrochloride. *Green Energy & Environ.* 5, 232–239. doi:10.1016/j.gee.2020.03.010

- Winterton, N. (2006). Solubilization of polymers by ionic liquids. *J. Mater. Chem.* 16, 4281–4293. doi:10.1039/b610143g
- Xiong, P., Zhao, K., Hu, L., Zhang, L., and Cheng, G. (2014). Dissolution of cellulose in aqueous NaOH/urea solution: role of urea. *Cellulose* 21, 1183–1192. doi:10.1007/s10570-014-0221-7
- Zhang, C., Liu, R., Xiang, J., Kang, H., Liu, Z., and Huang, Y. (2014). Dissolution mechanism of cellulose in N,N-dimethylacetamide/lithium chloride: revisiting through molecular interactions. *J. Phys. Chem. B* 118, 9507–9514. doi:10.1021/jp506013c
- Zhang, H., Lang, J., Lan, P., Yang, H., Lu, J., and Wang, Z. (2020). Study on the dissolution mechanism of cellulose by ChCl-based deep eutectic solvents. *Materials* 13, 278. doi:10.3390/ma13020278
- Zhang, J., Wu, J., Yu, J., Zhang, X., He, J., and Zhang, J. (2017). Application of ionic liquids for dissolving cellulose and fabricating cellulose-based materials: state of the art and future trends. *Mater. Chem. Front.* 1, 1273–1290. doi:10.1039/c6qm00348f
- Zhang, L., Yu, H., Liu, S., Wang, Y., Mu, T., and Xue, Z. (2023). Kamlet–Taft parameters of deep eutectic solvents and their relationship with dissolution of main lignocellulosic components. *Ind. Eng. Chem. Res.* 62, 11723–11734. doi:10.1021/acs.iecr.3c01309
- Zhao, H., Jones, C. L., Baker, G. A., Xia, S., Olubajo, O., and Person, V. N. (2009). Regenerating cellulose from ionic liquids for an accelerated enzymatic hydrolysis. *J. Biotechnol.* 139, 47–54. doi:10.1016/j.jbiotec.2008.08.009
- Zhong, Y., Wu, J., Kang, H., and Liu, R. (2022). Choline hydroxide based deep eutectic solvent for dissolving cellulose. *Green Chem.* 24, 2464–2475. doi:10.1039/d1gc04130d