

# Deliquescence Behavior of Deep Eutectic Solvents

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**Abstract:** Deep eutectic solvents (DESs) are formed by a hydrogen bond donor and an acceptor. The hydrogen bond interactions between these two components significantly depress the melting temperature of the mixture. DESs have been used as an alternative for organic solvents in various branches of the chemical industry. Many DESs are very hygroscopic and water is known to change the properties of DESs, but there has never been a systematic study performed on the deliquescence behavior of DESs. Therefore, this study investigated the thermal and deliquescent behavior of four DESs. The DES mixtures were stored in desiccators at different relative humidities (RH) to investigate the critical RH (RH<sub>0</sub>) for deliquescence. It was found that, due to the formation of a eutonic mixture, the RH<sub>0</sub> to induce deliquescence for a given DES mixture was lower compared to the individual components comprising the DES. The results showed that, even though all investigated DESs had eutectic melting temperatures above room temperature, but due to the low RH<sub>0</sub>, they were able to appear liquid at room temperature under ambient conditions. The eutonic and eutectic compositions were identified at different compositions for the DESs. The results emphasize that great care must be taken to control the process and storage conditions for DESs.

**Keywords:** deep eutectic solvents; deep eutectics; deliquescence; vapor sorption; phase behavior



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## 1. Introduction

Deep eutectic solvents (DESs) are a promising class of solvents suggested as alternatives for organic solvents in the chemical industry [1–4]. DESs are formed by intimate mixing of components with a hydrogen bond donor and an acceptor. The large melting point depression found in DESs is caused by the strong hydrogen bond interactions between the two components [3]. Due to the hydrogen bonds between the two DES components, the system does not follow the phase behaviour of simple eutectic systems that can be predicted by the simplified Schröder-Van Laar equation [5]. For melting temperature depressions larger than predicted, an interaction stronger than in the molten phase of the individual components is expected. For DESs, this interaction is a hydrogen bond between the two components. This means that only systems with negative deviations from an ideal phase behaviour can be defined as DESs. Systems that follow the predicted phase behaviour are classified as simple eutectics.

By combining different hydrogen bond donors and acceptors, it is possible to prepare DESs with specific eutectic melting points and/or solvation properties suitable for various technological applications. However, DESs are often hygroscopic, and the presence of sorbed moisture within DESs can change the DES properties and nanostructure [6,7]. After sorption of low amounts of water, a heterogeneous mixture is formed with domains of *water-in-DES* and *DES-in-water* because water acts as a second hydrogen bond donor/acceptor interacting with the DES-components. The relative prevalence of these domains changes with the concentration of water until the solution becomes an aqueous electrolyte-like mixture when the sorbed amount of moisture is able to fully hydrate both DES components [6–8]. The presence of water has also been reported to decrease the melting temperature, as illustrated by a DES consisting of choline chloride (ChCl) and urea.

The eutectic melting temperature of this DES decreased from 23.5 °C at 0 wt% water to 2 °C at 10 wt% water [9]. Other studies have reported that the presence of water within DESs dramatically decreases the viscosity and changes the polarity, conductivity, density, and solvation properties of organic compounds such as drugs [10–12]. The components used to form DESs are typically hygroscopic, able to form hydrates, or exhibit deliquescence at a low level of relative humidity (RH). Despite the impact of water on the properties of a DES, water sorption of DES during deliquescence has not been thoroughly studied.

Deliquescence of a solid crystalline material is a physical phenomenon, where a water-soluble material dissolves in the sorbed moisture at and above a critical relative humidity ( $RH_0$ ) [13]. If the RH decreases below the  $RH_0$ , the material will lose water and recrystallize. It has been reported that the  $RH_0$  for a given deliquescing material can decrease if said material is in contact with a second material [14]. The lowest  $RH_0$  of a binary mixture is called the eutonic point and is the binary composition at which both components reach their solubility limit in the solution [13–15].

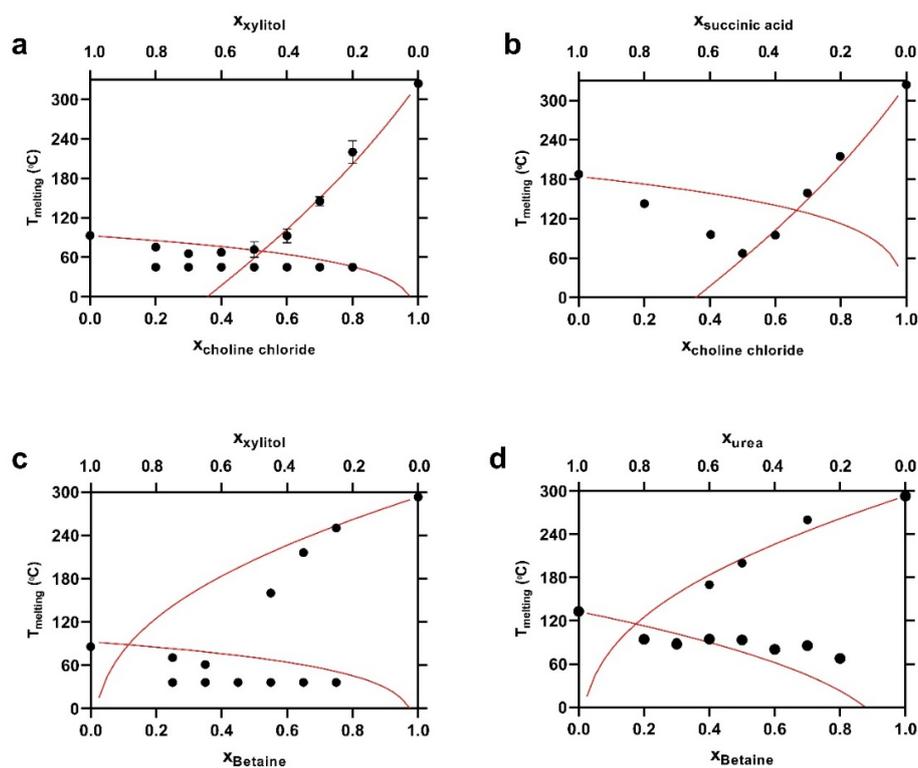
In our preliminary experiments, we experienced that many DESs reported to be liquid at room temperature were solid in our laboratory at dry conditions. However, at high absolute humidity conditions, the DESs become liquid. We believe that the liquid appearance of these mixtures was due to deliquescence and deliquescence lowering and not solely due to the eutectic behavior that these mixtures exhibit. Therefore, this study investigates the phase behaviour of four hygroscopic DESs (ChCl/xylitol, ChCl/succinic acid, betaine/xylitol, and betaine/urea) including two of which (ChCl/xylitol and betaine/urea) that have previously been reported to be liquid at room temperature but remained solid in our laboratory at dry conditions with eutectic melting temperatures above room temperature.

## 2. Results

In this study, we investigated the thermal phase behaviour of the dry DESs by thermomicroscopy, and, subsequently, investigated the  $RH_0$  by placing different molar compositions of the DES systems in desiccators with RHs ranging from 0% RH to 84% RH. Additionally, the precise quantity of moisture sorption at 72% RH was investigated in more detail to understand the relationship between moisture sorption and the  $RH_0$ .

### 2.1. Thermal Phase Behavior

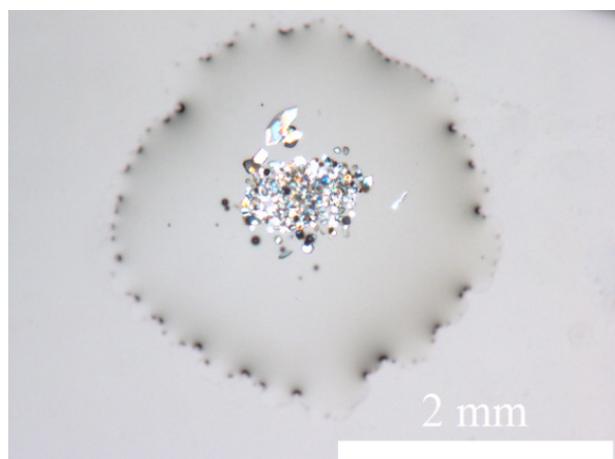
The binary phase diagrams in Figure 1 show the thermal phase behaviour of all the studied DESs in the absence of water. The black dots are experimentally measured melting temperatures, and the red solid-liquid equilibrium lines visualise the phase behaviour predicted by the simplified Schröder-Van Laar equation. The simplified Schröder-Van Laar equation assumes ideal phase behaviour. The experimentally obtained eutectic melting temperatures for ChCl/Succinic acid and betaine/xylitol were lower than those predicted, suggesting that these two systems are DESs. The experimental data for these two DESs were obtained from a previous study in our laboratory [16] and Abbott et al. (2004) [17] for ChCl/succinic acid and betaine/xylitol, respectively. The phase behaviour of ChCl/xylitol and betaine/urea followed almost the predicted phase behaviour. Nevertheless, lower eutectic melting temperatures were also observed for these two DES systems. From Figure 1, it can be seen that the eutectic melting temperatures for all four DESs were above room temperature. The lowest eutectic melting temperature was observed for the betaine/xylitol mixture, which had a eutectic melting temperature of 35 °C [16]. For the ChCl/xylitol system, the exact eutectic compositions were not identified. For all the investigated ChCl/xylitol compositions, the first melting event was observed at 45 °C, which was followed by a second melting event at a higher temperature.



**Figure 1.** Binary phase behavior of four different DESs: (a) ChCl/xylitol, (b) ChCl/succinic acid, (c) betaine/xylitol, and (d) betaine/urea. The red lines indicate the solid-liquid equilibrium line predicted by the simplified Schröder-Van Laar equation. The experimental data points (black dots) in diagram b were adapted from Reference [17] and diagram c was from a previous study in our lab [16].

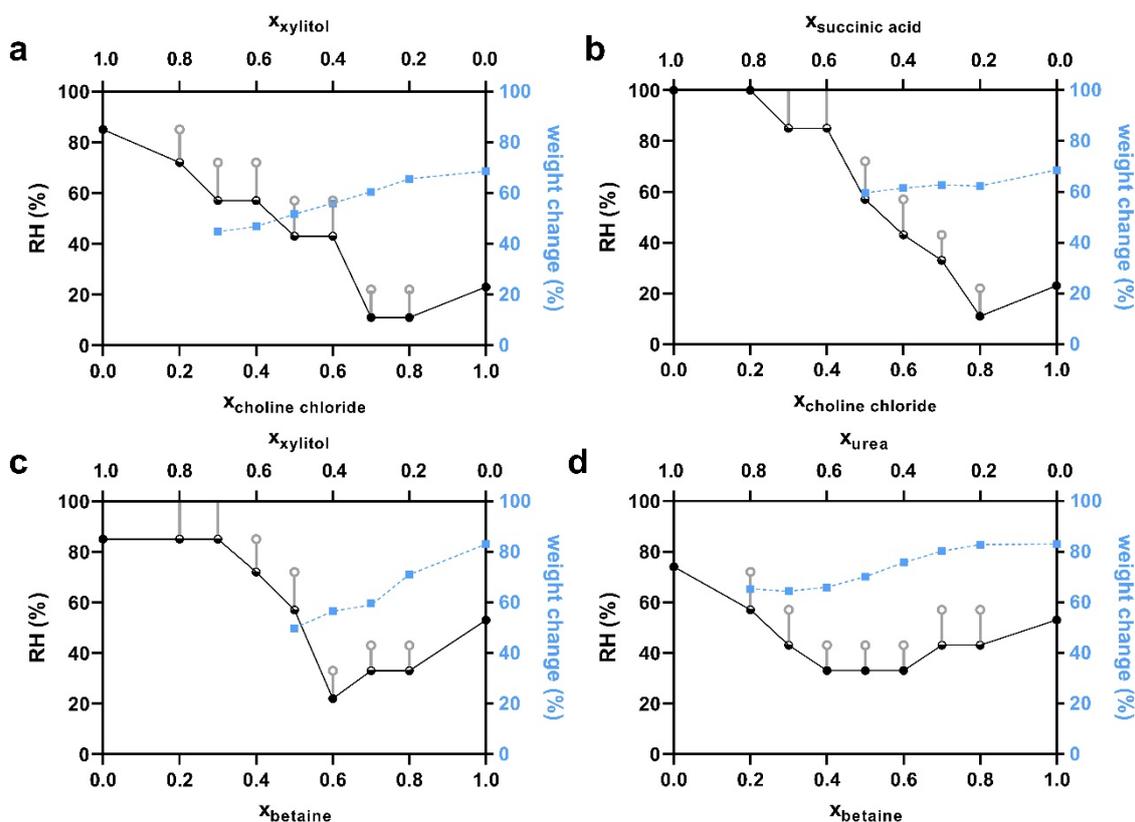
## 2.2. Deliquescence and Moisture Sorption

All the DES mixtures were initially solid physical mixtures but, when the samples were deliquesced at ambient conditions in our laboratory, this occurred for all DESs across the entire composition range with the only exception of ChCl/succinic acid (20:80). The deliquescence process of a 45:55 molar mixture of betaine/xylitol was exemplary captured (see Figure 2) under a microscope at ambient conditions measured to 25 °C and 55% RH.



**Figure 2.** Optical light microscopy image of the deliquescence process of a betaine/xylitol 45:55 mixture at ambient conditions measured to 25 °C and 55% RH under polarized light. Remaining crystals show birefringence in the middle of the image.

To study the deliquescence phase behaviour and to identify the eutonic composition, physical mixtures of the DES components at different molar ratios were stored in desiccators with various RHs. For comparison, the deliquescence of the individual components was also investigated. For all four DESs, a deliquescence lowering was observed compared with the individual components comprising the DESs (Figure 3). The deliquescence point of the eutonic composition was found to be lowered to between 11% and 22% RH for ChCl-based DESs and between 22% and 34% RH for betaine-based DESs. The eutonic compositions were between 0.7 and 0.8 mole fractions of ChCl for ChCl/xylitol and 0.8 for ChCl/succinic acid. For betaine/xylitol and betaine/urea, the eutonic compositions were 0.6 and between 0.4 and 0.6 mole fractions of betaine, respectively. The eutonic compositions were for all the DESs apart from the eutectic compositions seen in Table 1.



**Figure 3.** Deliquescence and moisture sorption behavior of deep eutectic solvents (DESs) at 25 °C. The deliquescence behavior (left y-axis) is plotted with markers representing observations of the physical appearance of the DESs as either solid (●), suspension (◐), or solution (○). The grey vertical line is connecting the observations where transitions in physical appearance have occurred, i.e., it indicates the RH range in which a transition from solid or suspension to solution occurred. The moisture sorption at 72% RH (right y-axis) is plotted as light blue squares (■). The DESs are: (a) ChCl/xylitol, (b) ChCl/succinic acid, (c) betaine/urea, and (d) betaine/xylitol.

**Table 1.** Eutectic and eutonic composition of deep eutectic solvents (DESs).

	Eutectic Composition *	Eutonic Composition *
ChCl/xylitol	n/a	0.7–0.8
ChCl/succinic acid	0.5	0.8
Betaine/xylitol	0.45	0.6
Betaine/urea	0.2–0.3	0.4–0.6

\* Mole fraction of betaine or ChCl.

Investigating the amount of sorbed water is important to understand the relationship between moisture sorption and the  $RH_0$ , and whether the systems at certain RH behaves as a DES or as an aqueous solution of DES components. The moisture sorption was investigated at a fixed RH of 72%. A relatively high RH was selected to be able to investigate a broad range of compositions. The amount of sorbed moisture was dependent on the composition seen in Figure 3 (on the right y-axis). Despite the lower  $RH_0$  for the DES mixtures, the highest sorption of moisture at 72% RH was observed for the hydrogen bond acceptors alone (choline chloride and betaine) and not for the DES. The sorbed amount of moisture was equal to a weight change of 81% for betaine and 69% for ChCl. The amount of sorbed moisture decreased across the composition range from betaine and ChCl toward higher contents of the hydrogen bond donors (urea, xylitol, and succinic acid).

### 3. Discussion

The experimental melting temperatures were significantly lower than those predicted by the simplified Schröder-Van Laar equation and confirmed the presence of a DES system for ChCl/succinic acid and betaine/xylitol. The phase behaviour of ChCl/xylitol and betaine/urea almost followed the predicted phase behaviour. However, the measured melting temperatures were slightly lower than predicted by the simplified Schröder-Van Laar equation. Thus, these two systems can also be classified as DESs. Often in the literature, DESs are referred to as liquid at room temperature without further information about their thermal phase behaviour or their water sorption behavior. However, under dry conditions, a distinction between a DES and a simple eutectic can only be made based on the phase behaviour rather than its physical appearance at room temperature. In addition, when preparing a physical mixture of two DES components under uncontrolled humidity, the physical appearance may be liquid as a result of deliquescence rather than a melting point depression below room temperature. All DESs characterised in this study had a eutectic melting temperature above room temperature for the dry physical mixtures. However, the DESs became liquid at ambient conditions as the humidity in our lab exceeded the  $RH_0$ , as captured by microscope in Figure 2. In the literature, betaine/urea has previously been reported to be liquid in a molar range from 50:50 to 25:75 [18]. In addition, ChCl/xylitol has been reported to be liquid at room temperature [19] even in a wide composition range from 33:66 to 66:33 [20]. Our data suggest that the liquid appearance at room temperature of these DESs is due to deliquescence and not alone due to the eutectic behaviour that these systems also exhibit. The preparation of DESs are often performed over a timespan of hours [11,19], possibly allowing sorption of a significant amount of water if proper humidity control was not in place.

The results showed that the  $RH_0$  was lowered for all the studied systems, making humidity control even more critical than for the individual hygroscopic DES-components. The eutonic compositions were not identical to the eutectic compositions. The eutonic compositions were observed at a larger mole fraction of the hydrogen bond acceptors when compared with the eutectic compositions. This means that sorption of water might also lead to unintentionally falsely reported DES compositions if preparation of the mixtures was done in an uncontrolled, humid environment. For example, the two DESs, known as ChCl/Glucose [21] and ChCl/acetylsalicylic acid [22], have been reported to be liquid at room temperature. However, other studies have reported the two DESs to have eutectic melting temperatures of 57.4 °C [23] and 63 °C [24], respectively. The difference in melting temperatures has also been previously explained by sorbed moisture [23]. For DESs liquid at room temperature at the eutectic composition, sorption of water can also broaden the composition range at which the DES appears liquid at room temperature. There was no correlation between the  $RH_0$  and the amount of sorbed moisture, and it was found that it depends alone on the affinity of the individual components towards water rather than the mixture. This is in line with the mechanism that water interrupts the DES nanostructure by formation of domains with water-in-DES and DES-in-water. Moisture sorption has also been investigated for other DESs with a melting temperature below room temperature

(at dry conditions). It was found that these systems sorbed moisture until the liquid-vapor equilibrium was established. In addition, here, the amount of sorbed moisture varied significantly even between DESs with a similar hydrogen bond acceptor [25]. A common strategy to prevent water within the DES is to dry the DES-components before preparation or subsequent drying of the prepared DES using vacuum [9,25].

In many studies, water has intentionally been added to tailor DESs for specific application purposes and to compensate for some of the disadvantages of DES, such as high viscosity [3,10]. Even after the intentional addition of water, strict humidity control cannot be neglected as further sorption or desorption of water might take place and change the desired physicochemical properties. The thermal phase diagrams and deliquescence phase diagrams presented in this study demonstrated that the difference in physical appearance between reported data on DESs could be explained by deliquescence. In this study, all four DESs would appear liquid at 43% RH at room temperature at the eutonic composition. However, all four DESs have eutectic melting temperatures well above room temperature. Thus, the preparation of DESs in uncontrolled RH conditions may result in variations in water content over time with potential critical consequences on the physico-chemical properties of the resulting DES. For technological applications of DESs, it will be important to operate in a controlled environment and clearly define the target product profiles (TPP) and related critical quality attributes (CQA), e.g., by implementing the quality-by-design (QbD) approach for product development, in order to control and obtain the desired product characteristics [26].

## 4. Materials and Methods

### 4.1. Materials

Phosphorpentoxide, lithium chloride, potassium acetate, magnesium chloride, potassium chloride, potassium carbonate, sodium bromide, potassium iodide, potassium chloride, succinic acid, urea, ChCl, betaine, and xylitol were all purchased from Sigma Aldrich (Darmstadt, Germany).

### 4.2. Thermomicroscopy

Physical mixtures of ChCl/xylitol and betaine/urea were prepared by mixing the DES-components with a pestle and mortar. Subsequently, the mixtures were stored in an open glass vial for 5 days in a desiccator with phosphorpentoxide before analysis. The thermal phase behavior was determined in a Mettler Toledo HS82 microscope hot-stage (Columbus, OH, USA) controlled by a Mettler Toledo FP90 central processor used in combination with a Zeiss Axiolab microscope (Copenhagen, Denmark) with a Carl Zeiss A-Plan 5×/0.12 objective and a polarized filter. The mixtures were heated at a heating rate of 10 °C/min from ambient temperature to the temperature at which the mixture became molten ( $n = 3$ ). The results were confirmed by heating 200 mg of the same samples in sealed glass vials from an ambient temperature to 300 °C in a silicon oil bath while visually examining the phase behavior.

### 4.3. Predicted Thermal Phase Behavior

The simplified Schröder-Van Laar equation (Equation (1)) was used to predict the theoretical phase diagram assuming no interaction between the DES-components [27].

$$\ln(x) = \frac{\Delta H_0}{R} \left( \frac{1}{T_0} - \frac{1}{T} \right) \quad (1)$$

To predict the phase behavior, the heat of fusion ( $\Delta H_0$ ), and fusion temperature ( $T_0$ ), information is required for all components. To predict the melting temperature ( $T$ ) at a given molar composition ( $x$ ), the gas constant ( $R$ ) was used. In this study, heat of fusion and temperature information from the literature were used for succinic acid ( $T_0 = 183.85$  °C,  $\Delta H_0 = 32.94$  kJ/mol) [28], xylitol ( $T_0 = 95.89$  °C,  $\Delta H_0 = 33.26$  kJ/mol) [29], urea ( $T_0 = 133.55$  °C,

$\Delta H_0 = 14.6$  kJ/mol [30], ChCl ( $T_0 = 323.85$  °C,  $\Delta H_0 = 4.30$  kJ/mol) [31], and betaine ( $T_0 = 293$  °C,  $\Delta H_0 = 17.98$  kJ/mol) [32] for the calculations.

#### 4.4. Desiccator

All samples were placed in desiccators with saturated salt solutions of: phosphorpentoxide (RH = close to 0%), lithium chloride (RH = 11%), potassium acetate (RH = 22%), magnesium chloride (RH = 33%), potassium carbonate (RH = 43%), sodium bromide (RH = 51%), potassium iodide (RH = 72%), and potassium chloride (RH = 84%). The RH was measured using a Testo 174H humidity sensor from Testo (Alton, UK). All samples of 500 mg were stored in the desiccators for 30 days before being visually analyzed and classified as either a clear solution without particles, a suspension, or a powder blend ( $n = 3$ ).

#### 4.5. Thermogravimetric Analysis

The sorbed amount of water for samples stored at 72% RH was analysed using a Discovery TGA from TA instruments (New Castle, DE, USA) under constant flow of 25 mL/min nitrogen. In addition, 20  $\mu$ L of the sample was heated in an aluminum pan on a titanium TGA pan from room temperature to 300 °C at a heating rate of 5 °C/min ( $n = 3$ ). The amount of sorbed moisture for ChCl and betaine was determined by keeping the solutions isothermal at 175 °C until a stable weight was observed.

#### 4.6. Dynamic Vapor Sorption Analysis

The deliquescence points of the pure components were determined in a VTI-SA+ Vapor Sorption Analyzer from TA instruments (New Castle, DE, USA). The components were dried for 180 min at 60 °C at 0% RH. The components were subsequently exposed to increasing levels of RH at 25 °C starting from 2% RH with incrementally increased humidity of +1% RH until an increase in the sample mass was observed. The components were kept at each RH for a maximum of 10 min ( $n = 1$ ). The deliquescence point of the pure components was used to construct the deliquescence phase diagram in Figure 3.

## 5. Conclusions

All four studied DESs were initially solid at room temperature at dry conditions. However, at humid conditions above the critical RH for deliquescence, a transition from solid to aqueous solution was observed at room temperature. The eutonic and eutectic compositions were not found at the same molar composition for the DESs. The results also showed that, although DESs may appear liquid at room temperature, it might be the result of sorbed moisture rather than melting temperature depressions. The hygroscopic nature of DESs requires strict humidity control during storage and handling of DESs in order to get reliable data and products.

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