

***aquo*-DESS: WATER-BASED BINARY NATURAL DEEP EUTECTIC SOLVENTS**

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ABSTRACT

Deep Eutectic Solvents (DESs) are a class of solvents that are increasing their relevance in the research activity thanks to their environmental-friendly features as well as to their structural characteristics and catalytic properties. Formed by no-solvent mixing of two substances, namely a hydrogen bond donor and a hydrogen bond acceptor, DESs are finding fruitful applications in many different topics as alternatives to common organic compounds.

In this work the realization, the characterization and the solubility applications of a novel water-based class of DESs are proposed. These innovative liquids, called *aquo*-DESs, are binary mixtures of water with glycolic acid (GA) and with trimethylglycine (TMG): GA/H₂O (1/4 molar ratio) and TMG/H₂O (1/5 molar ratio). The DES' identity of these mixtures was demonstrated by: shifts both in terms of the molar fraction and of the melting points in the experimental melting point curves from the theoretical ones; amounts of components over their reported maximum solubility in water; thermogravimetric profiles compared to the pure substances. The *aquo*-DESs were characterized in their viscosity and ionic conductivity in the temperature range 20-55 °C, showing really low viscosity and low ionic conductivity, with a peculiar behavior of the ionic conductivity of GA/H₂O DES. The solubilizing properties of aminoacids, phenols and carboxylic acids showed peculiar really high values whenever the solute can participate to the DES as DES component itself.

KEYWORDS

Deep Eutectic Solvents (DESs); water-based DESs; green solvents; physical properties.

1. INTRODUCTION

The development of novel technologies that can reduce the environmental impact of different chemical applications is nowadays mandatory to properly face the problems of the pollution of the planet[1–3]. From this point of view, the use of green liquids can reduce these matters because the solvent represents the most abundant part of the chemical applications, from transformations to extraction/preconcentration procedures and so on[4,5]. Their dispersion in the atmosphere, due to of their easy evaporation, and their accumulation in different environments, their toxicity and cancerogenicity are pushing the researchers towards novel green solvents in novel applications and towards the solvent shift of known technologies[6–8].

Deep Eutectic Solvents (DESs) are an innovative class of green solvents with interesting and peculiar structural features that are increasing their relevance in the recent years as substitutes of common volatile organic compounds (VOCs) and also of Ionic Liquids (ILs) that can be considered their forerunners[9–12]. These liquids are formed by mixing two hydrogen-bond capable molecules, namely a H-bond donor (HBD) and a H-bond acceptor (HBA) at the proper molar ratio to give stable liquids. The interactions occurring between the HBD and the HBA as well as between the same HBA-HBA and HBD-HBD lead to an impossible regular crystal lattice formation, therefore to liquid systems starting from high melting point components[13–16]. Also, other weak forces, such as halogen bonds or electrostatic interactions can occur in these liquids where the entropy and the inhomogeneity of the structures lead to liquids at the proper molar ratio, indicated as eutectic point[17–19]. The molecules that are reported in literature as capable for DESs formation are mainly carboxylic acids, polyols, alcohols, and so on as HBD, while ammonium or phosphonium salts, zwitterionic inner salts or neutral molecules such as acetamide as well as inorganic salts (also hydrates) are reported to be efficacious HBAs in the DESs formation[11,20–23]. The green properties of the DESs derive from their low or absent vapor pressure; their low or absent toxicity; their biocompatibility (there is also a relevant sub-class of DESs called NADESs for the natural source of the molecules forming them); their recycle possibility[24–29]. DESs share these green properties (also in part) with other green solvents such as the bio-mass derived ones, or with ILs as well, but the great advantage of DESs over all the other green solvents is represented by their synthesis that requires no solvent and it is made by simply mixing and heating the two pure substances with 100% yield and 100% of atom economy and with no purification procedures[30]. Therefore, even if the other solvents can be obtained by common procedures in the organic chemistry field, the higher

easiness and the greenness put the DESs nowadays in great advantage compared to the other green solvents also in industrial applications[31,32].

DESs can also show interesting catalytic features depending on the molecules forming them but also thanks to their structural features. In the literature cases of acidic catalyst DESs, basic ones (also ones formed by acidic molecules), reducing ones and also organocatalytic ones (in case of CDESs, chiral-DESs) are reported, with catalytic mechanisms that are dependent on the properties of the molecules forming them as well as to their association constants in terms of availability of the catalyst out of the DESs formation[33–43].

There are different classes of DESs reported in the literature in dependence of the class of the molecules forming them, and the number of novel mixtures is increasing in the recent years[44,45]. A theoretical-experimental melting point curves comparison approach is nowadays mandatory to define if a mixture is a DESs or a simple solution or eutectic mixture of the components, and this has also more relevance in the case one of the two components is a liquid itself[46,47]. A shift from the theoretical curves in terms both of the molar ratio and of the melting point (that must be deeply reduced from the theoretical) is the prove of the non-ideality of the mixture and of the DES' identity. One of the most interesting mixtures reported in the recent literature is represented by choline chloride/water liquid (ChCl/H₂O)[48]. Water, as the most relevant H-bond capable molecule as well as a really green substance, is used in mixture with ChCl at the ratio of 1/5 ChCl/H₂O to give a eutectic point with a melting temperature of 204 K. However, Coutinho and co-workers, in an extensive study performed on this liquid, did not call this system as "DES" as the temperature shift observed from the theoretical curves is really low and it should be related to the incorporation of water into the ChCl crystal according to their studies[49]. However, this liquid revealed to be useful and green for different applications such as organic transformations[50].

Following our recent results on the preparation and the characterization of a novel hydrophobic water-based DES (thymol/water mixture)[51], in this paper we realized, identified and characterized novel hydrophilic water-based binary Deep Eutectic Solvents, *aquo*-DESs: Glycolic Acid/Water (GA/H₂O) and Trimethylglycine/Water (TMG/H₂O) mixtures. Due to the natural occurrence of all the molecules forming them (both GA and TMG can be found for example in sugar beet), these liquids are also NADESs. The liquids, realized with two molecules already mixed together to give a relevant and widely used DES in the recent literature (GA/TMG)[40,52–57], were identified as DESs thanks to the theoretical-experimental curves comparison approach. They are formed with GA and TMG at amounts far over their maximum solubility in water (GA/H₂O 1/4 molar ratio; TMG/H₂O 1/5 molar

ratio). The thermogravimetric measures helped define them as DES for their peculiar thermal behavior. Then they were characterized in terms of their viscosity, ionic conductivity and ionicity (via Walden plot) in the temperature range 20-55 °C. Finally, measures of solubility of differently structured compounds in these DESs, compared to the values observed in water and in a 45% w/w water solution of GA/TMG DES, showed interesting results when DES-forming molecules are dissolved in them, opening for a new approach to the solubilization of these molecules in this class of green solvents.

2. EXPERIMENTAL

2.1 Reagents and DESs preparation

Glycolic Acid, Trimethylglycine, L-Menthol, Phenylacetic Acid, S-Mandelic Acid, Oxalic Acid dihydrate, Sorbic Acid, R-Carvone, L-Proline, L-Histidine, L-Tyrosine, Benzoic Acid were purchased from Sigma-Aldrich, Merck, Carlo Erba, Acros and they were used without further purifications (all purities >98%). All the DESs and all the mixtures were prepared mixing in small screw-sealed vials with low headspace the components with water at different molar ratios and then heating the samples at 130 °C with a heating gun with heavy shaking in order to prevent evaporation of the components. Then the mixtures were left cooling to room temperature to observe eventual reprecipitation of the components or solidification of the samples. The water contents were also confirmed via Karl-Fischer titrations with a Metrohm 684 KF Coulometer. The 45% w/w water dilution of GA/TMG DES was prepared by adding the proper amounts of water to the pre-formed DES and putting under magnetic stirring overnight at room temperature in order to have homogeneous samples.

2.2 Experimental and theoretical solid-liquid phase diagrams

The stable liquids were identified as DESs with the comparison of the experimental solid-liquid phase diagrams with the theoretical ones by measuring the melting points at different molar fractions. The samples were put in Dewar with CO₂/acetone mixture and the melting points were measured with a thermometer (± 0.1 °C). The melting points were taken in triplicate to avoid kinetic effect on the melting of the mixtures and the values showed standard deviation values <1°C.

The solid–liquid theoretical curves were determined by using the equation (1) that represents the solid-liquid equilibrium curve:

$$\ln(\chi_i \cdot \gamma_i) = \frac{\Delta_m H_i}{R} \cdot \left(\frac{1}{T_{m,i}} - \frac{1}{T} \right) + \frac{\Delta_m C p_i}{R} \cdot \left(\frac{T_{m,i}}{T} - \ln \frac{T_{m,i}}{T} - 1 \right) \quad (1)$$

where χ_i is the mole fraction of component i, γ_i is its activity coefficient in the liquid phase, $\Delta_m H_i$ and $T_{m,i}$ are its melting enthalpy and temperature, respectively, $\Delta_m C p_i$ is its heat capacity change upon melting, R is the ideal gas constant, and T is the absolute temperature of the system. The equation can be simplified by considering negligible the heat capacity change upon the melting of a substance, equation (2):

$$\ln(\chi_i \cdot \gamma_i) = \frac{\Delta_m H_i}{R} \cdot \left(\frac{1}{T_{m,i}} - \frac{1}{T} \right) \quad (2)$$

The theoretical melting temperatures were determined from the theoretical curves by considering the activity coefficients $\gamma_i = 1$. The experimental γ_i values were determined via equation (3) by using the experimentally observed melting temperatures:

$$\gamma_i = \frac{\exp\left[\frac{\Delta_m H_i}{R} \left(\frac{1}{T_{m,i}} - \frac{1}{T} \right)\right]}{\chi_i} \quad (3)$$

2.3 Thermogravimetric analysis

Thermogravimetric analyses (TGA) were performed using a Netzsch STA 2500 Regulus thermal analyzer, equipped with Al₂O₃ crucibles. The samples (10 mg) were heated from 25 °C to 600 °C, under nitrogen atmosphere with a heating rate of 10°C/min. T_{onset} was calculated from the intersection of the baseline weight and the tangent of the weight line when the decomposition of the samples occurred.

2.4 Density measures

The density values of the liquids were measured by weighting the samples in a 5 mL volumetric flask (± 0.025 mL). The flasks were held in a thermostated bath for 1 h then brought to volume by eliminating the suitable amount of liquid with a pipette. The flask was then thermostated at room temperature for 1 h and then weighed on analytical balance to obtain the density value at that temperature.

2.5 Viscosity measures

The viscosity of the samples was measured with a Fungilab Expert L viscometer, fitted with a thermostatic jacket and a temperature probe with a spindle attachment. The viscometer jacket was connected to an external thermostated bath. The different viscosity readings were taken after 20–25 minutes for each temperature selected and the profiles were drawn via subsequent superimposed heating and cooling cycles with standard deviations <1% of the mean value. The activation energies of viscosity E_η were obtained as the slope of the lines obtained via Arrhenius equation (4); all the profiles showed R^2 values >0.99.

$$\ln \eta = \ln \eta_0 + \frac{E_\eta}{RT} \quad (4)$$

2.6 Ionic conductivity and pH measures

Ionic conductivities and pH of the samples were measured with a Hach sensION+ MM374 conductivity and pH meter with the temperature controlled with an external thermostated bath. The different readings were taken after 20–25 minutes for each temperature selected and the profiles were drawn via subsequent superimposed heating and cooling cycles with standard deviations <1% of the mean value of the two cycles. The activation energies of conductivity E_Λ were obtained with the slope of the lines obtained via Arrhenius equation (5) whenever the profiles showed R^2 values >0.99.

$$\ln \sigma = \ln \sigma_0 + \frac{E_\Lambda}{RT} \quad (5)$$

2.7 Walden plot realization

The Walden plots were realized by plotting for each temperature the natural logarithm of molar ionic conductivity (ionic conductivity multiplied by molecular weight at the proper molar ratio divided by density) vs. the natural logarithm of inverse of viscosity values.

2.8 Solubility measures

The solubilities were evaluated by dissolving subsequent additions of the solutes to the solvents in screw-cap sealed vials, then they were gently heated at 60 °C for few seconds with a heating gun then left under magnetic stirring at 40 °C for 15 minutes, then left cooling at room temperature. The maximum solubility values were the ones before observing precipitation of solids after cooling to room temperature (25 °C).

3. RESULTS AND DISCUSSION

3.1 Screening of molecules for DESs formation with water

The first step of this study was a screening on differently structured molecules in order to find possible novel water-based Deep Eutectic Solvents. The set of tested molecules are already reported in literature to be capable to form hydrophobic and hydrophilic DESs both with HBD and HBA roles[46,57–60]. Glycolic Acid, Trimethylglycine, L-Menthol, Phenylacetic Acid, S-Mandelic Acid, Oxalic Acid dihydrate, Sorbic Acid, R-Carvone, L-Proline, L-Histidine, L-Tyrosine and Benzoic Acid were mixed with water in molar ratios spanning from 7/1 to 1/7. Following what we observed with the formation of the water-based hydrophobic DES thymol/water[51], the samples were heated at 130 °C in screw-cap sealed containers and heavily shaken in order to prevent any evaporation or sublimation of the reactants. These temperatures are higher than the ones commonly used for the DESs preparation, but are necessary in order to properly determine a DES formation. Most of the used molecules, in fact, are water soluble, therefore the simple solubilization process can be easily confused with a DES formation.

From this screening two molecules gave stable liquids at room temperature: glycolic acid (GA) and trimethylglycine (TMG); all the other ones gave semi solid unstable matrixes or non-liquid systems. In particular, glycolic acid/water mixture gave stable liquids in molar ratios spanning from 2/1 to 1/7 (GA/H₂O); trimethylglycine gave stable and homogeneous liquids in molar ratios from 1/4 to also 1/9 (TMG/H₂O). Glycolic acid and trimethylglycine molecules can form a DES when mixed together in 2/1 GA/TMG molar ratio, and this DES has found fruitful applications in chemical transformations, in extraction procedures, in membranes realization[40,51–57]. In particular, in the extraction of quercetin from onion skin waste, its 30% w/w water dilution was the best-performing in a screening on various DESs, underlining the water affinity of this solvent[61].

3.2 Solid-liquid phase diagrams and theoretical/experimental comparison

The second step of this work was the identification as DESs of the two GA/H₂O and TMG/H₂O mixtures. This is relevant in order to identify the eutectic point of the mixture and in order to demonstrate their DESs identity rather than water solution of the compounds. In Figure 1 the solid-liquid phase diagrams both experimental and theoretical of the two mixtures and the activity

coefficients are reported; in the same graphs the maximum water solubility of GA and TMG compounds at 25° C are also reported[62].

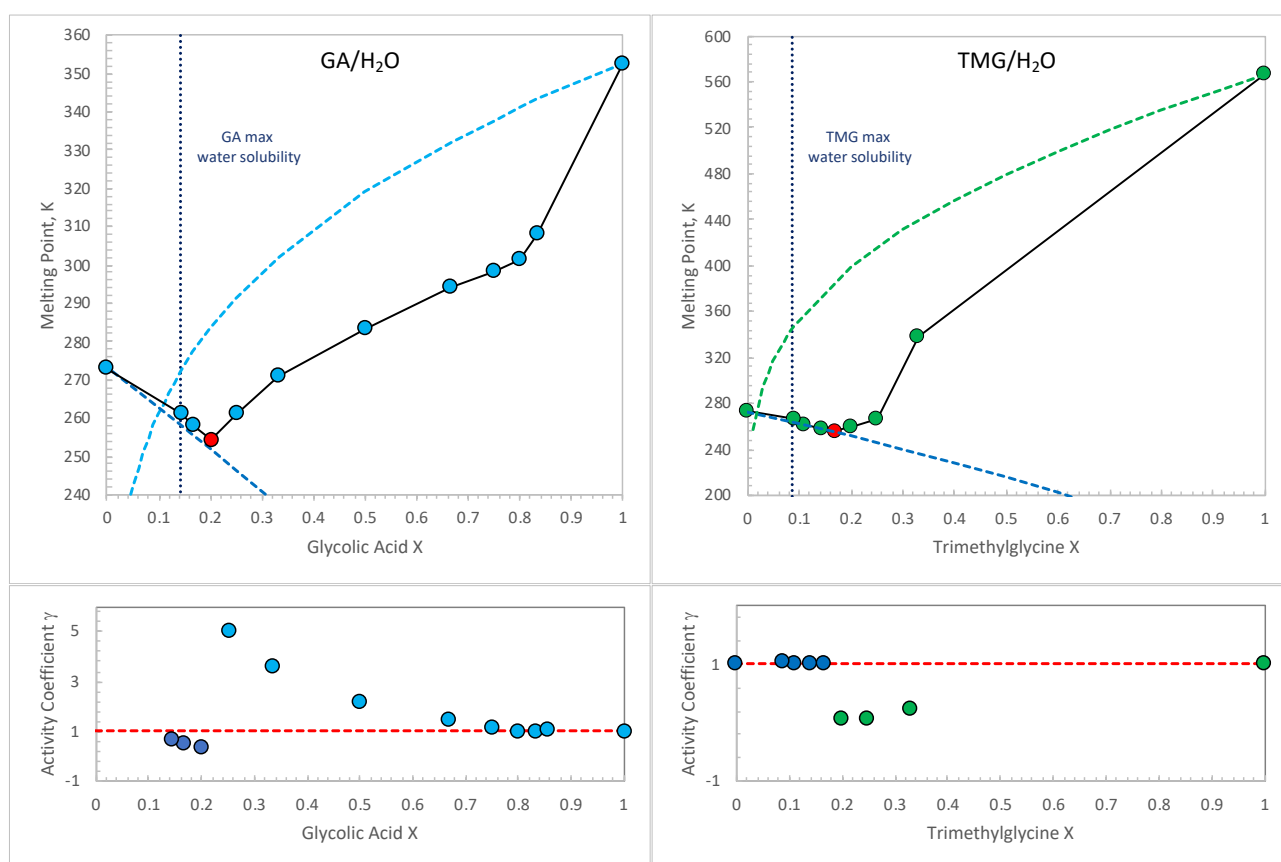
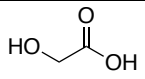

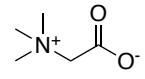



Figure 1. LEFT - Glycolic Acid/H₂O (GA/H₂O) DES, dots: experimental melting points (eutectic point in red); dashed lines: theoretical melting curves; vertical blue dashed line: maximum GA water solubility; bottom: experimental activity coefficients. RIGHT – Trimethylglycine/H₂O (TMG/H₂O) DES, dots: experimental melting points (eutectic point in red); dashed lines: theoretical melting curves; vertical blue dashed line: maximum TMG water solubility.

From the theoretical/experimental melting point curves comparison, it emerged that both the liquids can be defined as Deep Eutectic Solvents; a shift in the molar fraction of the eutectic and a lowering in the melting point from the cross in the theoretical melting curves is observed for both the systems. GA/H₂O DES showed a eutectic point at 0.2 molar fraction of acid (1/4 GA/H₂O molar ratio); the activity coefficients show an interesting profile because the mixture seems to behave ideally at low amounts of GA and then a great shift is observed at the eutectic point, indicating furtherly the non-ideality of the liquid. The same profile is observed for the activity coefficients of TMG/H₂O DES, and a eutectic is shown at 0.167 molar fraction of TMG (1/5 TMG/H₂O molar ratio). Also in this case, a shift of the eutectic both in terms of molar fraction and of the (lowered) melting point indicate clearly the DES identity of the liquid. As a further prove of the DES identity of the mixtures, the maximum solubilities in water of the two compounds are reported in the same graphs.

As it can be clearly seen, the liquids have amounts of the counterparts over their maximum solubility, and the liquids remain stable and transparent for undefined times (over months). The DESs preparations were made with high temperature heating (about 130°C) in few seconds, so this heat is probably necessary to properly form the DESs from the insolubilized compounds in water at room temperature. In Table 1 the structures of the molecules forming the DESs, the molar ratio of the eutectics, the freezing points of the same eutectics and the densities at 25° C are reported.

Table 1: Structures of the molecules forming the *aquo*-DESs; acronyms of the DESs; molar ratio at eutectic points; freezing points at eutectic points; densities at 25 °C.

Structures	Acronym	Eutectic molar ratio	Freezing point, °C	Density (25 °C), g/ml
 glycolic acid  water	GA/H ₂ O	1/4	-19	1.1195
 trimethylglycine  water	TMG/H ₂ O	1/5	-17	1.0474

3.3 Thermogravimetric analysis

The thermal behavior of the two *aquo*-DESs was analyzed via TGA analysis; in these experiments the thermal stabilities of the DESs were compared with the ones of their formers. TGA technique is generally employed for the characterization of novel DESs in order to determine their stability, therefore their possible applications, at different temperatures[63–65]. In Figure 2 the TGA analyses of the two DESs, as well as the thermal behavior of their formers are reported.

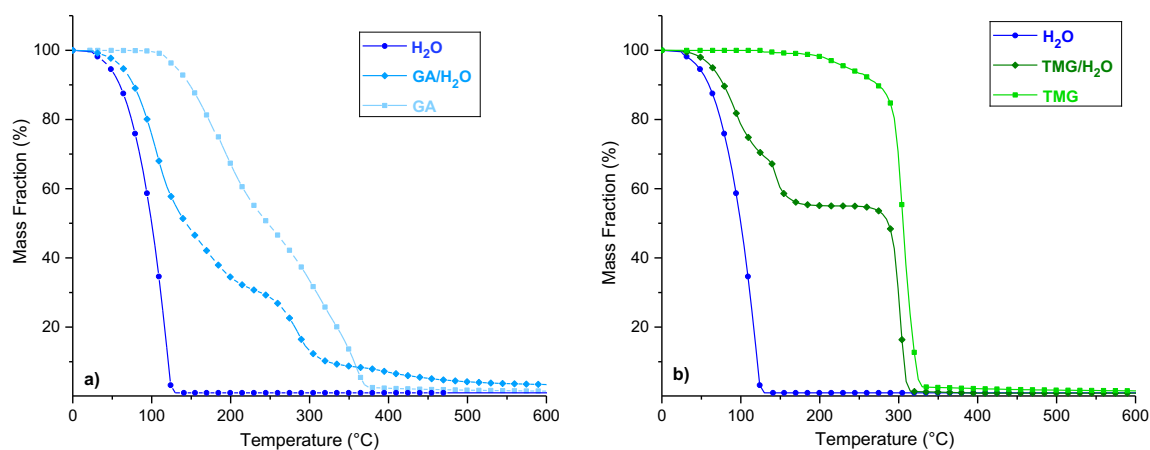


Figure 2. Thermogravimetric analysis of the novel *aquo*-DESs: LEFT – Glycolic Acid/Water (GA/H₂O, 1/4 molar ratio) mixture (blue diamonds) compared with the same analysis on neat water (dark blue circles) and Glycolic Acid (light blue squares); RIGHT – Trimethylglycine/Water (TMG/H₂O, 1/5 molar ratio) mixture (green diamonds) compared with the same analysis on trimethylglycine (light green squares) and water (dark blue circles) only.

The thermal behavior of neat glycolic acid only follows a two-step decomposition pathway[66], whereas only one mass loss step is observed in water and trimethylglycine curves. The TGA of the *aquo*-DESs shows more than two degradation steps probably due to the presence of clusters or the formation of products with different thermal stability[67].

Furthermore, GA/H₂O and TMG/H₂O DESs show intermediate decomposition curves between those of water and glycolic acid or trimethylglycine only. Table 2 shows the onset decomposition temperature (T_{onset}) for each step in the two *aquo*-DESs.

Table 2. Onset temperatures of the *aquo*-DESs.

Sample	Decomposition Step	T_{onset} , °C
GA/H ₂ O	I	76.7
	II	161.0
	III	263.4
	IV	355.2
TMG/H ₂ O	I	70.6
	II	140.7
	III	292.3

The T_{onset} value determines the maximum temperature at which a DES can maintain its liquid state without decomposition. In particular, the glycolic acid/water *aquo*-DES starts to decompose at 76.7 °C due to the water loss, followed by the decomposition of glycolic acid at 161.0 °C. The same trend was observed for the Trimethylglycine/Water DES, where water and trimethylglycine start to degrade at 70.6 °C and 292.3 °C, respectively.

In order to further underline the DES' nature of these novel liquids, the same analyses were performed in the water dilution of GA/TMG DES (2/1 molar ratio) by adding 45% w/w of water that is approximately in weight the amount of water present in the two *aquo*-DESs. Also in this case the results were compared with the formers, GA and TMG molecules as well as water. The graphs are reported in Supporting Information section. The thermal decomposition curves showed in this case two weight losses, the former (60.5 °C) related to the degradation of water and the second (235.2 °C) concerning the decomposition of the DES mixture. This result suggests a water dilution of the DES rather than the participation of H₂O in the DES' network, probably due to the lower temperatures used for the water dilutions preparation (magnetic stirring at r.t.).

3.4 Viscosity

The viscosity of a liquid is a fundamental property that can determine the easiness of application of it in many different topics. For example, low viscosities can promote the extraction procedures facilitating the mass transfer or generally they can determine more homogeneous and handy samples[68]. The viscosities of the two *aquo*-DESs GA/H₂O and TMG/H₂O were measured in the temperature range 20-55 °C; the results and the Arrhenius profiles are reported in Figure 3.

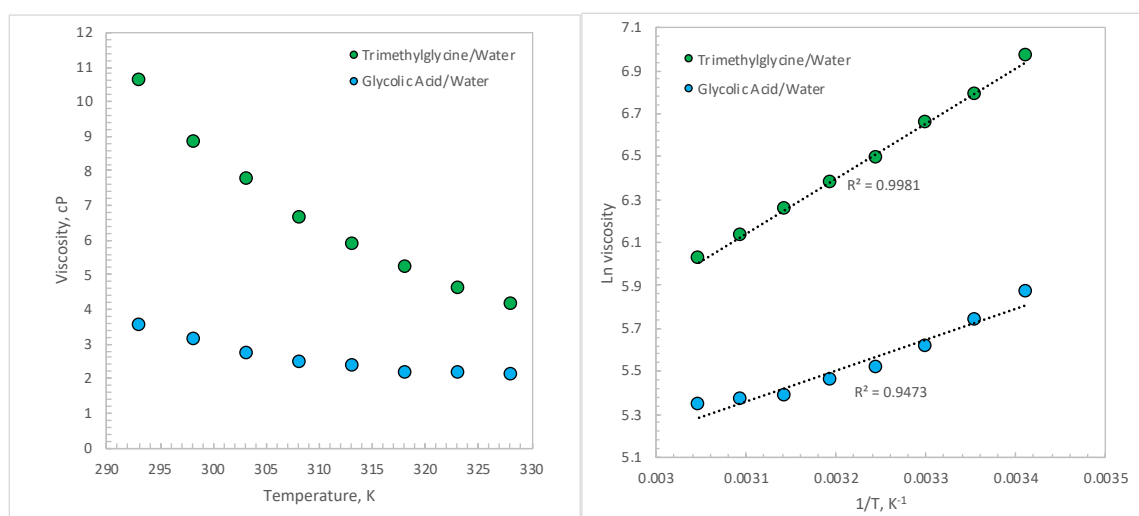


Figure 3. LEFT – Viscosity of Glycolic Acid/Water (1/4 molar ratio) mixture (blue dots) and of Trimethylglycine/water (1/5 molar ratio) mixture (green dots) in the temperature range 20-55 °C; RIGHT – Arrhenius profiles of the same mixtures Glycolic Acid/Water (1/4 molar ratio) mixture (blue dots) and of Trimethylglycine/water (1/5 molar ratio) mixture (green dots) in the temperature range 20-55°C, dashed black lines: linear correlation of the data with R^2 reported.

Both the systems show really low viscosities. TMG/H₂O DES showed a viscosity of 10.62 cP at room temperature and 4.14 cP at 55°C, while GA/H₂O mixture showed even lower values with 3.53 cP and 2.09 cP at room temperature and at 55 °C respectively. Other DESs mixtures reported in literature showed higher viscosity values, spanning from 100 cP to 2000 cP[69] also to over 6000 cP[70]. Water is reported to have lower viscosity (<1 cP) in the literature. By increasing the temperature, TMG/H₂O DES showed a high decrease of the viscosity following a common trend in the chemistry of DESs. The Arrhenius profiles showed really high R^2 values (0.9981) indicating a Newtonian behavior of the liquid. The viscosity activation energy value that can be determined from these measures showed a value of 21.37 kJ/mol for TMG/H₂O DES. This value in the same order of magnitude of other DESs liquids but lower than the common ones, indicating an easiness of holes and vacancies creations in the liquid structure, mainly due to the really low viscosity of the liquid.

On the other hand, GA/H₂O DES showed a little irregular viscosity decrease by increasing the temperature, and the Arrhenius profile showed a slight non-linearity. This can be easily observed from the graph and it can be numerically determined by its R^2 value (0.9473) which is lower than TMG/H₂O DES and lower than other DESs mixtures in the literature that showed really high linearity in these profiles. This shows a slight non-Newtonian behavior of the viscosity of GA/H₂O DES. This could be due to different reasons and it was observed also in ionic conductivity measures (see further).

3.5 Ionic Conductivities

Ionic conductivity of a liquid is a measure that can determine the amounts of free charges and the easiness of movement of them inside the liquid system. The ionic conductivity measures and the Arrhenius profiles in the temperature range 20-55 °C of the two TMG/H₂O and GA/H₂O *aquo*-DESs are reported in Figure 4.

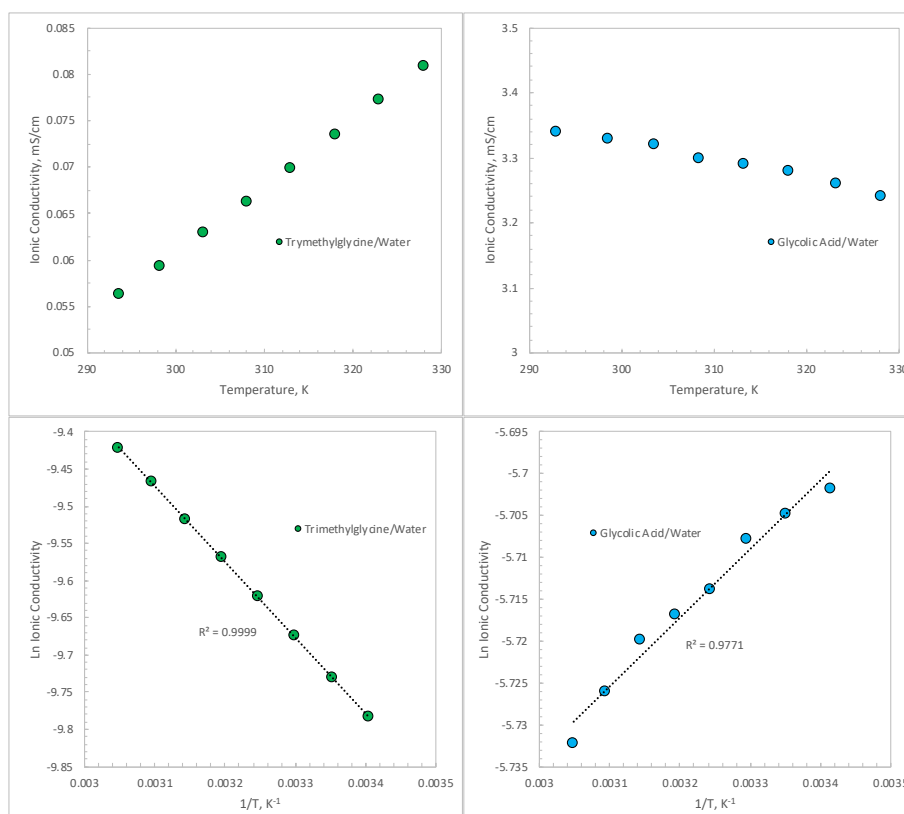


Figure 4. TOP LEFT – Ionic conductivity of Trimethylglycine/Water mixture (TMG/H₂O) in the temperature range 20-55 °C; BOTTOM LEFT – Arrhenius profile of ionic conductivity of Trimethylglycine/Water mixture (TMG/H₂O) in the temperature range 20-55 °C; TOP RIGHT – Ionic conductivity of Glycolic Acid/Water mixture (GA/H₂O) in the temperature range 20-55 °C; BOTTOM RIGHT – Arrhenius profile of ionic conductivity of Glycolic Acid/Water mixture (GA/H₂O) in the temperature range 20-55 °C.

TMG/H₂O DES showed low ionic conductivity values, spanning from 0.05 mS/cm at 20°C to 0.08 mS/cm at 55°C; this is because TMG is an inner salt, therefore the ions present in the liquid, that determine the values of ionic conductivity, are probably the ones coming from a partial protonation of trimethylglycine by water. The ionic conductivity increases slightly with the temperature and the Arrhenius plot showed really high linearity ($R^2 = 0.9999$); this is obviously determined by the increase in the mobility of the ions made by the increase of the temperature. The ionic conductivity activation energy of TMG/H₂O liquid revealed to be 8.45 kJ/mol, indicating a really easy movement of the charges inside the liquid, mainly due to their really low concentrations, therefore with low repulsion effects, as observed from the values of conductivity.

The ionic conductivity profile of GA/H₂O mixture showed a very peculiar result. The values are higher than those observed with TMG/H₂O and are around 3.3 mS/cm. However, contrary to what observed with the latter and with all the commonly-structured DESs liquid, its values decrease by increasing the temperature. This is in contrast with the increase of the mobility of the charges that occurs by increasing the temperature. The Arrhenius plot of ionic conductivity, as also observed with viscosity measures, shows a slight non-Newtonian behavior as it can be easily observed also from

R^2 value that is about 0.9771. This suggests a structural change in the system by increasing its temperature. The overall ionic conductivity value of this system can derive from a protonation of the water made by the GA; this is also consistent, and it confirms them, with the structural features of a DES in which the increase of the entropy (in terms of increase of different adducts) determines a lowering in the melting points because of the impossibility of regular crystal lattice formation. The pK_a values of Glycolic Acid, according to the literature, are slightly increasing by an increase of the temperature[71]. Moreover, DFT studies reported in literature show the existence of a wide number of differently structured GA-H₂O adducts[72]. These phenomena could be related to a facilitation in liquid formation thanks to the presence of different adducts and molecules. Therefore, from one side we have an increase of the values made by their increase in mobility, on the other side there is a decrease in its overall values because of the behavior of GA in water. We also measured the pH of this DES at different temperatures analyzed by ionic conductivity (see Supporting Information). Normally a measure of the pH of a DES has no meaning as the pH-meter measures the activity of H⁺ ions in water solutions; in this case because the DES is water-based it can have meaning and sense. We observe a slight increase of the values that passes from 0.79 at 25 °C to 0.85 at 60 °C, confirming a decrease of H⁺ species in the sample, that determine the ionic conductivity values with their counterions.

3.6 TMG/H₂O Walden Plot

The ionicity of TMG/H₂O DES mixture was evaluated by determining its Walden plot, that is drawn following the Walden's rule (Eq. 6) that correlates the molar ionic conductivity (Λ) with the viscosity (η) of a liquid system[73]:

$$\Lambda\eta = \text{constant} \quad (6)$$

With this approach, the liquid can be defined as "super-ionic" whenever the points fall in the upper side of the diagonal of the plot, indicating a neat charge separation in the liquid; if the points fall under the same diagonal, the liquid can be defined as "poor ionic" because the charges are intimate determining a low ionicity of the system. The diagonal itself represents KCl 0.01 M solution in water samples. The samples at the temperatures spanning from 20 °C to 55 °C of TMG/H₂O DES are reported in Figure 5. The GA/H₂O DES was not analyzed as the non-Newtonian behavior of it did not

permit to evaluate its ionicity via Walden plot. The density values at the different temperatures of TMG/H₂O DES are reported in Supporting Information section.

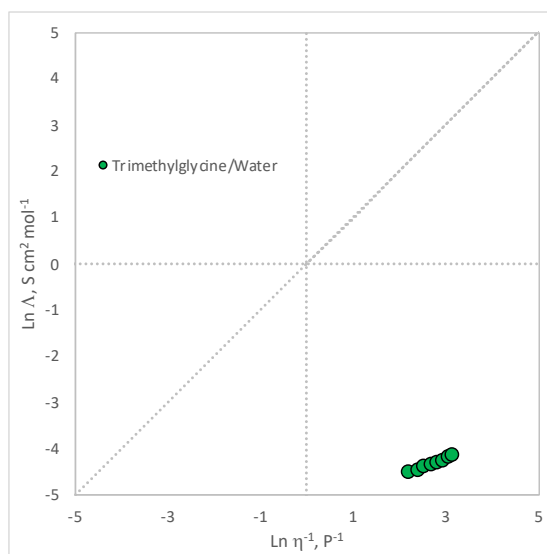


Figure 5. Walden plot (Ln inverse of viscosity η^{-1} vs. Ln molar ionic conductivity, $\text{Ln } \Lambda$) for TMG/H₂O DES in the temperature range 20-55 °C.

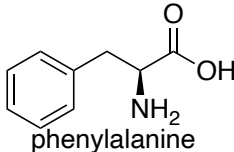
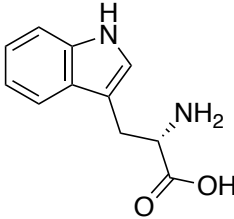
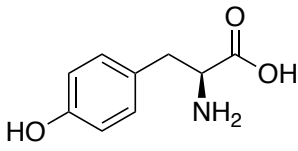
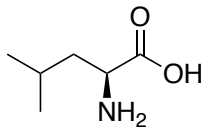
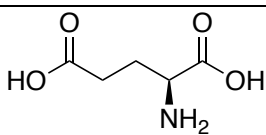
As it can be easily seen from its Walden plot, TMG/H₂O mixture is markedly a “poor ionic” liquid. Thanks to its low ionic conductivity and to its really low viscosity, the points fall in the Walden plot in the lower right portion of the graph. This means that in this liquid the charges are very intimate and not neat, and this is consistent with the zwitterionic inner salt nature of the charged part of the liquid itself. Commonly the DESs fall in the Walden plot close to the diagonal, except for the ones containing water that can be protonated by the HBD therefore slightly falling over the diagonal on the “super-ionic” portion of the Walden plot. GA/TMG DES fall down the diagonal but really close to it[57]. Ionic liquids usually also fall close to the diagonal.

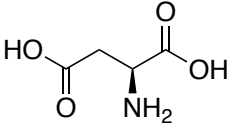
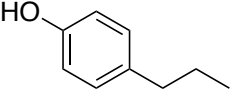
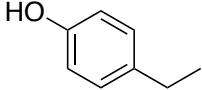
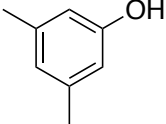
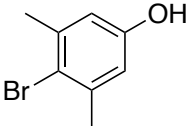
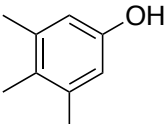
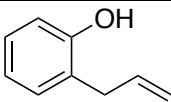
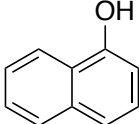
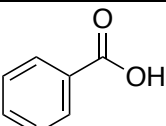
3.7 Solubility measures

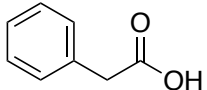
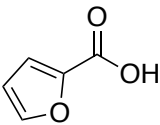
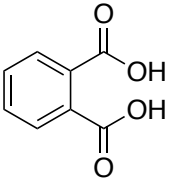
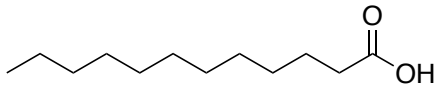
One of the most peculiar and relevant properties of DESs is their capability of solubilization of a wide number of differently structured molecules. In particular, they show a high affinity with aromatic structures and nanostructures thanks to the participation of the aromatic rings as HBAs in the H-bond network of the DES liquid[74]. In this work we investigated the solubilizing properties of the two novel *aquo*-DESs considering their peculiar structural properties. Therefore, several L-aminoacids, phenols and carboxylic acids were tested as solutes in these two solvents. An aqueous

dilution of the DES formed via the combination of GA and TMG (GA/TMG 2/1 DES) at 45% w/w of added water was used as a comparison in order to help to define if the solubilization process in a water-based DES can be similar to the one observed in a water-diluted DES. The amount of water used for the water dilutions of GA/TMG DES are still able to preserve its DES' identity according to the literature about water effect on deep eutectic solvents[75]. In Table 3 the solubility data are reported together with their solubility in water[62].

Table 3. Maximum solubility (grams of solute in 100 grams of solvent) of L-aminoacids, phenols and carboxylic acids in TMG/H₂O DES, in GA/H₂O DES, in GA/TMG DES +45% w/w water, in water[62] at 25°C.

Solutes	Solubility, g _{solute} /100 g _{solvent}			
	TMG/H ₂ O DES	GA/H ₂ O DES	GA/TMG DES +45% w/w H ₂ O	H ₂ O
Aminoacids				
 phenylalanine	0	25.5	5.3	2.6
 tryptophan	6.3	15.0	4.8	1.3
 tyrosine	30.4	25.9	0	0.05
 leucine	0	14.5	2.1	2.4
 glutamic acid	0	12.5	0	0.9

 aspartic acid	0	0	0	0.5
Phenols				
 4-propylphenol	0	0	0	0.1
 4-ethylphenol	0	2.1	69.1	0.3
 3,5-dimethylphenol	2.1	0	9.0	0.5
 4-bromo-3,5-dimethylphenol	0	0	0	0
 3,4,5-trimethylphenol	0	0	0	0
 2-allylphenol	0	0	5.2	0.1
 1-naphthol	0	0	6.4	0
Carboxylic Acids				
 benzoic acid	4.9	0	0	0.3

 phenylacetic acid	159	4.9	33.8	1.7
 2-furoic acid	130	11.2	28.6	4.7
 phthalic acid	27.1	0	7.8	0.7
 lauric acid	0	0	0	0.0002

The tested aminoacids revealed to be much more soluble in the GA/H₂O DES rather than in water and in the other systems, with solubilities in grams/100 grams of solvent over one order of magnitude higher. In this system, thanks to its acidic characteristics (see ionic conductivity paragraph), the aminoacids could also result protonated by the media, favoring their solubilization. TMG/H₂O DES showed significant solubilizing properties of tryptophan, but also in this case lower than the Glycolic Acid/Water DES. Also tyrosine revealed to be really soluble in the trimethylglycine-based DES, as observed also in GA/H₂O DES. The phenol moiety present in tyrosine could increase its solubility thanks to the affinity of this portions in DESs' structures[74]. Surprisingly, the water dilution of the GA/TMG DES revealed inefficient for the solubilization of this aminoacid, showing an anti-synergic effect. The water dilution of GA/TMG DES showed in some cases (phenylalanine, tryptophan, leucine) solubility values comparable with the ones reported in water but in other cases (tyrosine as reported above) anti-synergic effects are observed therefore lower solubilities than in water and in GA/H₂O DES. Aspartic acid showed no solubility in all the tested liquids, while the glutamic acid (that has one more methylene) showed a high solubility in GA/H₂O DES, suggesting a peculiar behavior of this last molecule in the GA-based DES.

Also the analyzed phenols showed peculiar and interesting results. 4-propylphenol is insoluble in all the DESs and in water a slight solubility is reported. Surprisingly, changing the aliphatic chain from

propyl- to ethyl- (4-ethylphenol) a change in the solubility is observed, with a really higher solubility than the one reported in water in GA/TMG water dilution (over two orders of magnitude) and also one order of magnitude more in GA/H₂O DES. In TMG/H₂O DES the phenol is insoluble, so in this case a synergic effect of the DESs' constituents is observed. 3,5-Dimethylphenol showed higher solubilities in GA/H₂O DES and in GA/TMG water dilutions than in water; no solubilization was observed for in TMG/H₂O DES. Therefore, it seems GA to play a role in its solubilization than can increase when interacting with TMG but not with TMG itself alone in TMG/H₂O DES. The bromide in position 4 of the same phenol (4-bromo-3,5-dimethylphenol) led to insolubility in all the systems, also in water. Also the methyl in 4 position (3,4,5-trimethylphenol) lead to insolubility in all the DESs systems as well as reported in water. 2-allylphenol and 1-naphtol showed one order of magnitude of more efficacious solubilization in the GA/TMG water dilutions rather than in water; the two *aquo*-DESs showed no solubilization at all of the two compounds.

The tested carboxylic acids solubilizations showed even more interesting results: their solubilities, in fact, showed values also three orders of magnitude higher than in water. Benzoic acid, that is reported by us to be a DES component when mixed with TMG[57], showed a solubility in TMG/H₂O DES much higher than in water, and much higher than GA/H₂O DES, suggesting to form a ternary DES when dissolved in this mixture. This data is supported by the insolubility of this acid in GA/H₂O DES and in GA/TMG water dilution. The same effect was observed also with other two DES-forming acids: phenylacetic acid and 2-furoic acid. Even if in these cases a solubility was observed also in GA/H₂O DES, these two acids showed really higher solubilities in TMG/H₂O DES, suggesting the same phenomena of ternary DES (or they can be interpreted as also water dilutions of the ACID/TMG DESs) formation. With these two acids also a good solubilization (higher than in water but lower than in TMG/H₂O DES) is observed in GA/TMG water dilutions, showing an anti-synergic effect of GA. The same effect is observed with phthalic acid, but this acid is not reported to form a DES with TMG according to our knowledge. Finally, lauric acid showed non solubility in the *aquo*-DESs as well as in the GA/TMG water dilution and really low in water.

In the literature are reported many cases of aminoacid-based, phenol-based and carboxylic acid-based DESs, with these molecules acting both as HBDs or HBAs in the mixtures[76–78]. The solubility values we observed in the novel *aquo*-DESs are in the order of magnitude of integers in molar ratios with the DES components. This suggests that the solute molecules can interact in the DESs solvents in a peculiar “DES-like” way, therefore increasing by much their solubilities. This data suggests further deeper analyses on the topic.

4. CONCLUSIONS

In this work novel water-based binary natural Deep Eutectic Solvents, *aquo*-DESs, were realized and characterized: Trimethylglycine/Water and Glycolic Acid/Water liquids. Their DES' identity was demonstrated thanks the shift, both in terms of molar fraction and decrease of the melting points, of the experimental eutectics from the theoretical melting points curves. Moreover, the Trimethylglycine and the Glycolic Acid amounts present in the *aquo*-DESs are higher than their reported water solubility. Finally, their thermal behavior was different from a typical water solution of a solute, showing multi-step degradation that is according to the multi-clustered structural feature of a DESs.

The properties of these liquids were analyzed in terms of their viscosity and their ionic conductivity in 20-55 °C temperature range, showing a really low viscosity promoting these solvents in different uses in different topics. Peculiar structural-changing effects were observed for GA/H₂O mixture by increasing its temperature. For TMG/H₂O DES it was possible to draw a Walden plot that indicated its marked "poor ionic" characteristic.

The solubilizing properties of these liquids were tested for different aminoacids, phenols and carboxylic acids, showing really good and interesting results on DES-forming capable solutes; this data could open for a novel approach in the solubilization of these types of molecules in this innovative class of environmental-friendly solvents.

CRedit AUTHORSHIP CONTRIBUTION STATEMENT

Eduardo Picciolini Investigation; **Genny Pastore** Investigation, Writing – original draft; **Tiziana Del Giacco** Writing – review & editing; Resources, Supervision, Validation; **Gianluca Ciancaleoni** Writing – review & editing, Validation; Software; **Matteo Tiecco*** Conceptualization, Data curation, Investigation, Writing – original draft, Project administration, Methodology, Formal analysis, Visualization; **Raimondo Germani** Resources, Supervision, Formal analysis, Writing – review & editing, Validation.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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