

## **Assessment and design of greener deep eutectic solvents – a multicriteria decision analysis**

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### **ABSTRACT**

Deep eutectic solvents (DES) are often considered as green solvents because of their properties, such as negligible vapor pressure, biodegradability, low toxicity or natural origin of their components. Due to the fact that DES are cheaper than ionic liquids, they have gained many applications in a short period of time. However, claims about their greenness sometimes seem to be exaggerated. Especially, bearing in mind lots of data gaps for DES properties as well as their individual components. To clarify the situation on their greenness status, a comprehensive assessment of commonly used hydrogen bond acceptors and donors separately and as DES is performed. The application of multicriteria decision analysis (TOPSIS ranking) with combination of biological effect modeling for DES to rank these alternatives according to greenness criteria is proposed. Also traditional organic solvents and ionic liquids as greenness reference points for better understanding are introduced. The ranking results show that many DES, which are synthesized by mixing sugars alcohols, alcohols, sugars and amides are promising environmentally friendly solvents, more than some imidazolium-based ionic liquids. Mixtures including components with metal ions and organic acids are less green.

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25 Keywords: green chemistry; deep eutectic solvents; MCDA; TOPSIS; green solvent

26

## 27 **1. Introduction**

28 Green chemistry refers to “design of chemical products and processes to reduce or eliminate  
29 the use and generation of hazardous substances” [1,2]. According to one of 12 principles of  
30 green chemistry, the use of harmful solvents should be avoided, replaced by more  
31 environmentally benign ones or their amount should be reduced [3]. The best replacement for  
32 conventional organic solvents is simply water, however usually more nonpolar solvents are  
33 required. Then, supercritical fluids, carbonates, bio-based solvents (from biomass or food  
34 waste), ionic liquids (ILs) or deep eutectic solvents (DES) are readily used. The last two  
35 groups of compounds have fairly similar physicochemical properties but ILs are more  
36 expensive [4] and harder to be obtained. Therefore, there is a noticeable growth of interest in  
37 DES, which are mixtures of two or more compounds with particular molar ratio – hydrogen  
38 bond acceptor (HBA) and hydrogen bond donor (HBD). In contrary to traditional organic  
39 solvents belonging to volatile organic compounds (VOCs), DES are rather nonvolatile, non-  
40 flammable due to the low vapour pressure [5]. Moreover, in comparison to ILs (as solvents of  
41 similar characteristic), apart from their low cost, they possess other advantages such as  
42 simpler synthesis and natural origin (mainly in case of natural deep eutectic solvent -  
43 NADES).

44 DES show excellent applicability in many areas, for instance separation processes, biodiesel  
45 production [6], electrochemistry [7], absorption and solubility of carbon dioxide [8], medical  
46 and pharmaceuticals usage [9], chemical synthesis [10], activation of enzymes and biocatalysis  
47 [11]. However, despite the wide range of applications, the claims about their low harmfulness,



48 non-toxicity or high biodegradability are not unequivocal. Several studies proved that not all  
49 DES are highly biodegradable or nontoxic and lack of data may be serious problem while  
50 environmental evaluations [12, 13, 14]. Estimation of DES greenness should be performed in  
51 more comprehensive way.

52 The tools that are helpful in assessments according to many factors simultaneously are  
53 multicriteria decision analysis algorithms (MCDA). Among many The Technique for Order of  
54 Preference by Similarity to Ideal Solution (TOPSIS) gained much interest due to its  
55 simplicity. MCDA methods have been already successfully applied in greenness assessments  
56 of solvents [15,16], derivatization agents [17], nanoparticles [18,19] and ionic liquids [20].

57 To authors best knowledge, it is the first study that considers variety of criteria (not only  
58 toxicity) to rank HBA and HBD as DES components and DES in respect to their  
59 environmental benignness. The results of this study may be useful for researchers and  
60 practitioners at the first stage of DES selection, especially for separation processes. The  
61 presented tools allow to assess how individual compounds, as well as their molar ratios can  
62 affect the greenness of DES.

## 63 **2. Materials and Methods**

### 64 ***2.1.Data collection***

65 Our study includes binary and ternary DES, which have been found in numerous scientific  
66 papers. An extensive search has been conducted particularly targeted library databases: ACS,  
67 Elsevier, Springerlink, RSC and Wiley – till first 150 hits, when available by the keywords  
68 “DES”, “Deep eutectic solvents”, “Green deep eutectic solvents” or “Environmentally  
69 friendly deep eutectic solvents”.

70 The dataset has been divided into HBAs and HBDs, as well as DES mixtures. In first case, for  
71 each of HBA and HBD properties referring to environmental and safety issues as hazardous



72 and precautionary statements, signal wording, flash point, hazardous decomposition products,  
 73 vapor pressure, toxicity towards *Daphnia magna*, algae, fish and rodents, octanol-water  
 74 partition coefficient, biodegradability and pH have been collected. Whereas, for each of  
 75 binary and ternary DES mixtures parameters such as melting point, density, viscosity,  
 76 conductivity, surface tension, pH, refractive index, Kamlet-Taft parameters, spectroscopic  
 77 polarity index as  $E_T^N$ , toxicity towards *Vibrio fischeri*, *Escherichia coli*, fish and cell line of  
 78 CCO fish and MCF-7 or HeLa human tumor, phytotoxicity towards wheat seeds - *Triticum*  
 79 *aestivum*, biodegradability and solubility of gases as carbon dioxide, sulphur dioxide,  
 80 ammonia has been gathered according to corresponding articles. All information are presented  
 81 in *Supplementary Information 2*. Due to many gaps in dataset some of initially collected data  
 82 was not included in the assessments. The criteria that have been taken for TOPSIS rankings  
 83 are summarized in **Table 1**.

84 **Table 1.** Criteria for HBDs and HBAs TOPSIS rankings.

| Criterion                        | Remarks   | Source                  |
|----------------------------------|---|-------------------------|
| H-stat                           | Descriptions are transferred into numerical values                                  | MSDS                    |
| P-stat                           | Descriptions are transferred into numerical values                                  | MSDS                    |
| Signal wording                   | Descriptions are transferred into numerical values                                  | MSDS                    |
| Flash point                      | The temperature in which compound flashes   | MSDS, papers            |
| Hazardous decomposition products | Descriptions are transferred into numerical values                                  | MSDS                    |
| Vapour pressure                  | In 25 °C  | MSDS, papers, databases |
| Toxicity <i>Daphnia magna</i>    | 48 h test data was preferable; if not available 24 h test data was taken            | Papers                  |
| Toxicity algae                   | 72 h test data was preferable; if not available 96 h test data was taken            | Papers                  |
| Toxicity fish                    | 96 h test data was preferable; if not available 48 h data was taken                 | Papers                  |
| Toxicity rodents via ingestion   | Rat was the preferable organism, if data was not available data for mouse was taken | Papers                  |
| logKow                           | Logarithm of partitioning coefficient between octanol and water                     | Papers, MSDS, databases |
| Biodegradability                 | 28 day test   | Papers, MSDS,           |

pH  
Solubility in water

-  
In 25 °C

databases  
MSDS, papers  
MSDS

85 For the specific references to paper, please see descriptions in Supplementary Information  
86 The majority of properties are taken from scientific papers, describing chemical  
87 characteristics of DES. Then information are supported by the chemical on-line databases  
88 such as ECHA, PubChem, Chemspider. Moreover, data for analysis in this work is provided  
89 by the Material Safety Data Sheets (MSDS) supplied by different companies, mainly Sigma-  
90 Aldrich, Merck, Thermo Fisher Scientific, Santa Cruz Biotechnology Inc., Iolitec. Especially  
91 information and parameters as: alternative names, CAS number, molecular formula,  
92 molecular weight, signal wording, special hazards arising from the substance or  
93 mixture/hazardous decomposition products.  
94 The properties of DES are not fully available, so in case of lack of data, parameters have been  
95 completed by predicted or estimated values (calculated in QSAR, EPISuite, etc.) or missing  
96 points are substituted with the values of the chemically similar compounds / group of  
97 compounds as proposed by Adler et al. [21] as summarized in **Tables S1, S5 and S7-S16**.  
98 Additionally, wherever several datapoints are available (for instance toxicity values for  
99 different fish / algae / rodent species), always the most unbeneficial one is selected, according  
100 to precautionary principle.  
101 Traditional organic solvents and ionic liquids are included in the dataset as reference points,  
102 for better understanding of a green nature of HBAs and HBDs being the DES components  
103 (the same properties as for the HBAs and HBDs are collected). Some of data require  
104 transformations from descriptions to numerical values, what is presented in **Tables S2-S6**.

## 105 ***2.2.TOPSIS algorithm***

106 TOPSIS is algorithm developed by Hwang and Yoon [22], it is based on finding an  
107 alternative characterised by the shortest distance from the positive ideal solution and

108 simultaneously the furthest distance from the negative ideal solution. This mathematical  
109 model allows for combination of different (often contradictory) criteria into a single score  
110 leading to creation of ranking of available alternatives. The ranking is defined by the values of  
111 similarity to ideal solution, for each alternative, ranged between 0 and 1. The value 0 is  
112 assigned to completely non-ideal alternative (the worst values for all criteria), while the value  
113 1 for an ideal solution (the best values for all criteria). Only basic information about TOPSIS  
114 algorithm are described above. Its mathematical algorithm is presented in Section 2 of  
115 *Supplementary Information 1*. More details may be found in the articles, including its  
116 fundamentals [23, 24]. The calculations involving TOPSIS are performed in Excel program  
117 (Microsoft 2016). TOPSIS was selected over other MCDA tools as it is fully applicable for  
118 many alternatives assessment, its outcome is easily interpretable and its algorithm is relatively  
119 simple.

### 120 ***2.3. TOPSIS algorithm for DES components – HBA and HBD***

121 Evaluation of HBAs and HBDs is carried out for each group separately. The number of  
122 alternatives is 95 for HBA, 181 for HBD, 16 and 14 for organic solvents and 7 for ILs. The  
123 difference in the amount of commercially used organic solvents is due to fact that n-butanol  
124 and phenol are also a DES component in case of HBDs assessment. The selection of ionic  
125 liquids is dictated by the data availability. Nevertheless, attempts are made to include salts  
126 with different cations and anions. Moreover, substances like 1-butyl-3-methylimidazolium  
127 chloride ( $[C_4C_1im][Cl]$ ) and tetrabutylphosphonium bromide ( $[P_{4444}][Br]$ ) may be classified as  
128 a ILs as well as a HBD.

### 129 ***2.4. TOPSIS algorithm for DES***

130 Environmental assessment of DES including binary and ternary mixtures are based on results  
131 obtained with TOPSIS analysis for HBAs and HBDs and calculations of common effects. Due

132 to fact, that DES are composed of HBA and one (for binary mixtures) or two HBDs (for  
133 ternary mixtures), the evaluation includes common responses, calculated with toxicological  
134 model, according to the equation:

$$135 \quad E(C_{mix}) = 1 - \prod_{i=1}^n (1 - E(C_i)) \quad (1)$$

136 where  $E(C_{mix})$  is combined effect at the mixture concentration ( $C_{mix}$ ), and  $E(C_i)$  is the  
137 similarity to ideal solution (calculated for HBA and HBD with TOPSIS) of individual mixture  
138 component (i) applied at the concentration ( $C_i$ ) [25]. Bearing in mind, fact that DES mixtures  
139 may have different ratios of HBA and HBD, this information is introduced by fractions,  
140 e.g. for HBA:HBD mixtures with ratios of 1:1 and 1:3, the fractions are equal  $\frac{1}{2}$  and  $\frac{1}{2}$  as well  
141 as  $\frac{1}{4}$  and  $\frac{3}{4}$ , respectively. Selected 35 binary and 2 ternary mixtures, considered by the  
142 authors of respective publications as green solvents are evaluated. All these DES are listed in  
143 **Table S18.** together with an information about areas of application and justification why  
144 authors consider them green. Ionic liquids and traditional organic solvents are also included as  
145 reference points. To obtain an adequate level of comparability with DES mixtures, combined  
146 value of addition effect for each solvent is calculated by multiplication values of similarity to  
147 ideal solution of HBA and HBD for particular solvent according to equation 1 (solvent is  
148 treated as mix of two individuals).

### 149 *2.5. Weights and confidence rankings*

150 The advantage of MCDA tools is possibility of assigning weights to criteria to give them  
151 relative importance in accordance to the purpose of the analysis. To provide a comprehensive  
152 ranking thirteen criteria with different importance are simultaneously considered in the  
153 assessment. Toxicity towards *Daphnia magna*, fish, algae and rats via ingestion are assessed  
154 to have higher influence on the greenness character of DES components (0.14), while  
155 biodegradability has weight value of 0.1. Information about hazard and precautionary

156 statements, vapor pressure are found to be less important with weight value equal 0.06. Then  
157 lower weights are considered for hazardous decomposition products (0.02), signal word  
158 (0.02), flash point (0.04), pH (0.04) and logK<sub>ow</sub> (0.04). The toxicity criteria are assigned with  
159 the highest weights as they refer more to the greenness assessment than other criteria. Hazards  
160 and precautionary statements, signal wordings, decomposition products, flash point, pH and  
161 logK<sub>ow</sub> are given low weights as they are characterized by lower variability and the criteria  
162 translated from descriptions can be treated as semi-quantitative information.

## 163 ***2.6.Sensitivity Analysis***

164 The sensitivity analysis is performed to investigate how changes in input values and/or  
165 weights influence the final ranking results. It is also applied to consider measurement errors of  
166 input variables. The input values are changed randomly for +10% or -10% and next analysis  
167 is performed to see if differences in ranking are significant.

## 168 **3. Results and discussion**

### 169 ***3.1.Results of TOPSIS ranking of HBA***

170 The results of TOPSIS analysis for HBAs with proposed criteria and assigned weight values  
171 are presented in **Table 2**. Traditional organic solvents and ionic liquids are highlighted light  
172 blue and light green, respectively.

173 It is found that the best alternative is triethylene glycol (0.5883), which is nontoxic to all  
174 evaluated organisms. Moreover, it does not undergo bioaccumulation due to low value of log  
175 K<sub>ow</sub> and it is easily biodegradable. This DES component is also described by small number of  
176 hazard and precautionary statements and in case of its decomposition there is no risk of  
177 arising hazardous products. Then for next 5 compounds the values of similarities to ideal  
178 solutions decrease from 0.18 to ~0.14. These compounds are mainly amino acids (betaine



179 hydrochloride, betaine, histidine) and traditional organic solvents such as methanol and  
 180 heptane. The high position of amino acids in the ranking is due to low toxicities towards at  
 181 least two of organisms, high flash points, small values of log  $K_{ow}$  and ease of biodegradation.  
 182 These two organic solvents are highly ranked because of low toxicity towards rats via  
 183 ingestion and good biodegradability. Moreover, methanol is characterized by low value of  
 184  $\log K_{ow}$  and is rather non-toxic towards other analyzed organisms.

185 The ranking scores for latter compounds are gradually decreasing from 0.0962 for serine to  
 186 0.0244 for glycerol. These compounds are monosaccharides, such as mannose, D-glucose and  
 187 D-fructose, which are characterized by small number of hazardous statements and low value  
 188 of  $K_{ow}$ , as well as by the high values of flash point and low toxicity towards majority of test  
 189 organisms. Moreover, mannose is favorable due to high biodegradability. Within this part of  
 190 ranking ethyl acetate is localized, because of low toxicities towards the most of evaluated  
 191 organisms and low risk of bioaccumulation. All ionic liquids included are located in the  
 192 second half of this ranking. For these salts the common features are low biodegradability and  
 193 considerable toxicities towards all organisms, as well as high number of decomposition  
 194 products and. Also HBA that are organometallic compounds are located in the second part of  
 195 the ranking. For the last ranks the scores change to  $<0.007$  for ammonium and phosphonium  
 196 salts, dodecanoic acid and solvents, like chlorobenzene, tetrahydrofuran and diethyl ether.  
 197 They are ranked low because of high toxicity in all included tests, in case of organic solvents  
 198 also high volatility.

199 **Table 2.** Results of TOPSIS analysis for HBA and comparison with traditional organic  
 200 solvents and ionic liquids combined with sensitivity analysis for changes in range of  $\pm 10\%$

| No. | Substance name (HBA/organic solvent/IL) | CAS number | Similarity to ideal solution | Ranking difference for $\pm 10\%$ changes |
|-----|---|------------|------------------------------|---|
| 1   | triethylene glycol                      | 112-27-6   | 0.5880                       | 0   |
| 2   | betaine hydrochloride                   | 590-46-5   | 0.1812                       | 3   |
| 3   | betaine                                 | 107-43-7   | 0.1734                       | 1   |



|    |                                       |                    |        |    |
|----|---------------------------------------|--------------------|--------|----|
| 4  | heptane                               | 142-82-5           | 0.1644 | 2  |
| 5  | histidine                             | 71-00-1            | 0.1485 | -3 |
| 6  | methanol                              | 67-56-1            | 0.1459 | -3 |
| 7  | serine                                | 56-45-1            | 0.0962 | 0  |
| 8  | mannose                               | 3458-28-4          | 0.0900 | 1  |
| 9  | L-proline                             | 147-85-3; 609-36-9 | 0.0597 | -1 |
| 10 | citric acid                           | 77-92-9            | 0.0542 | 0  |
| 11 | potassium carbonate                   | 584-08-7           | 0.0532 | 0  |
| 12 | D-glucose                             | 50-99-7            | 0.0383 | 0  |
| 13 | D-fructose                            | 57-48-7            | 0.0381 | 0  |
| 14 | acetamide                             | 60-35-5            | 0.0317 | 3  |
| 15 | ethylene glycol                       | 107-21-1           | 0.0293 | -1 |
| 16 | ethyl acetate                         | 141-78-6           | 0.0280 | 0  |
| 17 | glycerol                              | 56-81-5            | 0.0244 | -2 |
| 18 | hexane                                | 110-54-3           | 0.0209 | 0  |
| 19 | uea                                   | 57-13-6            | 0.0183 | 0  |
| 20 | calcium chloride hexahydrate          | 7774-34-7          | 0.0129 | 3  |
| 21 | alanine                               | 302-72-7           | 0.0124 | 3  |
| 22 | sodium glutamate                      | 6106-04-3          | 0.0123 | -2 |
| 23 | cyclohexane                           | 110-82-7           | 0.0117 | -2 |
| 24 | toluene                               | 108-88-3           | 0.0115 | 1  |
| 25 | L-carnitine                           | 541-15-1           | 0.0115 | -3 |
| 26 | polyethylene glycol                   | 25322-68-3         | 0.0111 | 1  |
| 27 | monoethanolamine hydrochloride        | 2002-24-6          | 0.0109 | 23 |
| 28 | acetic acid                           | 64-19-7            | 0.0108 | -2 |
| 29 | ethylammonium chloride                | 557-66-4           | 0.0107 | -1 |
| 30 | glycine                               | 56-40-6            | 0.0106 | 0  |
| 31 | lithium perchlorate                   | 7791-03-9          | 0.0104 | 1  |
| 32 | $\beta$ -alanine                      | 107-95-9           | 0.0103 | -1 |
| 33 | triethanolamine hydrochloride         | 637-39-8           | 0.0103 | 4  |
| 34 | malonic acid                          | 141-82-2           | 0.0102 | -1 |
| 35 | ethylammonium bromide                 | 593-55-5           | 0.0100 | -1 |
| 36 | magnesium chloride hexahydrate        | 7791-18-6          | 0.0100 | 2  |
| 37 | dimethylurea                          | 598-94-7           | 0.0100 | 4  |
| 38 | chloroethyltrimethylammonium chloride | 999-81-5           | 0.0100 | 1  |
| 39 | 1-ethyl-3-methylimidazolium           | 65039-03-4         | 0.0098 | -3 |
| 40 | L-menthol                             | 2216-51-5          | 0.0097 | 0  |
| 41 | anisole                               | 100-66-3           | 0.0096 | 12 |
| 42 | lithium nitrate                       | 7790-69-4          | 0.0096 | 7  |
| 43 | dimethylammonium chloride             | 506-59-2           | 0.0095 | 31 |
| 44 | tetraethylammonium chloride           | 56-34-8            | 0.0094 | 73 |
| 45 | tetramethylammonium chloride          | 75-57-0            | 0.0094 | 15 |
| 46 | cyclohexanone                         | 108-94-1           | 0.0094 | 16 |
| 47 | DL-menthol                            | 89-78-1; 1490-04-6 | 0.0093 | -5 |
| 48 | malic acid or DL-malic acid           | 617-48-1           | 0.0093 | -5 |
| 49 | 1,2-decanediol                        | 1119-86-4          | 0.0093 | -3 |
| 50 | tert-butanol                          | 75-65-0            | 0.0092 | -2 |
| 51 | diethylamine hydrochloride            | 660-68-4           | 0.0092 | -4 |



|    |   |             |        |     |
|----|---|-------------|--------|-----|
| 52 | caprolactam   | 105-60-2    | 0.0092 | 4   |
| 53 | n-butanol   | 71-36-3     | 0.0091 | -9  |
| 54 | lithium chloride                                      | 7447-41-8   | 0.0091 | 1   |
| 55 | zinc nitrate hexahydrate                              | 10196-18-6  | 0.0091 | 2   |
| 56 | furoic acid   | 88-14-2     | 0.0091 | 3   |
| 57 | lithium hexafluorophosphate                           | 21324-40-3  | 0.0091 | -12 |
| 58 | 1-butyl-3-methylimidazolium bromide                   | 85100-77-2  | 0.0089 | 30  |
| 59 | 1-butyl-3-methylimidazolium nitrate                   | 179075-88-8 | 0.0089 | -5  |
| 60 | choline iodide  | 2260-50-6   | 0.0089 | -2  |
| 61 | 1-tetradecanol  | 112-72-1    | 0.0088 | 7   |
| 62 | choline chloride                                      | 67-48-1     | 0.0088 | 1   |
| 63 | 1-ethyl-3-methylimidazolium chloride                  | 65039-09-0  | 0.0088 | -2  |
| 64 | tetrapropylammonium bromide                           | 1941-30-6   | 0.0088 | 2   |
| 65 | methyltriphenylphosphonium bromide                    | 1779-49-3   | 0.0088 | -1  |
| 66 | potassium thiocyanate                                 | 333-20-0    | 0.0088 | 1   |
| 67 | 1-butyl-3-methylimidazolium hexafluorophosphate       | 174501-64-5 | 0.0088 | -16 |
| 68 | lactic acid   | 79-33-4     | 0.0087 | 2   |
| 69 | guanidine   | 113-00-8    | 0.0087 | 14  |
| 70 | imidazole   | 288-32-4    | 0.0086 | 1   |
| 71 | iron(III) chloride hexahydrate                        | 10025-77-1  | 0.0086 | -19 |
| 72 | N-benzyl-2-hydroxy-N,N-dimethylethanaminium chloride  | 7221-40-1   | 0.0086 | -7  |
| 73 | 1-butyl-3-methylimidazolium trifluoromethanesulfonate | 174899-66-2 | 0.0085 | -4  |
| 74 | acetylcholine chloride                                | 60-31-1     | 0.0085 | 5   |
| 75 | guanidine hydrochloride                               | 50-01-1     | 0.0085 | 12  |
| 76 | tetraethylammonium bromide                            | 71-91-0     | 0.0085 | 34  |
| 77 | 1-butyl-3-methylimidazolium chloride                  | 79917-90-1  | 0.0085 | 39  |
| 78 | zirconyl chloride octahydrate                         | 13520-92-8  | 0.0085 | 2   |
| 79 | decanoic acid   | 334-48-5    | 0.0085 | 5   |
| 80 | manganese(II) chloride tetrahydrate                   | 13446-34-9  | 0.0084 | -8  |
| 81 | butyltriphenylphosphonium bromide                     | 1779-51-7   | 0.0084 | 1   |
| 82 | 4-methyl-imidazole                                    | 822-36-6    | 0.0084 | -4  |
| 83 | xylenes   | 1330-20-7   | 0.0084 | -10 |
| 84 | chromium(III) chloride hexahydrate                    | 10060-12-5  | 0.0084 | 6   |
| 85 | 1-ethyl-3-methylimidazolium acetate                   | 143314-17-4 | 0.0083 | -8  |
| 86 | thymol  | 89-83-8     | 0.0083 | -10 |
| 87 | triethylmethylammonium chloride                       | 56375-79-2  | 0.0083 | -6  |
| 88 | benzyltriethylammonium chloride                       | 56-37-1     | 0.0082 | -13 |
| 89 | benzyltrimethylammonium chloride                      | 56-93-9     | 0.0082 | 22  |
| 90 | lidocaine   | 137-58-6    | 0.0081 | -1  |
| 91 | atropine  | 51-55-8     | 0.0081 | -6  |
| 92 | tetraheptylammonium chloride                          | 10247-90-2  | 0.0080 | 1   |
| 93 | pyrazole  | 288-13-1    | 0.0080 | -2  |
| 94 | tetraoctylammonium bromide                            | 14866-33-2  | 0.0079 | -2  |
| 95 | tin(II) chloride                                      | 7772-99-8   | 0.0079 | -9  |
| 96 | guanidine thiocyanate                                 | 593-84-0    | 0.0079 | 4   |
| 97 | tetrabutylphosphonium bromide                         | 3115-68-2   | 0.0078 | -3  |

|     |   |             |        |     |
|-----|---|-------------|--------|-----|
| 98  | tetrabutylammonium bromide                                    | 1643-19-2   | 0.0078 | -3  |
| 99  | ethyltriphenylphosphonium iodide                              | 4736-60-1   | 0.0078 | -2  |
| 100 | iron(III) chloride  | 7705-08-0   | 0.0078 | 3   |
| 101 | 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide | 174899-83-3 | 0.0077 | 12  |
| 102 | zinc bromide  | 7699-45-8   | 0.0077 | 0   |
| 103 | aluminum trichloride  | 7446-70-0   | 0.0077 | -7  |
| 104 | tetrabutylphosphonium chloride                                | 2304-30-5   | 0.0076 | 3   |
| 105 | 1-butyl-3-methylimidazolium tetrafluoroborate                 | 174501-65-6 | 0.0076 | -7  |
| 106 | phenol  | 108-95-2    | 0.0076 | -7  |
| 107 | 1-naphthol  | 90-15-3     | 0.0076 | -6  |
| 108 | tetrahexylammonium bromide                                    | 4328-13-6   | 0.0075 | -3  |
| 109 | lithium bis[(trifluoromethyl)sulfonyl]imide                   | 90076-65-6  | 0.0074 | -5  |
| 110 | benzyltributylammonium chloride                               | 23616-79-7  | 0.0074 | -1  |
| 111 | tetrabutylammonium chloride                                   | 1112-67-0   | 0.0073 | -5  |
| 112 | zinc chloride   | 7646-85-7   | 0.0073 | -4  |
| 113 | chlorobenzene   | 108-90-7    | 0.0072 | -1  |
| 114 | benzyltriphenylphosphonium chloride                           | 1100-88-5   | 0.0068 | 1   |
| 115 | methyltrioctylammonium chloride                               | 5137-55-3   | 0.0068 | -1  |
| 116 | dodecanoic acid   | 143-07-7    | 0.0063 | 2   |
| 117 | tetrahydrofuran   | 109-99-9    | 0.0038 | -82 |
| 118 | diethyl ether   | 60-29-7     | 0.0014 | -89 |

201

202

### 3.2. Results of TOPSIS ranking of HBD

203 The results of TOPSIS analysis for HBD including proposed criteria and assessed weight  
 204 values are presented in **Table 3**. ILs and organic solvents, which are also highlighted with  
 205 light green and light blue, respectively.

206 The first rank is mannitol (0.5743), which is characterized by very low toxicities towards all  
 207 evaluated organisms. Moreover, this sugar is not bioaccumulative and does not decompose to  
 208 form harmful products and is described only by very few hazard and precautionary statements  
 209 and no signal wording. The second, the third and the fourth ranks are disaccharides:  
 210 isomaltose (0.4024), maltose (0.4009), D-sucrose (0.3675) which are non-toxic to *Daphnia*  
 211 *magna* and rodents via ingestion, highly biodegradable. Furthermore, they are characterized  
 212 by high flash point, low value of logK<sub>ow</sub>.



213 After few alternatives with clearly higher values of similarities to ideal solution, there are  
214 betaine, m-aminobenzoic acid, serine, L-proline, citric acid and stearic acid with score values  
215 0.11-0.23. These amino acids and are favorable due to low toxicity towards at least two of  
216 tested organisms, higher flash point, small value of logK<sub>ow</sub> and average to high percentage of  
217 biodegradation. Organic acids also appear in this range and the reason for their high positions  
218 is high biodegradability and each of compound has low and average toxicity towards tested  
219 organisms.

220 Then, straight-chain alcohols (1,2-propanediol, 1,4-butanediol), sugar alcohols (glycerol,  
221 sorbitol), sugars (D-fructose, D-glucose) and their derivatives (glucosamine) are placed in the  
222 ranking. They are characterized by high to average toxicity endpoints at least for two  
223 organisms, low values of logK<sub>ow</sub> and acceptable to high biodegradability level for almost all  
224 sugar-like HBDs. Between these compounds there are also traditional organic solvents as  
225 ethyl acetate, hexane or acetic acid, which are rather green solvents. Gradually, aminoacids  
226 appear, which begin the dominance of compounds containing an amino group as amino acids  
227 (e.g. alanine), amines (e.g. triethanolamine) and amides (e.g. urea). The majority of these  
228 chemicals have small values of logK<sub>ow</sub>, average level of toxicity, pH value close to neutral  
229 and are biodegradable. In the next part of the ranking organic acids occur (nicotinic, myristic,  
230 L-tartaric, succinic, itaconic), which are characterized by certain greenness issues, related to  
231 pH value, toxicity and hazards or precautionary statements.

232 In lower part ranking ionic liquids are located, indicating that they cause more problems than  
233 the most of HDB. Imidazolium salts owe their low position due to unfavourable toxicity  
234 endpoints, as well as great numbers of hazard and precautionary statements together with  
235 hazardous decomposition products. The ranking is closed with diethyl ether that is non-  
236 biodegradable and toxic to algae, flammable and very volatile. The majority of inorganic salts  
237 with metal cations as magnesium chloride hexahydrate, chromium(III) chloride hexahydrate,

238 iron(III) chloride, zinc bromide, zinc chloride, zinc chloride hydrate, cobalt(II) chloride  
 239 hexahydrate are localized in latter parts of HBD ranking.

240 **Table 3.** Results of TOPSIS analysis for HBD and comparison with traditional organic  
 241 solvents and ionic liquids combined with sensitivity analysis for changes in range of  $\pm 10\%$ .  
 242 Comparison of different toxicity evaluation – marked by colors: green, yellow, red (more  
 243 details in *Discussion – Comparison of obtained results* section)

| No. | Substance name (HBD/organic solvent/IL) | CAS number         | Similarity to ideal solution | Ranking difference for $\pm 10\%$ changes |
|-----|---|--------------------|------------------------------|---|
| 1   | mannitol                                | 69-65-8            | 0.5743                       | 0   |
| 2   | isomaltose                              | 499-40-1           | 0.4024                       | 1   |
| 3   | maltose                                 | 6363-53-7          | 0.4009                       | -1  |
| 4   | D-sucrose                               | 57-50-1            | 0.3675                       | 0   |
| 5   | betaine                                 | 107-43-7           | 0.2353                       | 2   |
| 6   | m-aminobenzoic acid                     | 99-05-8            | 0.2208                       | -1  |
| 7   | heptane                                 | 142-82-5           | 0.1979                       | -1  |
| 8   | serine                                  | 56-45-1            | 0.1455                       | 1   |
| 9   | L-proline                               | 147-85-3; 609-36-9 | 0.1293                       | -1  |
| 10  | citric acid                             | 77-92-9            | 0.1230                       | 0   |
| 11  | stearic acid                            | 57-11-4            | 0.1120                       | 0   |
| 12  | methanol                                | 67-56-1            | 0.0463                       | 1   |
| 13  | xylose                                  | 58-86-6            | 0.0447                       | 1   |
| 14  | methionine                              | 63-68-3            | 0.0332                       | -2  |
| 15  | tricarballic acid                       | 99-14-9            | 0.0297                       | 0   |
| 16  | ethyl acetate                           | 141-78-6           | 0.0290                       | 1   |
| 17  | aconitic acid                           | 499-12-7           | 0.0282                       | 2   |
| 18  | lanthanum(III) chloride hexahydrate     | 17272-45-6         | 0.0251                       | -2  |
| 19  | D-glucose                               | 50-99-7            | 0.0249                       | -1  |
| 20  | D-fructose                              | 57-48-7            | 0.0246                       | 2   |
| 21  | glucosamine                             | 3416-24-8          | 0.0242                       | -1  |
| 22  | meso-erythritol                         | 149-32-6           | 0.0230                       | -1  |
| 23  | 1,2-propanediol                         | 57-55-6            | 0.0221                       | 0   |
| 24  | D-sorbitol                              | 50-70-4            | 0.0214                       | 1   |
| 25  | $\alpha$ -cyclodextrin                  | 10016-20-3         | 0.0206                       | -1  |
| 26  | cis-9-octadecenoic acid                 | 112-80-1           | 0.0205                       | 2   |
| 27  | L-sorbose                               | 87-79-6            | 0.0203                       | 2   |
| 28  | 1,2-butanediol                          | 26171-83-5         | 0.0196                       | -1  |
| 29  | pentaerythritol                         | 115-77-5           | 0.0195                       | -3  |
| 30  | alanine                                 | 302-72-7           | 0.0189                       | 0   |
| 31  | hexane                                  | 110-54-3           | 0.0189                       | 1   |
| 32  | diethylene glycol                       | 111-46-6           | 0.0182                       | 3   |
| 33  | raffinose                               | 512-69-6           | 0.0179                       | 0   |
| 34  | phytic acid                             | 83-86-3            | 0.0178                       | 0   |
| 35  | adonitol                                | 488-81-3           | 0.0176                       | 5   |
| 36  | toluene                                 | 108-88-3           | 0.0174                       | 1   |

|    |                                |                        |        |     |
|----|--------------------------------|------------------------|--------|-----|
| 37 | mannose                        | 3458-28-4              | 0.0173 | 1   |
| 38 | calcium chloride hexahydrate   | 7774-34-7              | 0.0172 | 7   |
| 39 | urea                           | 57-13-6                | 0.0172 | 9   |
| 40 | polyethylene glycol            | 25322-68-3             | 0.0170 | 1   |
| 41 | D-trehalose                    | 99-20-7                | 0.0168 | 2   |
| 42 | cyclohexane                    | 110-82-7               | 0.0167 | -3  |
| 43 | acetamide                      | 60-35-5                | 0.0166 | 1   |
| 44 | ethylene glycol                | 107-21-1               | 0.0165 | -8  |
| 45 | acetic acid                    | 64-19-7                | 0.0163 | -14 |
| 46 | D-isosorbide                   | 652-67-5               | 0.0162 | 0   |
| 47 | triethanolamine                | 102-71-6               | 0.0161 | 6   |
| 48 | DL-glutamic acid               | 617-65-2               | 0.0161 | -1  |
| 49 | glycerol                       | 56-81-5                | 0.0159 | 0   |
| 50 | $\beta$ -alanine               | 107-95-9               | 0.0159 | 10  |
| 51 | 1,4-butanediol                 | 110-63-4               | 0.0158 | 0   |
| 52 | D-galactose                    | 59-23-4                | 0.0157 | 0   |
| 53 | nicotinic acid                 | 59-67-6                | 0.0156 | 3   |
| 54 | arginine                       | 74-79-3                | 0.0155 | -4  |
| 55 | zinc nitrate hexahydrate       | 10196-18-6             | 0.0155 | 11  |
| 56 | threonine                      | 72-19-5                | 0.0155 | 2   |
| 57 | 1,3-propanediol                | 504-63-2               | 0.0155 | -3  |
| 58 | magnesium chloride hexahydrate | 7791-18-6              | 0.0154 | 4   |
| 59 | myristic acid                  | 544-63-8               | 0.0154 | 2   |
| 60 | 1,6-hexanediol                 | 629-11-8               | 0.0154 | 9   |
| 61 | formamide                      | 75-12-7                | 0.0154 | 14  |
| 62 | DL-aspartic acid               | 617-45-8               | 0.0154 | 15  |
| 63 | L-tartaric acid                | 87-69-4                | 0.0153 | 11  |
| 64 | N-methylacetamide              | 79-16-3                | 0.0153 | -7  |
| 65 | succinic acid                  | 110-15-6               | 0.0153 | -23 |
| 66 | malonic acid                   | 141-82-2               | 0.0152 | 2   |
| 67 | itaconic acid                  | 97-65-4                | 0.0152 | 4   |
| 68 | triethylene glycol             | 112-27-6               | 0.0152 | 8   |
| 69 | L-diethyl tartrate             | 87-91-2                | 0.0152 | 17  |
| 70 | 1,3-dimethylurea               | 96-31-1                | 0.0152 | 10  |
| 71 | p-hydroxybenzaldehyde          | 123-08-0               | 0.0151 | -1  |
| 72 | aluminum trichloride           | 7446-70-0              | 0.0151 | -9  |
| 73 | N-methyldiethanolamine         | 105-59-9               | 0.0151 | 0   |
| 74 | A-L-rhamnose                   | 3615-41-6; 116908-82-8 | 0.0151 | 7   |
| 75 | vanillin                       | 121-33-5               | 0.0150 | -11 |
| 76 | malic acid or DL-malic acid    | 617-48-1               | 0.0150 | 3   |
| 77 | suberic acid                   | 505-48-6               | 0.0150 | 5   |
| 78 | 1,5-pentanediol                | 111-29-5               | 0.0150 | -11 |
| 79 | glutaric acid                  | 110-94-1               | 0.0150 | -1  |
| 80 | gallic acid                    | 149-91-7               | 0.0149 | -25 |
| 81 | p-ethylphenol                  | 123-07-9               | 0.0149 | -16 |
| 82 | adipic acid                    | 124-04-9               | 0.0149 | -23 |
| 83 | anisole                        | 100-66-3               | 0.0148 | -11 |

|     |   |                    |        |     |
|-----|---|--------------------|--------|-----|
| 84  | phenylacetic acid                               | 103-82-2           | 0.0148 | 1   |
| 85  | propionamide                                    | 79-05-0            | 0.0148 | 7   |
| 86  | methylurea                                      | 598-50-5           | 0.0148 | -3  |
| 87  | 1-butyl-3-methylimidazolium nitrate             | 179075-88-8        | 0.0147 | 15  |
| 88  | o-chlorobenzoic acid                            | 118-91-2           | 0.0147 | 6   |
| 89  | glycolic acid                                   | 79-14-1            | 0.0147 | -5  |
| 90  | 3-amino-1-propanol                              | 156-87-6           | 0.0147 | 15  |
| 91  | caffeic acid                                    | 331-39-5           | 0.0146 | 6   |
| 92  | p-chlorobenzoic acid                            | 74-11-3            | 0.0146 | -1  |
| 93  | coumarin  | 91-64-6            | 0.0146 | 11  |
| 94  | pyruvic acid                                    | 127-17-3           | 0.0146 | 1   |
| 95  | ammonium thiocyanate                            | 1762-95-4          | 0.0145 | -7  |
| 96  | tetramethylammonium chloride                    | 75-57-0            | 0.0145 | 3   |
| 97  | DL-lactic acid                                  | 50-21-5            | 0.0145 | 17  |
| 98  | DL-mandelic acid                                | 90-64-2; 611-72-3  | 0.0144 | 13  |
| 99  | 1-butyl-3-methylimidazolium bromide             | 85100-77-2         | 0.0144 | 9   |
| 100 | 1-butyl-3-methylimidazolium hexafluorophosphate | 174501-64-5        | 0.0144 | 15  |
| 101 | chromium(III) chloride hexahydrate              | 10060-12-5         | 0.0143 | -12 |
| 102 | allylurea                                       | 557-11-9           | 0.0143 | -2  |
| 103 | p-toluenesulfonic acid                          | 104-15-4           | 0.0143 | 3   |
| 104 | guaiacol  | 90-05-1            | 0.0143 | -14 |
| 105 | succinonitrile                                  | 110-61-2           | 0.0143 | 4   |
| 106 | p-coumaric acid                                 | 7400-08-0          | 0.0143 | 12  |
| 107 | lactic acid                                     | 79-33-4            | 0.0143 | -6  |
| 108 | benzamide                                       | 55-21-0            | 0.0143 | 4   |
| 109 | furoic acid                                     | 88-14-2            | 0.0143 | -6  |
| 110 | oxalic acid                                     | 144-62-7           | 0.0143 | -23 |
| 111 | m-chlorobenzoic acid                            | 535-80-8           | 0.0143 | -18 |
| 112 | DL-menthol                                      | 89-78-1; 1490-04-6 | 0.0142 | -14 |
| 113 | pentaethylenehexamine                           | 4067-16-7          | 0.0142 | 13  |
| 114 | levulinic acid                                  | 123-76-2           | 0.0142 | -18 |
| 115 | cinnamic acid                                   | 621-82-9           | 0.0142 | -5  |
| 116 | copper(II) chloride dihydrate                   | 10125-13-0         | 0.0141 | 6   |
| 117 | p-hydroxybenzoic acid                           | 99-96-7            | 0.0141 | 13  |
| 118 | trans-cinnamic acid                             | 140-10-3           | 0.0141 | -11 |
| 119 | decan-1-ol                                      | 112-30-1           | 0.0140 | -2  |
| 120 | oxalic acid dihydrate                           | 6153-56-6          | 0.0140 | 7   |
| 121 | 2,2,2-trifluoroacetamide                        | 354-38-1           | 0.0139 | -2  |
| 122 | triazole  | 288-88-0           | 0.0139 | 6   |
| 123 | 1-hexadecanol                                   | 36653-82-4         | 0.0139 | 13  |
| 124 | caprolactam                                     | 105-60-2           | 0.0139 | 22  |
| 125 | butanoic acid                                   | 107-92-6           | 0.0139 | 39  |
| 126 | dodecyl alcohol                                 | 112-53-8           | 0.0139 | -2  |
| 127 | aminomethylpropanol                             | 124-68-5           | 0.0138 | -11 |
| 128 | octanol   | 111-87-5           | 0.0138 | -15 |
| 129 | diethanolamine                                  | 111-42-2           | 0.0138 | -8  |
| 130 | diethylene triamine                             | 111-40-0           | 0.0138 | 12  |



|     |   |             |        |     |
|-----|---|-------------|--------|-----|
| 131 | cyclohexanone   | 108-94-1    | 0.0138 | 1   |
| 132 | 1-tetradecanol  | 112-72-1    | 0.0138 | 1   |
| 133 | sulfolane   | 126-33-0    | 0.0137 | 2   |
| 134 | 1-butyl-3-methylimidazolium chloride                          | 79917-90-1  | 0.0137 | 5   |
| 135 | chloroethyltrimethylammonium chloride                         | 999-81-5    | 0.0137 | -15 |
| 136 | potassium thiocyanate   | 333-20-0    | 0.0137 | -2  |
| 137 | 1-butyl-3-methylimidazolium trifluoromethanesulfonate         | 174899-66-2 | 0.0137 | -12 |
| 138 | $\alpha$ -tocopherol  | 59-02-9     | 0.0136 | 3   |
| 139 | butyltriphenylphosphonium bromide                             | 1779-51-7   | 0.0136 | 9   |
| 140 | phenylpropanoic acid  | 501-52-0    | 0.0136 | 0   |
| 141 | ethanolamine  | 141-43-5    | 0.0135 | -18 |
| 142 | decanoic acid   | 334-48-5    | 0.0135 | -11 |
| 143 | propionic acid  | 79-09-4     | 0.0135 | 1   |
| 144 | ibuprofen   | 15687-27-1  | 0.0135 | -7  |
| 145 | hexanoic acid   | 142-62-1    | 0.0134 | -2  |
| 146 | 1-ethyl-3-methylimidazolium acetate                           | 143314-17-4 | 0.0134 | 17  |
| 147 | imidazole   | 288-32-4    | 0.0134 | 2   |
| 148 | m-cresol  | 108-39-4    | 0.0133 | 2   |
| 149 | hexan-1-ol  | 111-27-3    | 0.0133 | 5   |
| 150 | lidocaine   | 137-58-6    | 0.0133 | -21 |
| 151 | cyclohexanol  | 108-93-0    | 0.0133 | 0   |
| 152 | p-cresol  | 106-44-5    | 0.0133 | 7   |
| 153 | tin(II) chloride  | 7772-99-8   | 0.0132 | -6  |
| 154 | resorcinol  | 108-46-3    | 0.0132 | -2  |
| 155 | 10-undecanoic acid  | 112-38-9    | 0.0132 | 0   |
| 156 | bis(trifluoromethylsulfonyl)imide                             | 82113-65-3  | 0.0132 | -11 |
| 157 | acetic acid   | 64-19-7     | 0.0132 | -4  |
| 158 | iron(III) chloride  | 7705-08-0   | 0.0132 | -1  |
| 159 | xylenes   | 1330-20-7   | 0.0131 | -21 |
| 160 | octanoic acid   | 124-07-2    | 0.0131 | -4  |
| 161 | ethambutol  | 74-55-5     | 0.0131 | 0   |
| 162 | atropine  | 51-55-8     | 0.0130 | 12  |
| 163 | benzyltriethylammonium chloride                               | 56-37-1     | 0.0130 | -3  |
| 164 | tert-butanol  | 75-65-0     | 0.0130 | -2  |
| 165 | 1-butanol   | 71-36-3     | 0.0130 | -7  |
| 166 | furfuryl alcohol  | 98-00-0     | 0.0129 | 3   |
| 167 | zinc bromide  | 7699-45-8   | 0.0129 | 0   |
| 168 | valeric acid  | 109-52-4    | 0.0129 | 12  |
| 169 | salicylic acid  | 69-72-7     | 0.0129 | 4   |
| 170 | chloroacetic acid   | 79-11-8     | 0.0129 | -4  |
| 171 | tetrabutylphosphonium bromide                                 | 3115-68-2   | 0.0129 | 6   |
| 172 | 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide | 174899-83-3 | 0.0128 | -7  |
| 173 | 1-butyl-3-methylimidazolium tetrafluoroborate                 | 174501-65-6 | 0.0128 | 8   |
| 174 | thiourea  | 62-56-6     | 0.0128 | -3  |
| 175 | benzoic acid  | 65-85-0     | 0.0127 | 0   |
| 176 | thymol  | 89-83-8     | 0.0127 | 0   |

|     |                                 |            |        |     |
|-----|---------------------------------|------------|--------|-----|
| 177 | DL-camphor                      | 21368-68-3 | 0.0127 | -5  |
| 178 | o-cresol                        | 95-48-7    | 0.0126 | -8  |
| 179 | trifluoromethanesulfonic acid   | 1493-13-6  | 0.0125 | 3   |
| 180 | p-chlorophenol                  | 106-48-9   | 0.0125 | -1  |
| 181 | trichloroacetic acid            | 76-03-9    | 0.0125 | -3  |
| 182 | zinc chloride                   | 7646-85-7  | 0.0124 | 7   |
| 183 | phenol                          | 108-95-2   | 0.0123 | 3   |
| 184 | acrylic acid                    | 79-10-7    | 0.0123 | 7   |
| 185 | 2,3-xylenol                     | 526-75-0   | 0.0122 | -1  |
| 186 | tetramethyl urea                | 632-22-4   | 0.0121 | -3  |
| 187 | 2,6-dimethylphenol              | 576-26-1   | 0.0120 | -2  |
| 188 | cobalt(II) chloride hexahydrate | 7791-13-1  | 0.0120 | 5   |
| 189 | diazabicyclo[5.4.0]undec-7-ene  | 6674-22-2  | 0.0120 | 3   |
| 190 | zinc chloride hydrate           | 29604-34-0 | 0.0120 | -3  |
| 191 | 1-propanol                      | 71-23-8    | 0.0119 | 3   |
| 192 | tetraethylenepentamine          | 112-57-2   | 0.0118 | -2  |
| 193 | chlorobenzene                   | 108-90-7   | 0.0116 | -5  |
| 194 | ethylenediamine                 | 100-36-7   | 0.0115 | -26 |
| 195 | DL-borneol                      | 507-70-0   | 0.0111 | 0   |
| 196 | perfluorodecanoic acid          | 335-76-2   | 0.0102 | 0   |
| 197 | dodecanoic acid                 | 143-07-7   | 0.0096 | 1   |
| 198 | formic acid                     | 64-18-6    | 0.0085 | -1  |
| 199 | 2,2,2-trifluoroethanol          | 75-89-8    | 0.0065 | 0   |
| 200 | tetrahydrofuran                 | 109-99-9   | 0.0046 | 0   |
| 201 | hexafluoroisopropanol           | 920-66-1   | 0.0026 | 0   |
| 202 | diethyl ether                   | 60-29-7    | 0.0018 | 0   |

244

245 

### 3.3. Results of TOPSIS ranking of DES

246 The results of DES mixtures evaluation including proposed criteria and modeling of their  
247 combined greenness, calculated with equation 1, are presented in **Table 4**. ILs and organic  
248 solvents are included in the analysis and they are marked light green and light blue,  
249 respectively.

250 The best alternative among selected set is citric acid:D-sucrose (1:3), followed by the citric  
251 acid:D-maltose (4:1) and glycerol:L-proline:D-sucrose (9:4:1). On the other hand, last three  
252 DES are represented by the iron(III) chloride hexahydrate:ethylene glycol (2:1), choline  
253 chloride:zinc chloride (1:1.2) and tetrabutylammonium bromide:formic acid (1:1). In general,  
254 places in the ranking for DES mixtures are similar to those obtained for separate analyses of  
255 HBA and HBD. For instance, citric acid as HBA and D-maltose as HBD have high positions,

256 their mixture is also in the top. Tetrabutylammonium bromide and formic acid take lower  
 257 positions in the rankings of HBA and HBD, then their mixture is also unsatisfactorily ranked.  
 258 In case of DES with choline chloride as a HBA (choline chloride:1,2-propanediol, choline  
 259 chloride:ethylene glycol, choline chloride:1,4-butanediol), the ranking positions decrease with  
 260 changing ratios towards the growing presence of hydrogen bond donors in the compounds.  
 261 Based on values of similarities to ideal solution of HBA and HBD, DES consisting of any  
 262 combination of constituents, can be assessed in this way. Traditional organic solvents are  
 263 found along the entire list of compounds with similar order as in case of individual assessment  
 264 of HBA and HBD. Location of DES next to solvents of rather green character (alcohols, esters  
 265 or aliphatic hydrocarbons) indicates that DES are also not so problematic. On the other hand,  
 266 ILs are in the second half of the list.

267 **Table 3.** Results of environmental assessment for DES mixtures using toxicological model  
 268 and TOPSIS analysis and comparison with traditional organic solvents and ionic liquids

|    | DES/IL/traditional organic solvents name    | Combined greenness effect |
|----|---|---------------------------|
| 1  | citric acid:D-sucrose (1:3)                 | 0.2855                    |
| 2  | heptane                                     | 0.1730                    |
| 3  | citric acid:D-maltose (4:1)                 | 0.1201                    |
| 4  | methanol                                    | 0.0944                    |
| 5  | glycerol:L-proline:D-sucrose (9:4:1)        | 0.0766                    |
| 6  | betaine:1,2-butanediol (1:3)                | 0.0574                    |
| 7  | betaine:ethylene glycol (1:4)               | 0.0474                    |
| 8  | ethyl acetate                               | 0.0283                    |
| 9  | glycerol:xylitol:D-fructose (3:3:3)         | 0.0218                    |
| 10 | potassium carbonate:glycerol (1:7)          | 0.0205                    |
| 11 | hexane                                      | 0.0198                    |
| 12 | choline chloride:1,2-propanediol (1:4)      | 0.0194                    |
| 13 | choline chloride:1,2-butanediol (1:5)       | 0.0178                    |
| 14 | choline chloride:1,2-propanediol (1:2)      | 0.0175                    |
| 15 | choline chloride:polyethylene glycol (1:20) | 0.0166                    |
| 16 | zirconyl chloride octahydrate:urea (1:5)    | 0.0157                    |
| 17 | choline chloride:1,2-propanediol (1:1)      | 0.0154                    |
| 18 | lactic acid:1,2-propanediol (1:1)           | 0.0154                    |
| 19 | choline chloride:1,4-butanediol (1:5)       | 0.0146                    |
| 20 | choline chloride:ethylene glycol (1:3)      | 0.0146                    |
| 21 | toluene                                     | 0.0144                    |

|    |   |        |
|----|---|--------|
| 22 | choline chloride:urea (1:2)                                   | 0.0142 |
| 23 | cyclohexane   | 0.0141 |
| 24 | choline chloride:ethylene glycol (1:2)                        | 0.0138 |
| 25 | glycine:lactic acid (1:5)                                     | 0.0136 |
| 26 | acetic acid   | 0.0135 |
| 27 | choline chloride:glycerol (1:2)                               | 0.0134 |
| 28 | choline chloride:1,4-butanediol (1:2)                         | 0.0133 |
| 29 | choline chloride:p-toluenesulfonic acid (1:4)                 | 0.0132 |
| 30 | L-menthol:acetic acid (1:1)                                   | 0.0130 |
| 31 | choline chloride:glycerol (1:1)                               | 0.0123 |
| 32 | choline chloride:lactic acid (1:2)                            | 0.0123 |
| 33 | choline chloride:levulinic acid (1:2)                         | 0.0122 |
| 34 | anisole   | 0.0122 |
| 35 | choline chloride:malic acid (1:1)                             | 0.0119 |
| 36 | 1-butyl-3-methylimidazolium nitrate                           | 0.0118 |
| 37 | 1-butyl-3-methylimidazolium bromide                           | 0.0116 |
| 38 | choline chloride:phenol (1:4)                                 | 0.0116 |
| 39 | choline chloride:tin(II) chloride (1:2)                       | 0.0116 |
| 40 | cyclohexanone   | 0.0115 |
| 41 | 1-butyl-3-methylimidazolium hexafluorophosphate               | 0.0115 |
| 42 | choline chloride:oxalic acid (1:1)                            | 0.0115 |
| 43 | lactic acid:D-glucose (5:1)                                   | 0.0114 |
| 44 | tetrabutylammonium chloride:decanoic acid (1:2)               | 0.0113 |
| 45 | lactic acid:D-fructose (5:1)                                  | 0.0113 |
| 46 | methyltrioctylammonium chloride:decanoic acid (1:2)           | 0.0112 |
| 47 | tert-butanol  | 0.0111 |
| 48 | 1-butyl-3-methylimidazolium chloride                          | 0.0111 |
| 49 | iron(III) chloride hexahydrate:ethylene glycol (2:1)          | 0.0111 |
| 50 | 1-butyl-3-methylimidazolium trifluoromethanesulfonate         | 0.0111 |
| 51 | n-butanol   | 0.0110 |
| 52 | 1-ethyl-3-methylimidazolium acetate                           | 0.0108 |
| 53 | choline chloride:zinc chloride (1:1.2)                        | 0.0107 |
| 54 | xylenes   | 0.0107 |
| 55 | tetrabutylphosphonium bromide                                 | 0.0103 |
| 56 | 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide | 0.0103 |
| 57 | 1-butyl-3-methylimidazolium tetrafluoroborate                 | 0.0102 |
| 58 | phenol  | 0.0099 |
| 59 | chlorobenzene   | 0.0094 |
| 60 | tetrabutylammonium bromide:formic acid (1:1)                  | 0.0081 |
| 61 | tetrahydrofuran   | 0.0042 |
| 62 | diethyl ether   | 0.0016 |

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270

### 3.4. Results of sensitivity analysis and comprehensive ranking



271 Sensitivity analysis allows to assess the reliability of conducted analysis based on reliability  
272 of input data. Results of sensitivity analysis rankings are presented in **Tables 2** and **3**. In both  
273 cases, the changes of input data within  $\pm 10\%$  of original values are insignificant, as they do  
274 not affect the ranking. Therefore, the ranking results can be considered as reliable. There are  
275 some shifts in HDB positions in the middle of ranking results, where the differences in values  
276 of similarities to ideal solution are very low.

### 277 ***3.5. Discussion - Comparison of obtained results***

278 HBD taken into evaluation are chemicals of a variety of characteristics, because they belong  
279 to different groups of compounds. However, it can be seen that in the first part sugars alcohols  
280 and straight-chain alcohols appear, they gradually pass through sugars and amides to organic  
281 acids. These groups do not create a clear boundaries but interpenetrate gradually increasing  
282 the predominance. Poor ecotoxicological profile of organic acids as a HBD is also reported by  
283 Radošević et al. in *in vitro* study of cholinium-based IL and DES towards fish cell line [26].

284 Similar results are presented by Halder et al. [27] in *in silico* modeling study of HDB  
285 toxicity. They divide evaluated chemicals into three groups, based on their toxicity level -  
286 low, intermediate and high. Their findings are marked in **Table 3** with green (low toxicity),  
287 yellow (moderate toxicity) and red (high toxicity) colours, respectively. The reason for some  
288 differences in comparison to this study may be fact, that Hadler's et al. assessment involves  
289 only toxicity criteria measured for different organisms (11 different mammalian cell lines -  
290 and 12 different microbial organisms) what results in poor coverage of this study assessment  
291 criteria. Hadler et al. also evaluate some HBA as preliminary studies, as they claim more  
292 experimental data is needed: choline chloride, menthol, N,N-diethylethanol ammonium  
293 chloride (DEAC), and methyltriphenyl phosphonium bromide (MTPB). MTPB and DEAC,  
294 are found to impart toxicity towards the most of the organisms, while N,N-diethylethanol



295 ammonium chloride followed by choline chloride were found to be less toxic DES  
296 components. However, it is difficult to compare both results due to fact that our evaluation  
297 includes only choline chloride and MTPB. Nevertheless, ChCl and MTPB are ranked on  
298 45<sup>th</sup> and 63<sup>rd</sup> place in the HBA list (out of 125 positions). The majority of evaluated HBA and  
299 HBD that are metalorganic compounds are ranked lower. The reason is that in our assessment  
300 toxicities are the most significant criteria and metal-containing DES are generally toxic to  
301 different organisms [28].

302 Perales et al. (2017) evaluated toxicity endpoints in combination with some physicochemical  
303 data (volatility and boiling point, flashpoint, biodegradability, bioconcentration factor, etc.)  
304 using the Environmental Health and Safety Approach (EHSA) used for identification of risks  
305 related to the environment and the human health) [29]. Using both types of information, each  
306 chemical compound receives a score for the categories health, safety and environment, then  
307 the best candidates considered as least dangerous for a short exposure time may be found.  
308 Herein, glycerol (rank 17 in HBA ranking) - derived solvents as 3-ethoxy-1,2-propanediol,  
309 3-butoxy-1,2-propanediol and 1,3-diethoxy-2-propanol are the most favourable  
310 (1,2-propanediol ranked 23 and 1,3-propanediol ranked 57 but ethoxy derivatives are not  
311 included in ranking).

312 DES mixtures may show some effects between the DES constituents (HBA and HBD) – the  
313 interactions, such as synergism and antagonism. More often synergistic effects are described  
314 due greater toxicity level of a mixture than toxicity level of its constituents. However, these  
315 two effects occur, which has also been discussed in the literature [30, 31]. In our study the  
316 synergistic or antagonistic effects are neglected, because still little is known on these types of  
317 interactions. In other words, only independent actions of the HBA and HBD are considered.

318 We also conduct evaluation of DES applications where authors claim their solvent is green  
319 and these results are summarized in **Table S17**. The number of publications that describe

320 choline chloride-based DES application is significantly higher than the others (30 out of 46  
321 examples). Then, betaine, citric acid, glycerol and lactic acid as HBA are of great interest,  
322 probably due to the natural origin. NADES generally belong to plant-based primary  
323 metabolites, i.e. organic acids, sugars, alcohols, amines and amino acids. Often they are  
324 considered as those with lower environmental impact and low toxicity than other DES. It has  
325 been reported in many papers, for instance in comparison of cytotoxicity profile of choline  
326 chloride:fructose and choline chloride:glucose as NADES and N,N-diethyl ethanolammonium  
327 chloride:triethylene glycol as DES towards different hepatic cell lines [32].

328 The problem with DES greenness assessment is that reports usually refer to physicochemical  
329 properties, such as density, viscosity, electrical conductivity, surface tension, solvatochromic  
330 parameters or refractive index [33]. Unfortunately, there is still lack of data on toxicological  
331 and environmental fate parameters (biodegradability, octanol-water partition coefficients,  
332 etc.). In this area DES are poorly characterized as ILs. The comparison of results on the  
333 cytotoxic effects on Channel Catfish Ovary cell line indicate that the cytotoxicity of  
334 cholinium-based IL and DES is generally lower than that of imidazolium- and pyridinium-  
335 based IL [26]. It is an implication that cholinium-based DES are promising and beneficial  
336 class of solvents in terms of ecotoxicological impact. However, it only refers to this specific  
337 type of DES and single of species of tested organism. Our results show that selected ionic  
338 liquids, mainly imidazolium salts, are placed in second part of list. Moreover, some choline-  
339 based DES as choline chloride with oxalic acid (1:1) or zinc chloride (1:1.2) are ranked  
340 between ILs.

341 All of the above-mentioned issues explain that it is not possible to unambiguously resolve the  
342 dispute, which of the solvents are more green - ILs or DES. DES properties depend on the  
343 specific case, criteria taken into evaluation, including tested organisms, etc. Therefore, the  
344 terms as non-toxic, biodegradable, environmentally friendly must be carefully used. Each of

345 the mixtures should be tested and evaluated individually. Naming the solvent green because it  
346 belongs to DES group is an abuse. The interpretation of data gathered in Table S18 shows that  
347 only very few of authors claims about the greenness of the used DES mixture is presented  
348 without justification. This is a significant improvement in a reference to greenness evaluation  
349 of ionic liquids [20]. In case of DES solvents, more authors explain the use of the term  
350 "green" extensively, giving solid justifications.

#### 351 **4. Conclusions**

352 In this study, the TOPSIS algorithm combined with calculation of additive effects is applied  
353 for DES components and DES ranking by their greenness. The comprehensive assessments  
354 that includes simultaneously safety, biodegradability and toxicological criteria indicate that  
355 DES formed by mixing sugars alcohols, straight-chain alcohol, sugars and amides may be  
356 promising green solvents, in contrary to those that include metal ions and organic acids.  
357 Those ranked first are more environmentally advantageous than some of the selected  
358 imidazolium ionic liquids, which makes them a potential alternative solvents for many  
359 applications. However, according to our results, due insufficient characteristics, especially  
360 concerning toxicity level, a general flat assertion of DES mixtures as a green solvent is  
361 inappropriate. Moreover, lack of data of some physiochemical properties may limit the  
362 number of fields for they usage in chemical practice or industry. Therefore, additional studies  
363 measuring environmental impact are required to understand the nature of DES mixtures  
364 including properties and biological effects between their components.

365 Although the described approach provides general information about solvent greenness and  
366 allows for ease comparison of variety of solvents in terms of greenness performance, the  
367 proposed assessment procedure may be only treated as a screening tool for preliminary  
368 selection of a green alternative, due to simplified model of additivity that is used for DES



369 mixtures calculations. More targeted evaluation for specific purpose is also possible, but need  
370 providing more newly obtained data (variety of properties and environmental fate of  
371 particular chemical) that may be easily incorporated into the performed algorithm.

### 372 **Conflict of interests**

373 There are no conflicts of interests to declare.

### 374 **Supplementary Information**

375 Supplementary Information 1 – Summary of different authors claims on DES being green,  
376 numerical transformation involved criteria and alternative substances (objects) taken into  
377 consideration in case of lack of data.

378 Supplementary Information 2 – Gathered data concerning physiochemical and environmental  
379 properties as a evaluated criteria of DES components and their mixtures.

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