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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 synthetized 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.

1. Introduction

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

DES show excellent applicability in many areas, for instance separation processes, biodiesel production [6], electrochemistry [7], absorption and solubility of carbon dioxide [8], medical and pharmaceutics usage [9], chemical synthesis [10], activation of enzymes and biocatalysis [11]. However, despite the wide range of applications, the claims about their low harmfulness, non-toxicity or high biodegradability are not unequivocal. Several studies proved that not all DES are highly biodegradable or nontoxic and lack of data may be serious problem while environmental evaluations [12–14]. Estimation of DES greenness should be performed in more comprehensive way.

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

To authors best knowledge, it is the first study that considers variety of criteria (not only toxicity) to rank HBA and HBD as DES components and DES in respect to their environmental benignness. The results of this study may be useful for researchers and practitioners at the first stage of DES selection, especially for separation processes. The presented tools

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allow to assess how individual compounds, as well as their molar ratios can affect the greenness of DES.

2. Materials and methods

2.1. Data collection

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

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

For the specific references to paper, please see descriptions in Supplementary Information.

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
Vapor pressure	In 25 °C	MSDS, papers, databases
Toxicity *Daphnia magna*	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, databases
pH	–	MSDS, papers
Solubility in water	In 25 °C	MSDS

The majority of properties are taken from scientific papers, describing chemical characteristics of DES. Then information are supported by the chemical on-line databases such as ECHA, PubChem, Chemspider. Moreover, data for analysis in this work is provided by the Material Safety Data Sheets (MSDS) supplied by different companies, mainly Sigma-Aldrich, Merck, Thermo Fisher Scientific, Santa Cruz Biotechnology Inc., Iolitec. Especially information and parameters as: alternative names, CAS number, molecular formula, molecular weight, signal wording, special hazards arising from the substance or mixture/hazardous decomposition products.

The properties of DES are not fully available, so in case of lack of data, parameters have been completed by predicted or estimated values (calculated in QSAR, EPISuite, etc.) or missing points are substituted with the values of the chemically similar compounds/group of compounds as proposed by Adler et al. [21] as summarized in Tables S1, S5 and S7-S16. Additionally, wherever several datapoints are available (for instance toxicity values for different fish/algae/rodent spices), always the most unbeneficial one is selected, according to precautionary principle.

Traditional organic solvents and ionic liquids are included in the dataset as reference points, for better understanding of a green nature of HBAs and HBDs being the DES components (the same properties as for the HBAs and HBDs are collected). Some of data require transformations from descriptions to numerical values, what is presented in Tables S2-S6.

2.2. TOPSIS algorithm

TOPSIS is algorithm developed by Hwang and Yoon [22], it is based on finding an alternative characterized by the shortest distance from the positive ideal solution and simultaneously the furthest distance from the negative ideal solution. This mathematical model allows for combination of different (often contradictory) criteria into a single score leading to creation of ranking of available alternatives. The ranking is defined by the values of similarity to ideal solution, for each alternative, ranged between 0 and 1. The value 0 is assigned to completely non-ideal alternative (the worst values for all criteria), while the value 1 for an ideal solution (the best values for all criteria). Only basic information about TOPSIS algorithm are described above. Its mathematical algorithm is presented in Section 2 of Supplementary Information 1. More details may be found in the articles, including its fundamentals [23,24]. The calculations involving TOPSIS are performed in Excel program (Microsoft 2016). TOPSIS was selected over other MCDA tools as it is fully applicable for many alternatives assessment, its outcome is easily interpretable and its algorithm is relatively simple.

2.3. TOPSIS algorithm for DES components – HBA and HBD

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

2.4. TOPSIS algorithm for DES

Environmental assessment of DES including binary and ternary mixtures are based on results obtained with TOPSIS analysis for HBAs and HBDs and calculations of common effects. Due to fact, that DES are composed of HBA and one (for binary mixtures) or two HBDs (for ternary

mixtures), the evaluation includes common responses, calculated with toxicological model, according to the equation:

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

where E(Cmix) is combined effect at the mixture concentration (Cmix), and E(Ci) is the similarity to ideal solution (calculated for HBA and HBD with TOPSIS) of individual mixture component (i) applied at the concentration (Ci) [25]. Bearing in mind, fact that DES mixtures may have different ratios of HBA and HBD, this information is introduced by fractions, e.g. for HBA:HBD mixtures with ratios of 1:1 and 1:3, the fractions are equal ½ and ½ as well as ¼ and ¾, respectively. Selected 35 binary and 2 ternary mixtures, considered by the authors of respective publications as green solvents are evaluated. All these DES are listed in Table S18. together with an information about areas of application and justification why authors consider them green. Ionic liquids and traditional organic solvents are also included as reference points. To obtain an adequate level of comparability with DES mixtures, combined value of addition effect for each solvent is calculated by multiplication values of similarity to ideal solution of HBA and HBD for particular solvent according to Eq. (1) (solvent is treated as mix of two individuals).

2.5. Weights and confidence rankings

The advantage of MCDA tools is possibility of assigning weights to criteria to give them relative importance in accordance to the purpose of the analysis. To provide a comprehensive ranking thirteen criteria with different importance are simultaneously considered in the assessment. Toxicity towards *Daphnia magna*, fish, algae and rats via ingestion are assessed to have higher influence on the greenness character of DES components (0.14), while biodegradability has weight value of 0.1. Information about hazard and precautionary statements, vapor pressure are found to be less important with weight value equal 0.06. Then lower weights are considered for hazardous decomposition products (0.02), signal word (0.02), flash point (0.04), pH (0.04) and $\log K_{OW}$ (0.04). The toxicity criteria are assigned with the highest weights as they refer more to the greenness assessment than other criteria. Hazards and precautionary statements, signal wordings, decomposition products, flash point, pH and $\log K_{OW}$ are given low weights as they are characterized by lower variability and the criteria translated from descriptions can be treated as semi-quantitative information.

2.6. Sensitivity analysis

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

3. Results and discussion

3.1. Results of TOPSIS ranking of HBA

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

It is found that the best alternative is triethylene glycol (0.5883), which is nontoxic to all evaluated organisms. Moreover, it does not undergo bioaccumulation due to low value of log K_{OW} and it is easily biodegradable. This DES component is also described by small number of hazard and precautionary statements and in case of its decomposition there is no risk of arising hazardous products. Then for next 5 compounds the values of similarities to ideal solutions decrease from 0.18 to ~0.14. These compounds are mainly amino acids (betaine hydrochloride, betaine, histidine) and traditional organic solvents such as methanol and heptane. The high position of amino acids in the ranking is due to low toxicities towards at least two of organisms, high flash points, small values of log K_{OW} and ease of biodegradation. These two organic solvents are highly ranked because of low toxicity towards rats via ingestion and good biodegradability. Moreover, methanol is characterized by low value of $\log K_{OW}$ and is rather non-toxic towards other analyzed organisms.

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

3.2. Results of TOPSIS ranking of HBD

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

The first rank is mannitol (0.5743), which is characterized by very low toxicities towards all evaluated organisms. Moreover, this sugar is not bioaccumulative and does not decompose to form harmful products and is described only by very few hazard and precautionary statements and no signal wording. The second, the third and the fourth ranks are disaccharides: isomaltose (0.4024), maltose (0.4009), D-sucrose (0.3675) which are non-toxic to *Daphnia magna* and rodents via ingestion, highly biodegradable. Furthermore, they are characterized by high flash point, low value of $\log K_{OW}$.

After few alternatives with clearly higher values of similarities to ideal solution, there are betaine, m-aminobenzoic acid, serine, L-proline, citric acid and stearic acid with score values 0.11–0.23. These amino acids and are favorable due to low toxicity towards at least two of tested organisms, higher flash point, small value of $\log K_{OW}$ and average to high percentage of biodegradation. Organic acids also appear in this range and the reason for their high positions is high biodegradability and each of compound has low and average toxicity towards tested organisms.

Then, straight-chain alcohols (1,2-propanediol, 1,4-butanediol), sugar alcohols (glycerol, sorbitol), sugars (D-fructose, D-glucose) and their derivatives (glucosamine) are placed in the ranking. They are characterized by high to average toxicity endpoints at least for two organisms, low values of $\log K_{OW}$ and acceptable to high biodegradability level for almost all sugar-like HBDs. Between these compounds there are also traditional organic solvents as ethyl acetate, hexane or acetic acid, which are rather green solvents. Gradually, aminoacids appear, which begin the dominance of compounds containing an amino group as amino acids (e.g. alanine), amines (e.g. triethanolamine) and amides (e.g. urea). The majority of these chemicals have small values of $\log K_{OW}$, average level of toxicity, pH value close to neutral and are biodegradable. In the next part of the ranking organic acids occur (nicotinic, myristic, *L*-tartaric, succinic, itaconic), which are characterized by

Table 2
Results of TOPSIS analysis for HBA and comparison with traditional organic solvents and ionic liquids combined with sensitivity analysis for changes in range of ±10%.

No.	Substance name (HBA/organic solvent/IL)	CAS number	Similarity to ideal solution	Ranking difference for ±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	β-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

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-napthol	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

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-napthol	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

certain greenness issues, related to pH value, toxicity and hazards or precautionary statements.

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

3.3. Results of TOPSIS ranking of DES

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

The best alternative among selected set is citric acid:D-sucrose (1:3), followed by the citric acid:D-maltose (4:1) and glycerol:L-proline:D-sucrose (9:4:1). On the other hand, last three DES are represented by the iron(III) chloride hexahydrate:ethylene glycol (2:1), choline chloride:zinc chloride (1:1.2) and tetrabutylammonium bromide:formic acid (1:1). In general, places in the ranking for DES mixtures are similar to those obtained for separate analyses of HBA and HBD. For instance, citric acid as HBA and D-maltose as HBD have high positions, their mixture is also in the top. Tetrabutylammonium bromide and formic acid take lower positions in the rankings of HBA and HBD, then their mixture is also unsatisfactorily ranked. In case of DES with choline chloride as a HBA (choline chloride:1,2-propanediol, choline chloride:ethylene glycol, choline chloride:1,4-butanediol), the ranking positions decrease with changing ratios towards the growing presence of hydrogen bond donors in the compounds. Based on values of similarities to ideal solution of HBA and HBD, DES consisting of any combination of constituents, can be assessed in this way. Traditional organic solvents are found along the entire list of compounds with similar order as in case of

individual assessment of HBA and HBD. Location of DES next to solvents of rather green character (alcohols, esters or aliphatic hydrocarbons) indicates that DES are also not so problematic. On the other hand, ILs are in the second half of the list.

3.4. Results of sensitivity analysis and comprehensive ranking

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

3.5. Discussion - Comparison of obtained results

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

Similar results are presented by Halder et al. [27]in in silico modeling study of HDB toxicity. They divide evaluated chemicals into three groups, based on their toxicity level - low, intermediate and high. Their findings are marked in Table 3 with green (low toxicity), yellow

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

No.	Substance name (HBD/organic solvent/IL)	CAS number	Similarity to ideal solution	Ranking difference for ±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	tricarballylic 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	α-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

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	α-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

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

(moderate toxicity) and red (high toxicity) colors, respectively. The reason for some differences in comparison to this study may be fact, that Hadler's et al. assessment involves only toxicity criteria measured for different organisms (11 different mammalian cell lines - and 12 different microbial organisms) what results in poor coverage of this study assessment criteria. Hadler et al. also evaluate some HBA as preliminary studies, as they claim more experimental data is needed: choline chloride, menthol, N,N-diethylethanol ammonium chloride (DEAC), and methyltriphenyl phosphonium bromide (MTPB). MTPB and DEAC, are found to impart toxicity towards the most of the organisms, while N, N-diethylethanol ammonium chloride followed by choline chloride were found to be less toxic DES components. However, it is difficult to compare both results due to fact that our evaluation includes only choline chloride and MTPB. Nevertheless, ChCl and MTPB are ranked on 45th and 63rd place in the HBA list (out of 125 positions). The majority of evaluated HBA and HBD that are metalorganic compounds are ranked lower. The reason is that in our assessment toxicities are the most significant criteria and metal-containing DES are generally toxic to different organisms [28].

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

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

We also conduct evaluation of DES applications where authors claim their solvent is green and these results are summarized in Table S17.

Table 4
Results of environmental assessment for DES mixtures using toxicological model 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

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

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

All of the above-mentioned issues explain that it is not possible to unambiguously resolve the dispute, which of the solvents are more green - ILs or DES. DES properties depend on the specific case, criteria taken into evaluation, including tested organisms, etc. Therefore, the terms as non-toxic, biodegradable, environmentally friendly must be carefully used. Each of the mixtures should be tested and evaluated individually. Naming the solvent green because it belongs to DES group is an abuse. The interpretation of data gathered in Table S18 shows that only very few of authors claims about the greenness of the used DES mixture is presented without justification. This is a significant improvement in a reference to greenness evaluation of ionic liquids [20]. In case of DES solvents, more authors explain the use of the term “green” extensively, giving solid justifications.

4. Conclusions

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

Although the described approach provides general information about solvent greenness and allows for ease comparison of variety of solvents in terms of greenness performance, the proposed assessment procedure may be only treated as a screening tool for preliminary selection of a green alternative, due to simplified model of additivity that is used for DES mixtures calculations. More targeted evaluation for specific purpose is also possible, but need providing more newly obtained data (variety of properties and environmental fate of particular chemical) that may be easily incorporated into the performed algorithm.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.molliq.2020.114878.

Declaration of Competing Interest

There are no conflicts of interests to declare.

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