

Deep eutectic solvents vs ionic liquids: Similarities and differences

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Abstract

Deep eutectic solvents (DES) were introduced as an alternative to ionic liquids (IL) to overcome the drawbacks of IL solvents. However, some authors consider them to be a subclass of ILs. In contrast, other authors emphasize that these are by their nature independent, different groups of substances. Thus, the question arises: Which solvent group should DESs belong to? Maybe a new class should be added to the existing ones. The aim of this work is to attract the attention of researchers using DES in their studies to the need for a proper use of terms.

Keywords

Deep eutectic solvents; ionic liquids; analytical chemistry; solvents

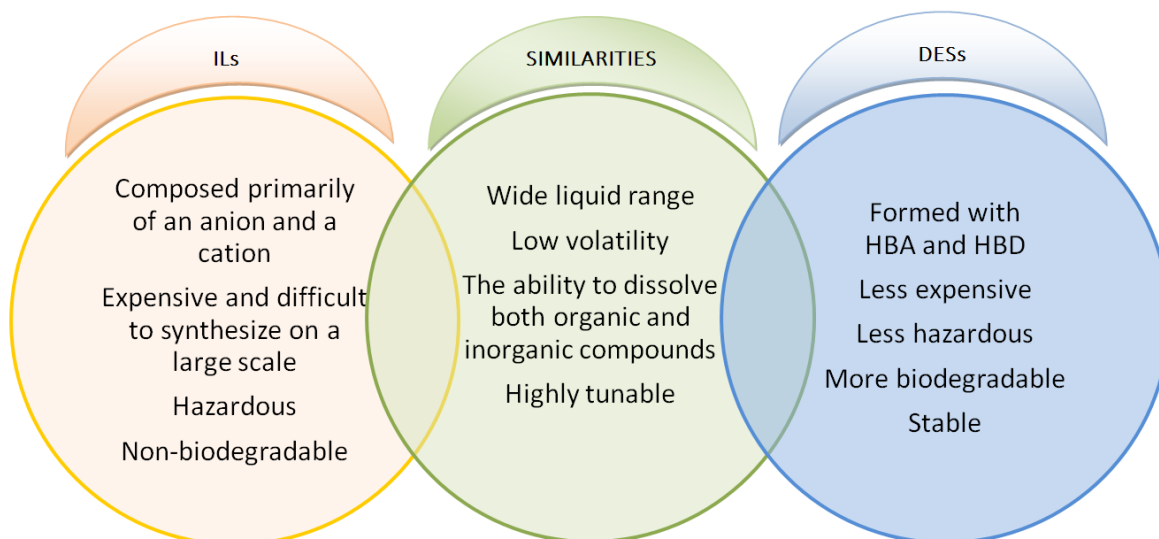
1 Introduction

At the beginning of our century, Abbott's group published a few papers that triggered research in the area we call today *Deep Eutectic Solvents* (DES) [1-3]. They examined the properties of these systems and also indicated the possibility of their use as solvents with interesting features. There are also other terms and denominations, **which may or may not denote** the substances we now consider to be DESs: Low Transition Temperature Mixtures (LTTM) [4], Low Melting Mixtures (LMM) [5] or Deep Eutectic Ionic Liquids (DEIL) [6]. When a DES is composed of components of natural origin, it is defined as a natural deep eutectic solvent (NADES) [7, 8].

35 On the other hand, *Ionic Liquids* (IL), which could be considered as the parents of DESs, were
36 reported for the first time by Paul Walden in 1914 [9]. At that time, no one knew that ILs would
37 become a very hot topic of chemistry one century later. Nowadays, some important fundamental
38 points of view are different from the original concepts, as insights into the nature of ILs have become
39 deeper. For instance, ILs were known to be non-volatile, non-flammable and stable on air and in
40 water, and were considered as green solvents. Recently, it is well known that many of them are, in
41 fact, volatile, flammable, unstable and even toxic. This situation is attributed to the large
42 combinations of cations and anions that meet the definition of ILs, leading to an adverse suite of
43 behaviors. As the chemical variety of ILs has grown, they have been further divided into many types.
44 Worth mentioning are: task-specific ILs (TSILs) [10], room-temperature ILs (RTILs) [11] and polyionic
45 liquids (PILs) [12]. Very recently Singh and Savoy summarized the literature on the structural
46 classification of ILs, their synthesis pathways and the potential applications [13].

47 DESs were introduced as an alternative to ILs to overcome the drawbacks of ILs. Some
48 authors consider them to be a subclass of ILs, and sometimes they consider these terms
49 interchangeable. On the other hand, other authors emphasize that despite the many similarities (See
50 Figure 1), they are by their nature independent, different groups of substances [14, 15]. Thus, the
51 question arises: Which solvent group should DESs belong to? The aim of this work is to attract the
52 attention of researchers using DES in their studies to the need for a proper use of terms. Although ILs
53 and DESs have a lot in common, especially when it comes to physical properties as well as
54 applications, from the chemical point of view, these are two separate groups of substances.
55 Therefore, it is still necessary to understand the specific chemical nature of DES systems in order to
56 prevent a mechanistic understanding of how these systems work. In our opinion there are many
57 more differences than similarities. In considering the differences between these two type of solvents,
58 the chemical formation process as well as the source of their starting materials need to be
59 mentioned [16].

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62 **Figure 1.** Similarities and differences of ILs and DESs

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64 **2 Starting materials and mechanism of synthesis**

65 DESs differ from ILs in two basic ways, namely the nature of the starting materials and the methods
 66 of their formation. ILs are a combination of organic heterocyclic cations and organic or inorganic
 67 anions (Figure 2), while DESs are a combination of various hydrogen bond acceptors (HBAs) (Figure 3)
 68 and hydrogen bond donors (HBDs) (Figure 4). The number of potential mixtures is virtually unlimited
 69 for both ILs and DESs [17]. With such a large number of suitable starting materials as well as their
 70 possible combinations, they have both advantages and disadvantages which allow the properties of
 71 these substances to be changed to meet the requirements of specific application (which is precisely
 72 why both ILs and DESs have found wide use in various fields of science, research and technology).
 73 The huge advantage of DESs, however, is that they are made of generally nontoxic, easily accessible,
 74 cheap and sustainable compounds. Furthermore, common components of DESs are naturally
 75 occurring biocompatible compounds that are not hazardous if they are released back into nature
 76 [18]. It is also important to note that the components of DESs, unlike ILs, must not react with each
 77 other; therefore, it is necessary to avoid combinations of such compounds where this is possible.

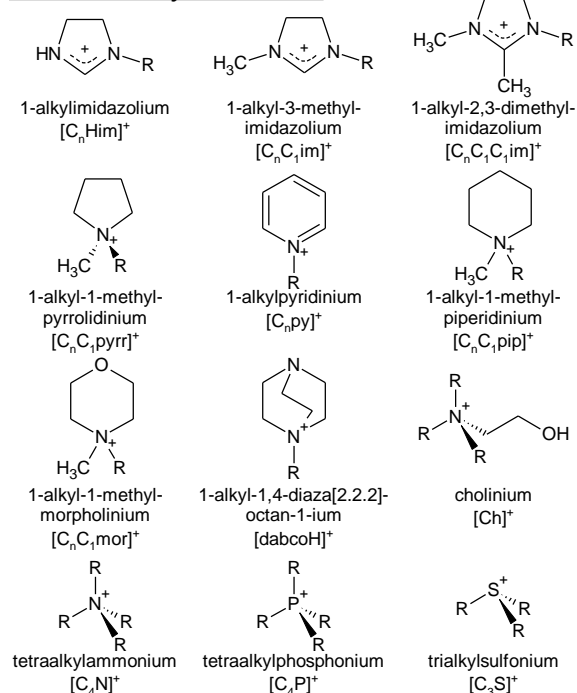
78 The synthesis of ILs often involves several synthetic steps using various reagents, organic
 79 volatile solvents; in addition, by-products and waste are generated. Generally, the reaction time is
 80 long (up to 48 h) with the temperature varying from 25 to 100 °C. The synthesis of ILs (Figure 5)
 81 consists of two main steps: (i) cation formation (by protonation of the amine by an acid or
 82 quaternization reaction of the amine with a haloalkane) and (ii) anion exchange (by treatment of
 83 halide salt with a Lewis acid or by anion metathesis) [19]. In contrast, DESs can be simply prepared by
 84 heating or the grinding method (Figure 6). The heating method is the most used; the compounds are
 85 mixed and heated at temperatures between 50 °C to 100 °C under constant stirring for times

spanning from minutes to hours until a homogeneous liquid forms. The grinding method is based on mixing the compounds at room temperature and grinding them in a mortar with a pestle. A liquid formed by the heating or grinding method is obtained with a yield of 100% and with an atom economy of 100% [20]. Another method – freeze-drying (Figure 2) – is also known, but it is a bit more complicated. The separated aqueous solutions of components are mixed together, frozen and freeze-dried to form a clear viscous liquid [21]. From the above stated, it is clear that ILs and DESs differ not only in the nature of the components, but also in the methods of their formation.

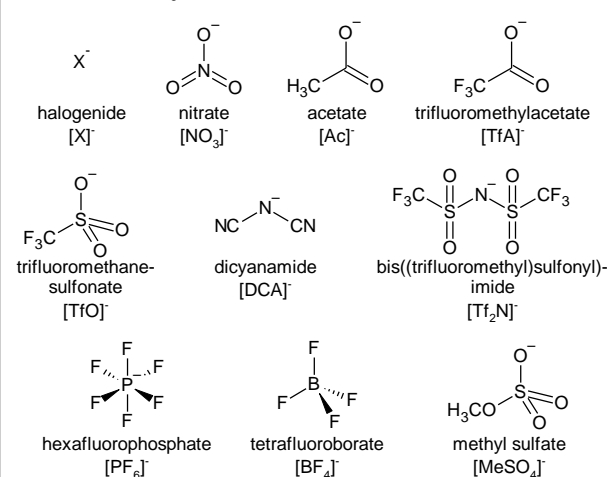
The synthesis of ILs is, in general, more costly and difficult than the preparation of DESs. The production of DESs is relatively straightforward and inexpensive and does not pose any significant post purification or disposal problems.

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Some commonly used cations



Some commonly used anions



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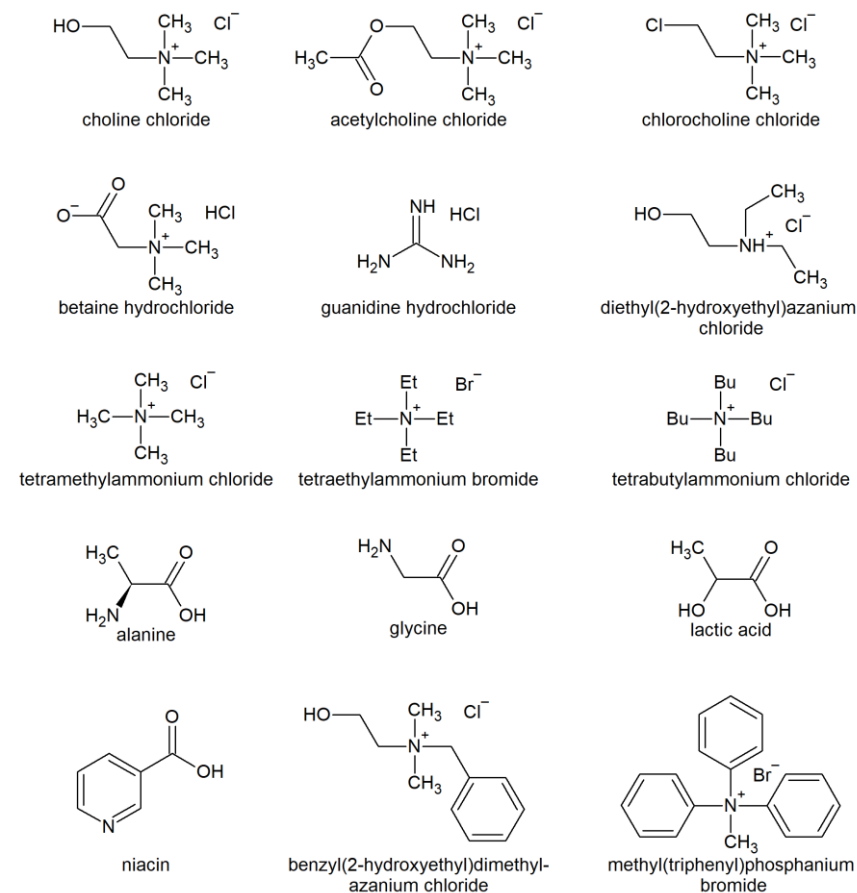
99 **Figure 2.** Selected cations and anions used for the synthesis of ILs

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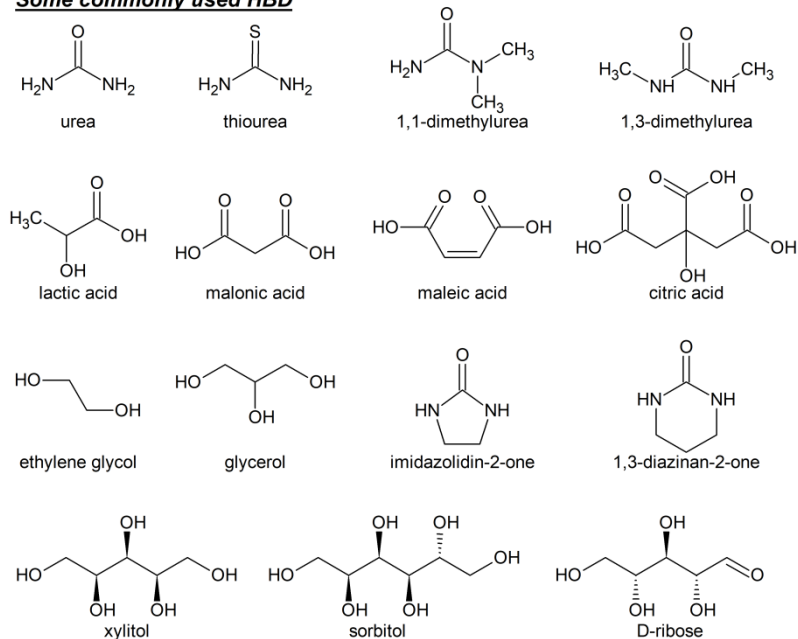
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Some commonly used HBA

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105 **Figure 3.** Selected HBAs for the synthesis of DESs

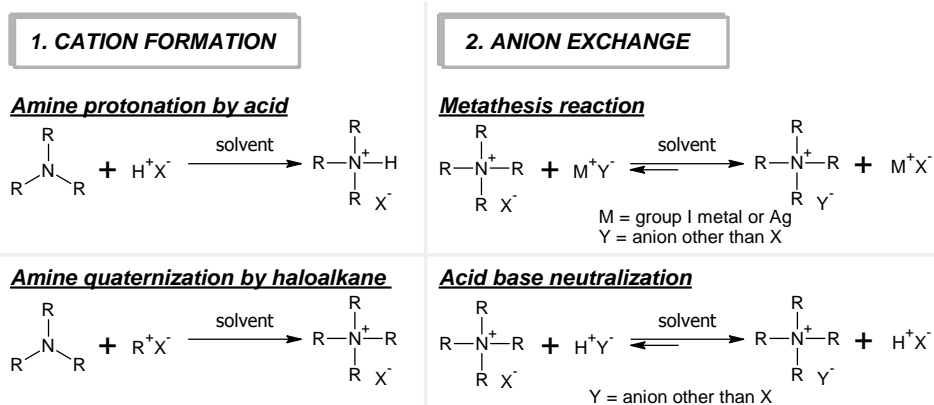
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Some commonly used HBD

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109 **Figure 4.** Selected HBDs for the synthesis of DESs

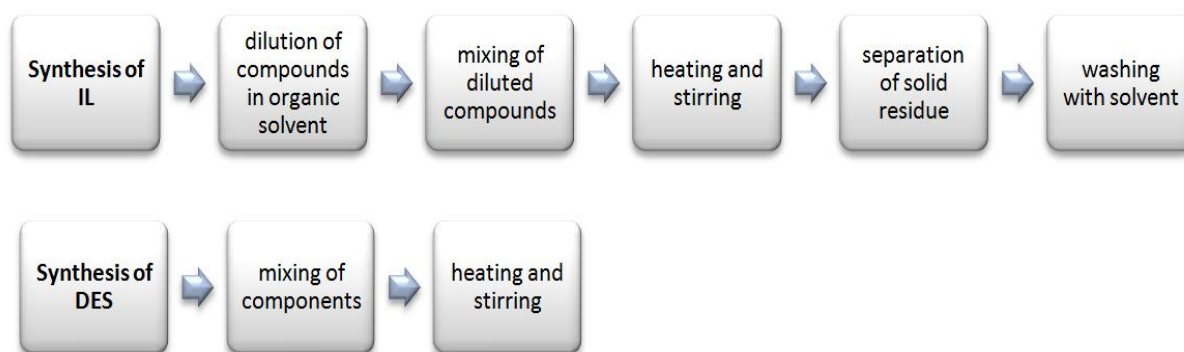


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111 **Figure 5.** The main methods of preparing ILs

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116 **Figure 6.** A comparison of the main synthesis processes of ILs and DESs.

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119 **3 Properties**

120 The structure and properties of ILs as well as DESs are determined by intermolecular interactions:
 121 Coulomb forces, hydrogen bonding and dispersion forces. By definition, the behavior of ILs is
 122 dominated by ionic interactions (Coulomb forces), whereas DESs, as eutectic mixtures of two or more
 123 distinct components, exhibit a strong contribution from hydrogen bonding [22]. Although ILs and
 124 DESs differ in the nature of their constituents and the type of dominant intermolecular forces, they
 125 share many interesting properties, which can be adjusted by selecting the nature and ratio of the
 126 constituents.

127 However, due to the large number of possible ILs and DESs resulting from the large number of
 128 possible combinations of starting substances, it is very difficult to unambiguously characterize and
 129 generalize their physical properties. We can only define some general rules and conclusions. Both ILs
 130 and DESs have low melting points. ILs melt below 100 °C, while the melting temperature of DES is far

131 below that of either individual component. The density and viscosity of these solvents also have
132 similar values and are strongly dependent on their composition and temperature. Therefore, the
133 selection of IL and DES constituents is essential, since high viscosity and density are the main
134 drawbacks for the practical use of these solvents [23-25]. Although the viscosity problem can be
135 solved quickly and easily in the case of DESs by using water as an additional component, a large
136 excess of water can in some cases lead to the complete decomposition of the DES [26]. In general, ILs
137 and DESs present high polarity. This is a great advantage of both solvents, because they can solubilize
138 a wide range of organic and bioactive substances. On considering other similarities between DESs
139 and ILs, it could be highlighted that both systems concern a low vapor pressure and wide liquid
140 range. Moreover, they are highly tunable.

141 As we can see, the physical properties of ILs and DESs are close to each other, and what is even
142 more important, thanks to the large number of possible combinations of starting materials, they are
143 also highly tunable depending on the requirements for specific use. On the other hand, this makes it
144 impossible to generalize about their chemical properties, such as toxicity, stability, biodegradability,
145 flammability, greenness, etc. From an environmental perspective, DESs are superior to ILs due to
146 their higher biodegradability and lower toxicity. The natural origin of the constituents gives DESs a
147 great edge over ILs, because they are clearly less toxic and more environmentally friendly. Whereas
148 IL components are onium salts, which show high toxicity [27]. Beside toxicology, biodegradability and
149 recyclability factors, there are several other assessments that influence the green-chemistry quality
150 of ILs: the long reaction time at high temperatures, the use of volatile and non-renewable solvents,
151 the large quantities of chemicals, large quantity of by-products as waste, and high stability in water
152 (ILs become persistent pollutants in wastewaters). Moreover, their different chemical properties
153 encourage application areas which are significantly more varied (for example many enzymes exhibit
154 both high activity and unexpected promising stability in DESs [28]).

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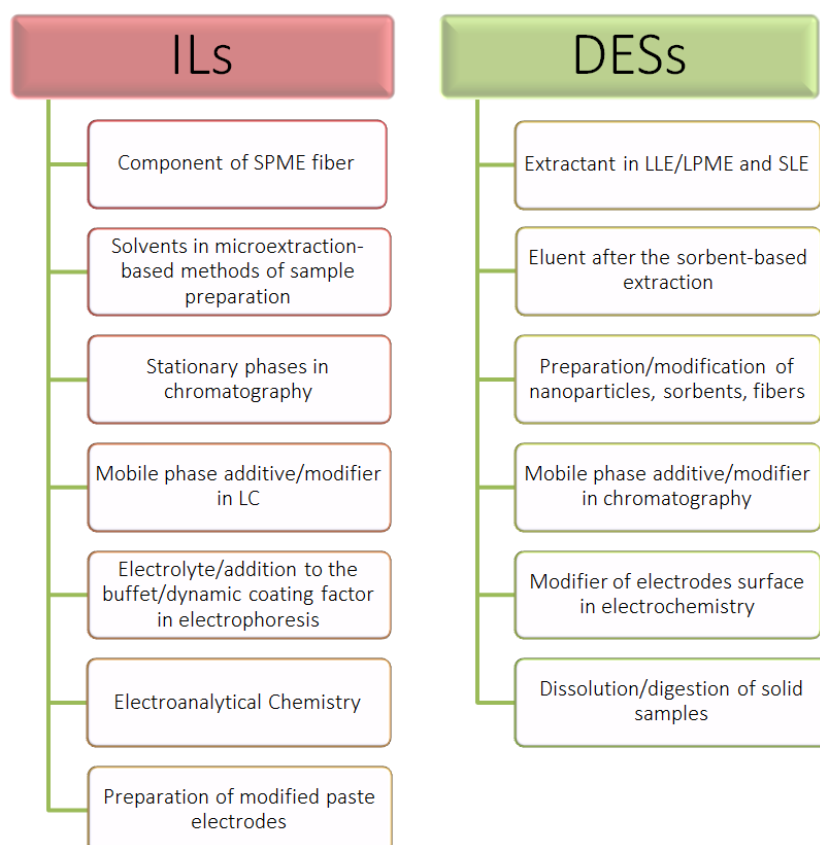
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157 **4 Applications in analytical chemistry**

158 Without a doubt, DESs and ILs share many interesting properties [20] which allow them to be applied
159 in many fields of analytical chemistry (Figure 7) [29, 30]. These solvents are used in analytical
160 chemistry mainly at the sample preparation stage for solvent-based and sorption-based extraction of
161 target analytes from aqueous or solid samples, as stationary phase modifiers in GC, and also as
162 mobile phase additives in LC, but in the case of DESs also for the dissolution or digestion of solid
163 samples.

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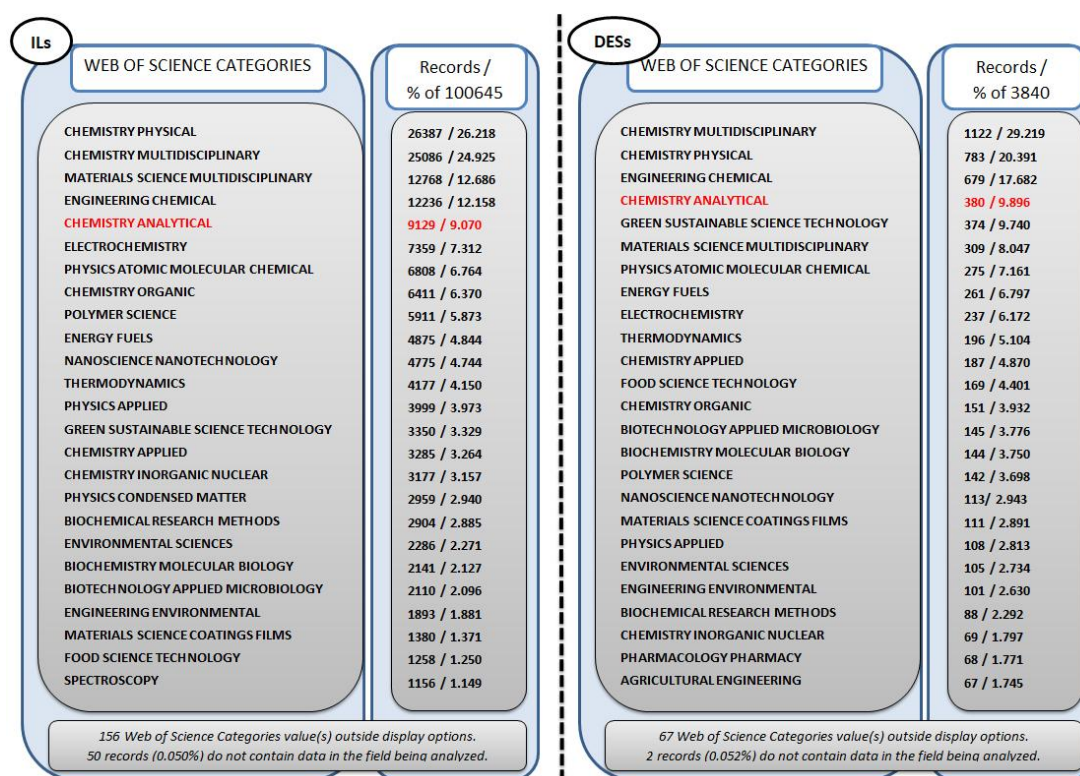
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166 Figure 7. Application of ILs and DESs in the analytical chemistry

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168 Despite the fact that the application areas of DESs are very close to those of ILs [13], the
 169 number of publications devoted to ILs is more than one order of magnitude higher than for DESs
 170 (Figure 8) especially concerning their use in analytical chemistry. This is probably because IL
 171 compounds were introduced into analytical science several years before the introduction of DESs.
 172 However, if we do not compare the absolute number of published papers in each category but their
 173 percentage distribution, the order of the categories for both solvents becomes very close. The
 174 category “chemistry analytical” is in the highest positions for both solvents. However, for example,
 175 the category of “green sustainable science technology” is much higher for DES than for IL.

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179 **Figure 8.** Schematic representation of the type of chemistry categories versus percentage number of
 180 publications for ILs and DESs (*performed by application of Web of Science with permission. Keywords:*
 181 *Ionic Liquid, Deep Eutectic Solvent*).

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184 4. Advantages and drawbacks

185 ILs and DESs were found to be greener options when compared to conventional solvents. In
 186 comparison to ILs, the advantages of DESs concern their easy synthesis by simply mixing the
 187 components with gentle heating. In addition, no future purification is required, in contrast to ILs.
 188 Additionally, the cost of production is low due to the low prices of synthetic raw materials.
 189 Unfortunately, their high viscosity and solid state at room temperature could be detrimental.
 190 However, the physicochemical properties of DESs can be tailored by the selection of proper HBA and
 191 HBD and their molar ratio or the addition of water.

192 Although authors often report that most of these solvents, both ILs and DESs, are non-toxic,
 193 biocompatible and biodegradable, others state that more investigation is required on this matter,
 194 since the toxicity and cytotoxicity of DESs vary depending on the components. Therefore, cautious
 195 handling of the terms *non-toxicity* and *biodegradability* must be considered [31]. However, despite
 196 everything, DESs are believed to be more effective and environmentally friendly solvents than ILs.

197 While ILs are well understood, there are still some aspects that need further studies. In the
198 case of DESs, studies are still limited and many unknowns exist. This is why there is a continuous
199 need for research in this area. On the other hand, the potential of the solvents described herein
200 opens interesting perspectives for further research in analytical chemistry as well as in industrial
201 applications.

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204 **Conclusions**

205 The aim of this work is to attract the attention of researchers using DES in their studies to the need
206 for a proper use of terms. Although ILs and DESs have a lot in common, especially when it comes to
207 physical properties and applications, from a chemical point of view, these are two separate groups of
208 substances. However, from our point of view, it is important to focus on the mechanisms of DESs and
209 ILs formation, as this could explain a lot of unknowns, e.g. their differences. It also would help to look
210 for new applications in many fields of chemistry and, especially in analytical chemistry, while at the
211 same time, correctly evaluating the greenness of these new solvent systems. Considering DESs as a
212 subtype of ILs will lead to the forming of confused criteria for the selection of the applications in
213 which they can be employed to enhance analytical perspectives.

214 In addition to analytical chemistry, we can expect new applications of DESs in pharmacy,
215 medicine, cosmetics, food science and, very importantly, new knowledge in the field of theoretical
216 study of DESs concerning their composition and extraction mechanism as well.

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