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Chapter

Fluorinated Ionic Liquids as Task-Specific Materials: An Overview of Current Research

Nicole S.M. Vieira, Margarida L. Ferreira, Paulo J. Castro, João M.M. Araújo and Ana B. Pereiro

Abstract

This chapter is focused on the massive potential and increasing interest on Fluorinated Ionic Liquids (FILs) as task-specific materials. FILs are a specific family of ionic liquids, with fluorine tags equal or longer than four carbon atoms, that share and improve the properties of both traditional ionic liquids and perfluoro surfactants. These compounds have unique properties such as three nanosegregated domains, a great surfactant power, chemical/biological inertness, easy recovery and recyclability, low surface tension, extreme surface activity, high gas solubility, negligible vapour pressure, null flammability, and high thermal stability. These properties allied to the countless possible combinations between cations and anions allow the design and development of FILs with remarkable properties to be used in specific applications. In this review, we highlight not only the unique thermophysical, surfactant and toxicological properties of these fluorinated compounds, but also their application as task-specific materials in many fields of interest, including biomedical applications, as artificial gas carries and drug delivery systems, as well as solvents for separations in engineering processes.

Keywords: fluorinated ionic liquids, task-specific materials, artificial gas carriers, drug delivery systems, separation processes

1. Introduction

Perfluorocarbons (PFCs) consists of a large group of man-made chemicals available worldwide in many different fields since the 1940's [1]. The numerous applications of PFCs in different areas relies on their distinctive physical and chemical characteristics (water and oil repellence, thermal and chemical stability, surfactant behaviour, low polarity, weak intermolecular interactions, and reduced surface tension), [1–3] highly fomented by the fluor-carbon moiety [1–3]. These compounds are widespread in consumers life through plastics, fire retardants, dyes, surfactants, polymers, and pharmaceuticals, among others [1–6]. Benign PFCs have been used in the development of biomedical applications, such as emulsions, [7, 8] imaging agents, [9, 10] biocompatible lubricants, [11] oxygen therapeutics, [12] pulmonary delivery agents, [13] and theranostic agents [14]. On the other hand, perfluoroalkyl acids (PFAs) and fluorinated greenhouse gases (F-gases) belong to a class of persistent chemicals, widely used in industrial and commercial products [1, 2, 5, 6]. Due to

their high global warming potential (GWP), long atmospheric lifetime, persistency, and mobility, these compounds have been found in several contaminated sites, [2, 15] including water, soils, biota and food [16–18]. Major concerns about their toxicity and bioaccumulation limit their use and encourages their replacement [1, 2, 5].

In the last decades ionic liquids (ILs) have emerged as new engineering solvents. The application of these compounds has aroused in many different subjects, including catalysis, electrochemistry, extraction and separation processes, pharmaceutical and biomedical applications [19–25]. This massive use of ILs is supported by their unique thermophysical properties and limitlessness combinations between anions and cations [19, 26, 27]. Their title of "green solvents" is corroborated by an almost negligible vapour pressure at room temperature and reduced flammability [19, 26]. Additionally, the increased research about the cytotoxicity and environmental toxicity of these compounds reinforces that their possible harmful behaviour is dependent on the cation-anion tested combination [28]. Due to their complexity and variety, ILs have been categorized in several families according either to their properties or to their applications [29].

This chapter is focused on the use of a less explored ILs family, the fluorinated ionic liquids (FILs), defined as ILs with fluorine tags equal or longer than four carbon atoms [30–33]. The fluorinated tags can create one nanosegregated domain distinct from polar and apolar (hydrogenated) [32, 33]. FILs combine the exceptional properties of conventional ILs (high thermal stability, negligible vapour pressure, reduced flammability, and greener potential) with the greatest properties of traditional PFCs (chemical and biological inertness, reduced surface tension and increased surfactant behaviour). In contrast to the low solubility and toxicity intrinsic to many highly fluorinated compounds, some novel FILs have been designed with completely water miscibility [34, 35] and negligible toxicity, [30, 36, 37] furthering its use in more green engineering processes and biomedical applications. In spite of these outstanding properties, scarce information is available in literature and research is mainly focused on their synthesis and characterization, [38] electrochemical properties, [39] gas solubilities [40] and application as reaction media [38, 41].

This chapter covers the main assets of these FILs, namely their thermophysical and structural properties, aggregation and surfactant behaviour, cytotoxicity, acute ecotoxicity and biodegradation. Additionally, a more detailed approach throughout the application of FILs as task-specific materials in several areas comprise the analysis of a series of works. It is evidenced the progress of FILs either in biomedical applications, or in engineering separation processes.

2. Properties of fluorinated ionic liquids

The characterization of FILs properties and the influence of the different cation/anion combinations on these properties is still critical to head these specific materials to the potential applications. FILs have enhanced properties due to the nanosegregated structuring into three different domains, one polar and two apolar (hydrogenated and fluorinated), making them an alternative solvent with new improved mechanisms of solubilization of different compounds (see **Figure 1**) [31–33]. The manipulation of the nanosegregation behaviour and intra- and intermolecular interactions of FILs allows the control of thermal and thermophysical properties, toxicity, solubility capacity or hydrophobicity of FILs.

In this section, it is emphasized how the formation of the new fluorinated domain and the structural features influence the properties of FILs. The properties

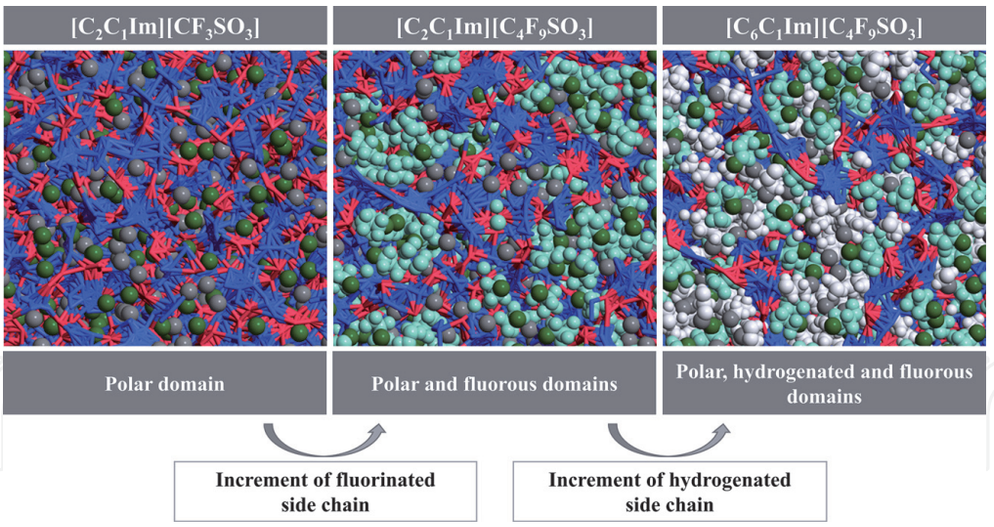


Figure 1.
Formation of three nanosegregated domains of $[C_2C_1Im][CF_3SO_3]$, $[C_2C_1Im][C_4F_9SO_3]$ and $[C_6C_1Im][C_4F_9SO_3]$ FILs. The red and blue sticks represent negative and positive charges, indicating the segregated polar network in the three ILs. The green space-filled areas represent the fluorinated domains. The grey space-filled areas indicate the hydrogenated moieties segregated. Adapted from [42].

of FILs, such as melting point, thermal stability, density, viscosity, refractive index, ionic conductivity and surface tension [30, 33, 42–50] are discussed along with the FILs self-aggregation behaviour in aqueous solutions [34, 35, 50–52]. A close sight on the biocompatibility of FILs by examining their toxicological and biodegradability properties is also included for discussion [30, 36, 37].

2.1 Thermophysical properties

2.1.1 Phase behaviour and thermal properties

The phase behaviour of pure FILs is determined by the melting, solid–solid and glass transitions while the thermal stability is defined by the decomposition temperature. These properties are determinant to define the liquid range of application, allowing a wisely choice of a fluid to a specific task. Several works include the thermal characterization of the FILs depicted in **Table 1** [30, 33, 42–47, 50]. In the case of FILs where the formation of three domains occurs, due to long enough hydrogenated (up to 6 carbons) and fluorinated (up to 4 carbons) chains (**Figure 1**), a rich phase behaviour is found, with a high number of solid–solid transitions. This indicates the ability of FILs domains to rearrange into different structures until the complete melting, proving the high influence of the nanosegregation [33, 46].

The different structural features of FILs can impact the melting and decomposition temperatures, and much work has been done to find trends to design FILs with tuned thermal properties [30, 42, 45, 47, 50]. The melting and decomposition temperatures of several FILs can be found in the **Table 2**. In the case of $[C_nC_1Im][C_4F_9SO_3]$ FILs family, it was found that the increment of the cationic hydrogenated chain increases the melting temperature and decreases the decomposition temperature [42, 47]. The increase of the anionic fluorinated chain also rises the melting point. However, the thermal stability is maintained constant at a considerable high temperature [42, 47]. Moreover, FILs based on $[C_nF_{2n+1}SO_3]^-$ anions have a much higher thermal stability than ILs conjugated with $[C_nF_{2n+1}CO_2]^-$ anions [42, 45, 50]. The type of cation and its functionalization also has a great

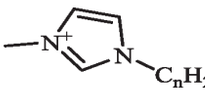
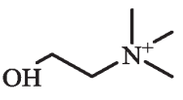
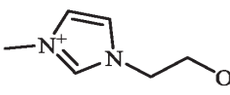
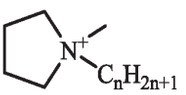
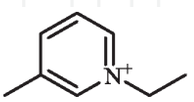
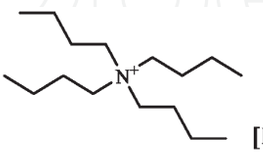
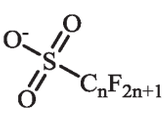
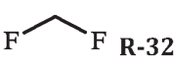
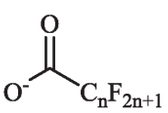
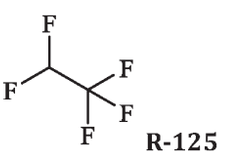
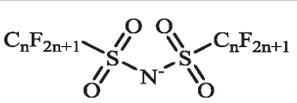
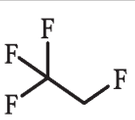
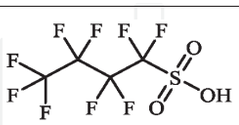
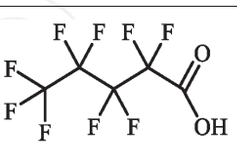
Cations structure	
 $[C_nC_1Im]^+$ n = 2, 4, 6, 8, 10 and 12 1-Alkyl-3-methylimidazolium	 $[N_{1112(OH)}]^+$ (2-Hydroxyethyl)trimethylammonium
 $[C_{2(OH)}C_1Im]^+$ 1-(2-Hydroxyethyl)-3-methylimidazolium	 $[C_nC_1pyr]^+$ n = 2 and 4 1-Alkyl-1-methylpyrrolidinium
 $[C_2C_1py]^+$ 1-Ethyl-3-methylpyridinium	 $[N_{4444}]^+$ Tetrabutylammonium
Anions structure	**F-gases**
 $[C_nF_{2n+1}SO_3]^-$ n = 1, 4 and 8 Perfluoroalkyl sulfonate	 **R-32** Difluoromethane
 $[C_nF_{2n+1}CO_2]^-$ n = 4 and 8 Perfluoroalkyl carboxylate	 **R-125** Pentafluoroethane
 $[N(C_nF_{2n+1}SO_2)_2]^-$, n = 1 and 4 Bis(perfluoroalkylsulfonyl)imide	 **R-134a** 1,1,1,2-Tetrafluoroethane
Perfluorinated acids	
 $[C_4F_9SO_3H]$ Nonafluoro-1-butanesulfonic acid	 $[C_4F_9CO_2H]$ n-Perfluoropentanoic acid

Table 1.
Structure and nomenclature of the ions constituting the FILs and of the F-gases studied for absorption in FILs and in deep eutectic solvents, prepared with the illustrated perfluorinated acids.

influence in both thermal properties, and a carefully analysis must be performed when choosing a FIL for a specific ending [30, 33, 42, 45, 46, 50].

The FILs based on long fluorinated chains (e. g. $[N(C_4F_9SO_2)_2]^-$) have a very high melting temperature, automatically reducing the liquid operating range. Eutectic mixtures of FILs can be the solution to solve this handicap. The evaluation of the solid–liquid phase behaviour of binary mixtures of FILs showed a high decline of the melting temperature to values close or below room temperature [44]. This does not only increase the liquid range of FILs, but also expands the tuneability of neat FILs.

	T_m K	T_{onset} K	ρ g·cm^{-3}	η m·Pas^{-1}	γ mN·m^{-1}
			$[C_nC_1Im][C_4F_9SO_3]$		
n = 2	293 [42]	627 [42]	1.547 [42]	163.0 [42]	25.14 [43]*
n = 4	286 [47]	638 [47]	1.460 [47]	307.3 [47]	22.83 [43]*
n = 6	297 [30]	627 [30]	1.392 [30]	401.7 [30]	21.36 [43]*
n = 8	308 [30]	621 [30]	1.338 [30]	374.6 [30]	20.57 [43]*
n = 10	307 [47]	627 [47]	1.310 [47]	597.1 [47]	22.05 [43]*
n = 12	311 [42]*	617 [42]*	1.247 [42]*	280.9 [42]*	23.42 [43]*
			$[C_4F_9SO_3]^-$		
$[C_2C_1py]^+$	278 [30]	629 [30]	1.515 [30]	201.8 [30]	26.35 [45]
$[N_{4444}]^+$	327 [30]	587 [30]	1.234 [30]	15319 [30]	22.77 [45]**
$[C_4C_1pyr]^+$	364 [46]	632 [46]			
$[N_{1112(OH)}]^+$	436 [45]	609 [45]			
$[C_{2(OH)}C_1Im]^+$	251 [50]	559 [50]	1.620 [50]	831.6 [50]	
			$[C_4F_9CO_2]^-$		
$[C_2C_1Im]^+$	278 [42]	392 [42]	1.487 [42]	107.5 [42]	
$[C_8C_1Im]^+$	297 [42]	399 [42]	1.292 [42]	307.9 [42]	
$[C_{2(OH)}C_1Im]^+$	295 [50]	433 [50]	1.541 [50]	712.8 [50]	
$[C_2C_1py]^+$	275 [45]	392 [45]	1.454 [45]	147.1 [45]	26.83 [45]
			$[C_8F_{17}SO_3]^-$		
$[N_{4444}]^+$	255 [30]	385 [30]	1.317 [30]	6690 [30]	21.98 [45]
$[C_2C_1Im]^+$	368 [42]	616 [42]			
			$[N(C_4F_9SO_2)_2]^-$		
$[C_2C_1pyr]^+$	428 [45]	619 [45]			
$[C_4C_1pyr]^+$	371 [45]	639 [45]			
$[N_{1112(OH)}]^+$	303 [45]*	622 [45]*	1.674 [45]*	947.1 [45]*	25.04 [45]*

*Experimental data obtained * at 313.15 K and ** at 333.15 K.*

Table 2.
Thermophysical and thermodynamic properties of fluorinated ionic liquids at 298.15 K and atmospheric pressure: melting temperature, T_m; decomposition temperature, T_{onset}; density, ρ; viscosity, η; and surface tension, γ.

2.1.2 Density, transport properties, free volume, and surface tension

Density, transport, free volume, and surface tension properties have high relevance in the biomedical field as well as in the separation and extraction processes for industrial proposes [30, 53]. The structural features of FILs can determine their density, [30, 42, 45, 47, 50] as can be seen in **Table 2**. While the increment of the fluorinated chains increases FILs density, [30, 42, 45] the opposite behaviour is found for the increment of hydrogenated side chain [30, 42, 45, 47]. The

carboxylate anions show a lower density comparing with the sulfonate anions [30, 45, 50]. The functionalization of imidazolium cation with a hydroxyl group has shown an increment on density [50]. The cation nature widely affects the density, and each family must be analysed case by case to infer on the applicability of each FIL [30, 42, 45].

The characterization of FILs viscosity, and consequently of their fluidity, was studied in several works, [30, 42, 45, 47, 50] and some of the results can be found in **Table 2**. The results indicate that FILs with longer aliphatic and fluorinated chains increase the viscosity [30, 42, 45, 47]. The FILs composed by $[C_nF_{2n+1}SO_3]^-$ anions also present high viscosity comparing with the $[C_nF_{2n+1}CO_2]^-$ anions [30, 42, 45]. The nature of the FIL cation affects tremendously the viscosity. In the case of bulkier cations, a lower fluidity is found [30, 42, 45]. The addition of a hydroxyl group in imidazolium cations increases the cohesive forces resulting in more viscous fluids [50].

The ionic conductivity has great importance, especially when correlating the molar conductivity with the fluidity obtaining the ionicity of FILs [30, 42]. The ionicity is evaluated by the Walden plot where FILs are classified depending on the distance to an ideal electrolyte [54]. From the ionicity can result information on the formation of aggregates between ions due to low mobility [54]. The analysis of the results shows that the increment of the cationic aliphatic and of the anionic fluorinated chains decrease the ionicity, diverging from the ideal behaviour [30, 42, 45, 47].

The free volume has a high relevance to FILs suitability as enhanced solvents of gases or other compounds with low molecular weight [55]. The relation between refractive index and density allows the calculation of molar free volume effects, evaluating the available space for dissolution of gases [30, 42, 45, 47, 50]. Therefore, the increase of both hydrogenated and fluorinated chain and bulkier cations rise the molar free volume values [30, 42, 45, 47, 50].

The surface tension of FILs is the property that most differs from the conventional ILs, in which the cation's nature has a predominant influence on this property [43, 45, 56]. The values of surface tension for some FILs can be found in **Table 2**. The surface tension of $[C_nC_1Im][C_4F_9SO_3]$ family showed the lowest values existing in the overall ILs literature [43]. The increment of the hydrogenated chain decreases the surface tension up to the lowest value, found for the $[C_8C_1Im][C_4F_9SO_3]$. The further increase of FILs aliphatic chain resulted in higher values of surface tension, revealing a global behaviour marked by a bowl-shaped trend [43]. The addition of a fluorinated domain in FILs induces a competition with the aliphatic domain to protrude the interface, which dramatically changes the values of surface tension [43]. As long as the hydrogenated chain increases to $[C_8C_1Im]^+$, a rearrangement in the organization between the non-polar domains happens, allowing both to protrude through the top layer. After $[C_8C_1Im]^+$, the aliphatic chain is much larger than the fluorinated chain, and occupies more space at the interface, increasing the values of surface tension [43]. In the case of quaternary ammonium-based FILs it was shown that they have lower values of surface tension comparing with pyridinium cation. In FILs based on ammonium, the increment of the fluorinated chain deeply decreases the surface tension [45].

The FILs properties can be tuned by choosing the cation, anion, length of side chains and functionalization of cation, increasing the possibilities of designing the best task-material. The complete determination of these properties is a complex assignment, requiring a lot of costs and time. To ease this task, theoretical models can be applied to predict their characteristics. An effort has been done in this direction obtaining several models that accurately reproduces the FILs properties of the neat FILs and of the mixtures with gases and aqueous solutions [47–50].

2.2 Aggregation and surfactant behaviour

The behaviour of FILs in aqueous solutions is enhanced in comparison with the PFCs and conventional ILs [34, 35, 50–52]. The selection of nontoxic FILs based on imidazolium, pyridinium (with short aliphatic chains) and cholinium cations conjugated with the $[C_4F_9SO_3]^-$ anion were used to study the self-aggregation behaviour. These compounds are completely miscible in water at all range of concentrations studied in the conductivity profile [34]. The same behaviour was later found for imidazolium-FILs functionalised with a hydroxyl group [50] and some examples are represented in **Figure 2a**. The Liquid + Liquid equilibria of binary systems FIL + water was also analysed to study the solubility of water [35, 52]. The increment of the aliphatic chain in $[C_nC_1Im][C_4F_9SO_3]$ family increases the solubility of water in the FIL-rich phase [35, 52].

The water-rich region was selected to determine the critical aggregation concentrations (CACs) of several FILs [34, 35, 50, 52]. $[C_2C_1Im][C_4F_9SO_3]$ showed three different transitions related to the formation of distinct aggregates. These aggregates were evaluated and associated to different self-assembled structures [34]. These stable self-assembled structures can be the greatest contribution to the full miscibility of FILs in water. **Figure 2b** represents the values of the first CAC, so-called critical micelle concentration (CMC) of FILs [34, 35, 50, 52] and conventional surfactants [57–59]. All the FILs show much lower CMC and FILs with only four carbon atoms have greater aggregation power than the conventional surfactants with eight carbon atoms. The increment of the hydrogenated chain in the $[C_nC_1Im][C_4F_9SO_3]$ family decreases the CMC value, promoting the formation of more, bulkier and better packed structures [35, 52]. The longer fluorinated chains also decrease the CMC values. However, the growth of both nonpolar chains hinders the solubility in water [34, 35, 52]. The pyridinium and tetrabutylammonium cations show slightly lower CMC values comparing with imidazolium, cholinium or pyrrolidinium cations [19, 20, 22].

The FILs behaviour in water was also inferred in the FIL-rich phase by investigating the hydrogen-bonding ability and polarizability through Kamlet-Taft parameters [51]. The results indicate that increasing the fluorinated chain restricts the impact of adding water into ILs, keeping the hydrogen bond acceptance ability constant. This result indicates that the rich aggregation of FILs promotes the aggregation of water in a bulky polar network. The water aggregates expand and drive to the proximity of the polar nanosegregated domains of the FILs due to the higher repulsion of the fluorinated counterparts [51].

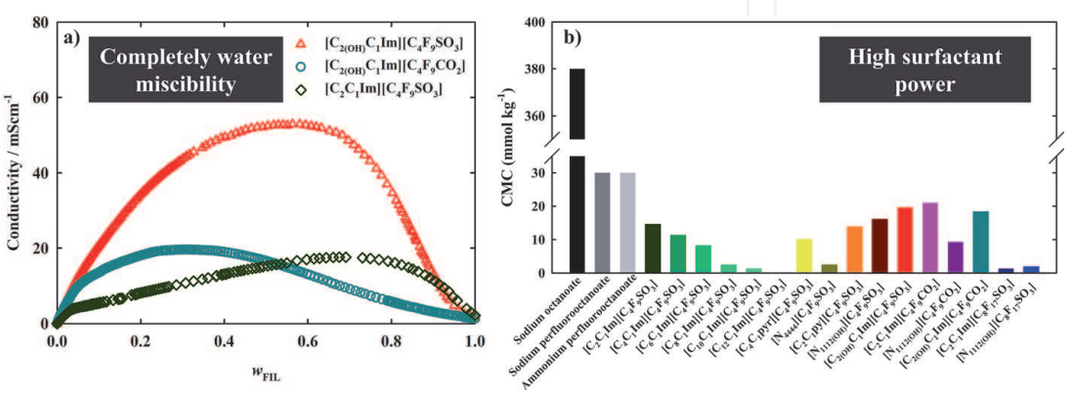


Figure 2.
(a) Complete conductivity profile of FILs in water at 298.15 K and (b) the values of critical micellar concentrations of PFCs (grey bars) and hydrogenated (black bar) surfactants [57–59] and of the FILs (coloured bars) [34, 35, 50, 52].

2.3 Cytotoxicity, ecotoxicity and biodegradation

Cytotoxicity, partition properties, acute ecotoxicity and biodegradation are key parameters to assess the health and environmental risks of these FILs. Knowledge about structure-toxicity relationships is of great interest for the design of biocompatible and greener FILs. The design of these new compounds aims to surpass the persistency, bioaccumulation, and toxicity drawbacks of PFCs [1, 2, 5, 6].

This section provides a critical review of the cytotoxicity in different human cell lines: human colon carcinoma cells (Caco-2), human hepatocellular carcinoma cells (HepG2), human umbilical vein cell line (EA.hy926), and spontaneously immortalized human keratinocyte cell line (HaCaT), representing the risks associated to different routes of biomedical administration [30, 37]. Cytotoxicity screenings, with 4 h [30] and 24 h [37] exposure, were performed in these cell lines. For short-chain based-FILs, such as $[C_2C_1Im][C_4F_9SO_3]$ and $[C_2C_1py][C_4F_9SO_3]$, the overall reduced toxicity can be justified by their high hydrophilicity and surfactant performance [30, 34, 35, 37, 52]. In HaCaT cells, higher EC_{50} values were obtained for both FILs mentioned before and these results can be associated to the intrinsic properties of this cell line [37]. A higher biocompatibility was attained with the cholinium cation conjugated with the $[C_4F_9SO_3]^-$ anion, due to the non-aromaticity and symmetry of this cation, which is also an essential nutrient for cell growth [25, 37, 60]. A similar behaviour was reported for several cholinium alkanoates [61, 62]. The non-aromatic and symmetric $[N_{4444}]^+$ as well as the alicyclic pyrrolidinium cations, conjugated with the $[C_4F_9SO_3]^-$ anion, maintain the cellular viability in Caco-2, HepG2 and EA.hy926 cells [30, 37]. The elongation of the imidazolium hydrogenated alkyl chain length from $[C_2C_1Im]^+$ up to $[C_{12}C_1Im]^+$ prompts the decrease of the cellular viability in the Caco-2 cell line, as depicted in **Figure 3a** [37]. This effect on cellular viability can be due to the presence of delocalized charges or due to the increment of lipophilicity which enhance the disruption of the cell wall [37, 63]. A more pronounced decay on the cellular viability is observed with the increment of the anionic fluorinated side chain length [30, 37]. This effect was noticed for the variation of $[C_4F_9SO_3]^-$ to $[C_8F_{17}SO_3]^-$ or $[N(C_4F_9SO_2)_2]^-$ anions, combined with imidazolium, cholinium and ammonium-based cations [30, 37]. The fluorinated elongation on carboxylate-based anions also engenders a significant reduction of the cellular viability in different cell lines [62]. The increment of the fluorinated domain also enhances the FILs lipophilicity and the charges delocalization, which is traduced in a higher permeation of the cell membranes [37, 64]. Inside the cell compartment, free fluoride ions are formed by

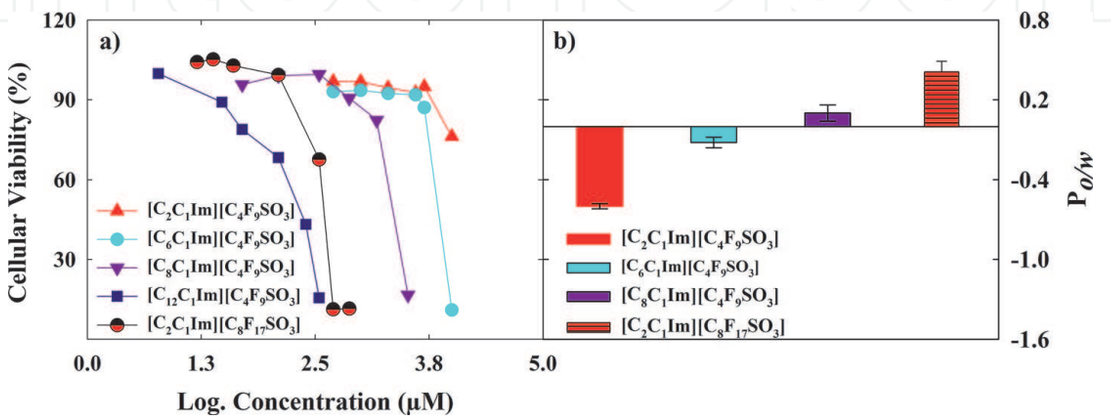


Figure 3.
(a) Cellular viability for imidazolium-based FILs with the increment of hydrogenated and fluorinated alkyl side chain length; (b) Effect of the hydrogenated and fluorinated alkyl side chain length on the 1-octanol/water partition coefficient ($P_{o/w}$) of imidazolium based FILs. Adapted from [37].

hydrolytic cleavage, which can interfere with the cellular mechanisms leading to cell death [37, 64].

The increment of the lipophilicity as result of the elongation of both hydrogenated and fluorinated alkyl side chain was confirmed through the 1-Octanol/water partition coefficients ($P_{o/w}$) of different FILs [37]. As depicted in **Figure 3b**, the $P_{o/w}$ increases with the increment of the hydrogenated side chain length from $[C_2C_1Im]^+$ to $[C_8C_1Im]^+$ [37]. This increment is associated to a greater lipophilic behaviour, caused by stronger van der Waals interactions between the FIL alkyl side chain and the hydrophobic region of the organic solvent, promoting their solubility in the organic media [37, 65]. This elongation also decreases the polarity and the acidity of these compounds, and consequently their interaction with water media [37, 65]. The increment on the anion core from $[C_4F_9SO_3]^-$ to $[C_8F_{17}SO_3]^-$ has a more pronounced effect in the partition properties, as illustrated in **Figure 3b** [37]. These results were associated to an enhanced solubility in lipophilic solvents endorsed by the fluorinated moiety [37, 66]. Finally, the partition properties of both $[C_2C_1Im]$ $[C_4F_9SO_3]$ and $[C_2C_1py][C_4F_9SO_3]$ are quite similar due to the highly acidic methylene groups in the constitutive rings [65]. Nevertheless, the partition properties of the studied FILs indicate that they not accumulate or concentrate in the environment [37].

An environmental hazard assessment is also essential in the context of sustainability and green chemistry. An ecotoxicological screening to evaluate the impact of FILs in aquatic environment was performed in marine bacterium *Vibrio fischeri*, crustacean *Daphnia magna*, and in *Lemna minor* plant [36]. This screening was made in aquatic species owing to the selected FILs unique water miscibility [34, 35]. Briefly, all tested FILs present a reduced ecotoxicity for the mentioned species [36]. The EC_{50} values indicate that FILs based on the imidazolium cation conjugated with $[C_4F_9SO_3]^-$ anion are more toxic than FILs based on other cations conjugated with the same anion [36]. The $[C_4F_9CO_2]^-$ anion is also less toxic than the sulfonate equivalent, except for the hydroxylated based imidazolium cations in *Daphnia magna and Lemna minor* [36]. Even so, the $[C_4F_9SO_3]^-$ based anion are less toxic than the bis(trifluoromethylsulfonyl)imide ($[N(CF_3SO_2)_2]^-$) anion for both *Vibrio fischeri* and *Daphnia magna* [36, 60]. Furthermore, both cholinium and hydroxylated imidazolium cations are the least toxic in the three aquatic species [61]. The functionalization of the imidazolium cation decreases the lipophilicity of these compounds, and consequently decreases their overall toxicity [36]. Finally, it must be stated that based on *Daphnia magna* and *Lemna minor* EC_{50} values and accordingly to the "Globally Harmonized System of Classification and Labelling of Chemicals", these FILs do not need to be categorized in terms of acute aquatic hazard [36]. It must be noticed that both cytotoxicity and ecotoxicity results are highly dependent on the target organisms and exposure times, [36, 37, 62] then different species and long-term effects of these compounds must be accessed prior to a large-scale application.

The microbial degradation of some FILs showed that short chain-based imidazolium FILs are highly resistant to biodegradation, even with the incorporation of hydroxyl groups. A certain biodegradability occurred in the short chained pyridinium-based FIL, associated to the oxidation of the alkyl side chain [36, 67, 68]. However, some variability is associated to the biodegradation of these cation that must be associated to the differences in microbial compositions involved in the degradation process [67, 68]. The higher degrees of biodegradation obtained with the cholinium-based FILs is only related to the cation core degradation that retains 75% of the oxidizable carbon [36]. To overcome the highly resistance associated to these compounds, removal or degradation alternative routes must be studied. According to these published results a proper combination between cations and

short chained fluorinated anions may result in biocompatible FILs with potential to be biodegradable by alternative routes. These biocompatible FILs can support the fields of FILs as task-specific materials in a broad range of fields, from biomedical to reaction media in industrial processes.

3. Applications of fluorinated ionic liquids

3.1 Biomedical applications

3.1.1 Artificial gas carriers

The need of new products to replace the blood transfusions appeared in the beginning of the 21th century as a consequence of cross-infections derived from the human immunodeficiency virus (HIV) [4, 69]. The lack of safety and trust allied with the severe shortages and increased demand of blood supplies have contributed to the search of an ideal artificial gas carrier (AGC) [4, 69]. PFCs-based emulsions are among the substances under clinical trials used to substitute the red blood cells in critical situations such as acute blood loss [4]. However, the PFCs have several handicaps that can restrict their usage as AGCs, such as high vapour pressures and poor solubility in water. With the aim to solve these limitations, FILs appeared as a solution to replace the PFCs fully or partially in AGC emulsions. Different works have been developed to infer on this prospect [34, 35, 49, 50, 70, 71]. The results show the possibility to design FILs with complete water miscibility, which solves one of the greatest handicaps [34, 35, 50]. The study of phase equilibria between FILs and two PFCs, perfluorodecalin and perfluorooctane, indicated that the enthalpic contributions are larger than the entropic contributions, which results in a favourable process of solvation of PFCs by FILs [70]. The high surfactant behaviour of FILs is also a huge advantage because it enables the stabilization of AGC emulsions, which can be favourable to reduce the usage of excipients and to enhance the solubilization of the respiratory gases [34, 35, 50]. The reduced cytotoxicity and ecotoxicity determined for FILs with the characteristics above mentioned strengths the possible use of these compounds in the biomedical field [30, 36, 37]. The greatest aspect that spurs the use of FILs as potential substitutes of PFCs in AGC emulsions is their higher ability to solubilize oxygen, carbon dioxide and nitrogen, compared to the conventional fluorine-containing ILs and with PFCs [49, 71]. However, the formulation of an emulsion with high efficacy and the implementation of tests on the physiological safety and other health studies must be carried out before applying FILs.

3.1.2 Drug delivery systems

Although there are several studies dealing with ILs for the solubilisation and stabilization of proteins, [23, 72] dissolution of low soluble active pharmaceutical ingredients (APIs), [23, 24] and development of drug formulations and delivery systems, [23–25, 73] the application of FILs in this field of pharmaceutical development is quite unexplored. Our research group initiated a pioneering research line to use FILs as drug delivery systems (DDSs) [74–76]. These novel biocompatible carriers can overcome the problems associated to proteins administration (e.g. sensibility to environmental conditions, short-half lives in blood stream, structural conformation and hydrophobic/hydrophilic nature that hamper the *in vivo* delivery) [77, 78] and their traditional delivery platforms (low stability, uncontrolled release, and low encapsulation efficiency) [79]. FIL-based DDSs have been shown

the potential to increase the safety and effectiveness of the therapeutic biomolecules, reducing the dosage needed and enabling a time and site-specific release [74–76].

The application of FILs as DDSs and stabilizing agents was firstly evaluated for two different model proteins, lysozyme, and bovine serum albumin (BSA) [74, 75]. Lysozyme is a protein with antiviral, antitumor and immunological properties, [80] whereas BSA is involved in organism homeostasis and in the transport of several components essential for several vertebrates' body functioning [81]. For these applications, FILs based on imidazolium, pyridinium and cholinium cations, conjugated with $[C_4F_9SO_3]^-$ and $[C_4F_9CO_2]^-$ anions were selected due to biocompatibility and improved surfactant behaviour [30, 31, 34–37]. The tested FILs concentrations cover values above and below their CMCs values (**Figure 2b**) [34, 52]. Concentrations above CMC were chosen due to their ability for self-assembling in micellar structures that can be used to protect, encapsulate, and deliver the therapeutic proteins [34, 52]. The stability of both proteins in the presence of FILs was determined based on the variations observed in the melting temperature of the biomolecules [74, 75]. The stability of lysozyme is not significantly affected by the incorporation of FILs, and only a slight decrease was achieved with $[C_2C_1py][C_4F_9CO_2]$ with a minor reduction of 2% in the melting temperature of the protein [74]. However, for BSA the melting temperature increases for all tested FILs concentrations, suggesting a stabilization of the protein [75]. These distinct results indicate a specific interaction between FILs and each tested protein [74, 75]. The differences among the interactions of the two biomolecules with FILs were also supported by structural studies. Both circular dichroism (CD) and fourier transformed infrared spectroscopy results suggest no substantial lysozyme structural modifications in the presence of cholinium and $[C_2C_1Im][C_4F_9SO_3]$ FILs, respectively [74]. For BSA, a slight increment on molar ellipticity and α helical content, followed by a β sheet and random coil reduction, observed in CD results, indicate a stabilization of the secondary structure, and a more compact state of the protein with $[N_{1112(OH)}][C_4F_9SO_3]$ [75, 82]. Furthermore, in the presence of FILs, the biological activity of lysozyme increased, even at concentrations where the encapsulation of the protein inside the micelles occurs [74]. Although there are differences in the interactions between the two different proteins and the FILs, the stability, activity and secondary structure of biomolecules are not negatively impacted by the selected fluorinated compounds [74, 75].

The aggregation behaviour of different FILs was analysed in the protein medium. No significant variations were achieved in the FILs self-aggregation process in aqueous solutions [34, 74, 75]. To prove the encapsulation of lysozyme in the aggregates of FILs, the self-assembled structures were studied through dynamic light scattering (DLS) [74]. As illustrated in **Figure 4a**, an encapsulation of the protein at a concentration approximately twice the FILs CMC (1.2% v/v) is expected based on the disappearance of the intensity peak of lysozyme (~ 4 nm) [74]. This encapsulation is driven by the fluorinated surfactant core of the FILs since the lysozyme characteristic peak remains present for the non-surfactant ILs [74]. This encapsulation was indorsed spectrophotometrically with the concentration of lysozyme in solution being reduced with the addition of 1.2% v/v $[C_2C_1Im][C_4F_9SO_3]$ [74]. Moreover, the FIL-protein aggregates became more stable after 24 h and a maximum stabilization was verified after 96 h [74]. The lysozyme encapsulation in $[C_2C_1Im][C_4F_9SO_3]$ was also evidenced, illustrated in **Figure 4b** and **c** [74]. **Figure 4b** depicts the solution of lysozyme with 1.2% v/v of $[C_2C_1Im][C_4F_9SO_3]$ analysed by transmission electron microscopy (TEM), where an external darker counter surrounding the aggregates of FILs is associated to the heavier elements present in the anion, in contrast to the lighter grey shades of the lysozyme

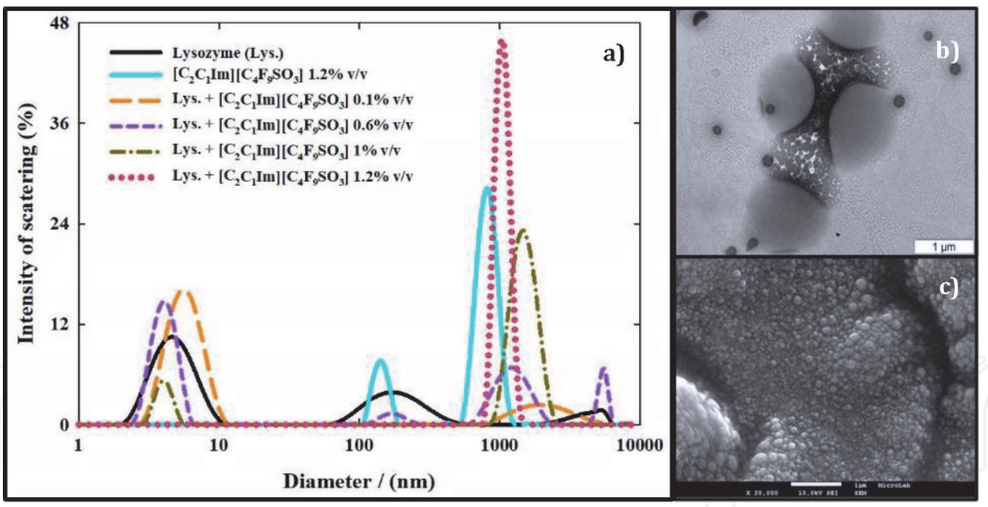


Figure 4.
(a) DLS spectra of lysozyme in buffered medium upon the addition of $[C_2C_1Im][C_4F_9SO_3]$ at several concentrations; (b) TEM image of $[C_2C_1Im][C_4F_9SO_3]$ 1.2% v/v with lysozyme; (c) SEM image of $[C_2C_1Im][C_4F_9SO_3]$ 1.2% v/v with lysozyme. Adapted from [74].

[74]. Moreover, the micellar sizes obtained by TEM are similar to the hydration diameters measured by DLS. A qualitative analysis through scanning electron microscopy (SEM), **Figure 4c**, reveals an external surface of the solution containing lysozyme with 1.2% v/v of $[C_2C_1Im][C_4F_9SO_3]$ similar to the FILs blank solution depicted in [74].

The interaction and the encapsulation between $[C_2C_1Im][C_4F_9SO_3]$ and BSA was proved through isothermal titration calorimetry (ITC) [75]. BSA interacts with the $[C_2C_1Im][C_4F_9SO_3]$ monomers causing conformational changes, as well as hydrogen bonding and hydrophobic interactions [75]. The aggregation of $[C_2C_1Im][C_4F_9SO_3]$ in buffer determined by conductimetry was also supported by the ITC measurements. However, ITC indicates that the interaction between BSA and FIL is stronger than the FIL self-aggregation [75]. A different interaction between BSA and the FIL aggregates, not identified in the conductivity measurements, strongly supports the encapsulation of this protein inside the FILs aggregates [75].

After the first proof of concept dealing with the encapsulation of lysozyme inside the FIL aggregates, the optimal incubation temperature of the protein during 24 h was determined at 4 °C without a significant loss of protein activity [76]. The encapsulation efficiencies of lysozyme in both $[C_2C_1Im][C_4F_9SO_3]$ and $[C_2C_1py][C_4F_9SO_3]$ at 1.8% v/v (3 times higher than CMC) range from 69.4 to 83.4%, values similar or higher than the obtained with other traditional platforms [76]. This lysozyme remains encapsulated up to 12 h post-incubation at 4 °C, without significant losses of biological activity [76]. This longer retention of the biomolecule inside the FILs aggregates can be caused by the high stability of the fluorinated counterpart of the IL, as well as by the interaction between FIL and protein [76]. Furthermore, the biomolecule release was accomplished after the application of several external stimuli [76]. With the increment of temperature up to 37 °C, simulating the average body temperature, lysozyme is completely released from the aggregated structures after 6 h [76]. This complete release was also achieved after the exposure to an ultrasound bath with a frequency of 80 kHz during 1 h [76]. This approach can be applied for a site specific and controlled delivery of therapeutic proteins through FILs based DDS. Furthermore, within the same time frame at 42 °C the protein released range from 57% and 39% to $[C_2C_1Im][C_4F_9SO_3]$ and $[C_2C_1py][C_4F_9SO_3]$ based DDS, respectively, suggesting that under a pathological condition the protein can be released at some relevant extent after 1 h post administration [76]. The biological activity of the released protein remains above 50% for all the tested

scenarios, except for the release after 12 h at 37 °C [76]. Then, biocompatible FILs can be designed to encapsulate different therapeutic proteins with good levels off encapsulation efficiencies promoting a site specific and thermo responsive release under different external stimuli. The differences among the effect of FILs in both lysozyme and BSA support the need to further study the interactions of these fluorinated compounds with other therapeutic biomolecules prior the design of the DDS.

3.2 Separation of fluorinated greenhouse gases using FILs

Currently, there is a great interest in the development of technologies to reduce the emissions of greenhouse gases (GHGs) into the atmosphere. F-gases, including hydrofluorocarbons (HFCs), PFCs, and sulphur hexafluoride (SF_6), are major contributors to GWP with long atmospheric lifetime. The most predominant F-gases used in refrigeration include 1,1,1,2-tetrafluoroethane (R-134a) and difluoromethane (R-32), alone or in blends with other F-gases, such as pentafluoroethane (R-125). In order to accomplish the international goals to reduce the emissions of GHGs, new refrigerants with lower GWP are being investigated and great research efforts are being made aiming to develop technologies to selective separate value-added F-gases from depleted refrigerants. These technologies lead to a reduction of gas emissions and promote the use of recycled F-gases. However, the separation of F-gases faces a major challenge, particularly in the cases of gas blends with an azeotropic or near-azeotropic behaviour. R-410A is widely used in the refrigeration sector but has a high GWP. Therefore, this refrigerant is one of the focus of the EU HFC phase-down [83]. This blend is a near-azeotropic system of R-32 and R-125 and therefore the separation of its individual components is hampered [83]. Consequently, there is a growing interest in the search for new efficient, low-energy, and sustainable separation processes.

The solubilization of F-gases in FILs is a poorly explored area. Most work has been done with imidazolium-based ILs composed of the $[N(CF_3SO_2)_2]^-$, tetrafluoroborate ($[BF_4]^-$) or hexafluorophosphate ($[PF_6]^-$) anions for the solubilization of different HFCs [84–87]. Gas solubility in ILs is an interplay of different phenomena with: (i) the enthalpic contribution of the intermolecular interactions between gas molecules and the absorbent and; (ii) the entropic contribution of the accommodation of gas molecules in the cavities of the absorbent. A positive correlation is found between the degree of fluorination of the ILs and the solubilization of HFCs [87, 88]. Additionally, the fluorination of the cation was shown to play a major role in the solubilization of PFCs [89] and HFCs [90] in 1-alkyl-3-methylimidazolium based ILs. The structures and the fluorination degree of the gases also strongly affect their solubilization into ILs. Solubilities of a variety of F-gases in $[C_2C_1Im][N(CF_3SO_2)_2]$ have been evaluated experimentally, and by modeling with soft-SAFT equation. These studies demonstrated the importance of the establishment of hydrogen bonds between the gas molecules and the absorbent. Both entropic effects, resulting from higher chain length/volume, and enthalpic effects, resulting from higher dipole moment, are suggested to increase gas solubility [91].

FILs present particular properties that distinguish them from mere fluoro-containing ILs, such as the ones with the $[N(CF_3SO_2)_2]^-$, $[BF_4]^-$, and $[PF_6]^-$ anions. Their ability to form three nanosegregated domains with different behaviours and the existence of countless cation/anion combinations increase the range of possible interactions (van der Waals, coulombic, and hydrogen bonding), making them ideal three-in-one solvent for the separation of F-gases [33].

When evaluating the absorption capacities of traditional ILs and of FILs for the selective capture of R-32 (**Table 1**), a positive relation between the fluorination

degree of the anion and the solubilization of this gas was reported [91]. This behaviour is similar to what is observed when the size of the hydrogenated alkyl chain in the cation of fluoro-containing imidazolium-based ILs increases, [86, 88, 92, 93] and can be explained by the entropic contribution of the accommodation of gas molecules in the cavities of absorbents with higher molar volume. Moreover, when the absorption of R-125 and R-134a in the abovementioned ILs was studied, a higher solubility capacity of FILs in comparison to mere fluoro-containing ILs was observed [83]. This demonstrates the relevance of the FILs nanosegregated domains for gas solubility, either by increasing the free volume for the accommodation of gas molecules or by increasing the number of possible gas-absorbent interactions. Lower solubilities have been obtained in mere fluoro-containing and in FILs to R-125 in comparison to R-134a. This has been explained by the decrease in the number of interactions with the absorbent as a consequence of the reduced number of hydrogen atoms in R-125, [89] or by a decrease in the flexibility of R-125, as consequence of a higher number of fluorine atoms [91]. By playing with the different factors involved in the solubilization of F-gases in ILs, namely the constitution of the cations and anions of the IL, temperature, pressure and others, it is possible to develop processes where the solubilization of one gas is favored in relation to other gas, or gases, present in the same mixture [91]. In this way, while the separation of the binary mixtures R-134a + R-125 and R-32 + R-125 was demonstrated to be improved using fluoro-containing ILs, lacking an alkyl fluorinated chain, the separation of the mixture R-134a + R-32 might be improved by utilizing FILs.

The increased solubility of F-gases in FILs supports the use of these absorbent as an alternative to conventional ILs with longer hydrogenated chains, which present higher toxicity [83]. Other study focused on evaluating the viability and costs of an absorption technology in near-industrial conditions for the capture of R-32 and R-134a (with HFC recoveries above 90%) from a dilute gas stream, using FILs or mere fluoro-containing ILs as absorbents. In this study a COSMO-based/Aspen Plus methodology was applied to evaluate the influence of ILs structure, HFC partial pressure, operating temperature, and FIL/IL mass flow on the recovery of HFCs [94].

The development of separation processes based on ILs may face some obstacles due to the unfavorable properties of some of these compounds, such as the toxicity of those with long fluorinated alkyl side chains, poor biodegradability, high viscosity, high-cost production, and high melting temperature. As aforementioned, the solubility of F-gases is favored when the number of fluorine atoms in ILs is increased, but this is also associated with higher melting temperature and to a decrease in the range of temperatures in which FILs can be operated at the liquid state. In this sense, deep eutectic solvents (DESs) are emerging as a versatile alternative to ILs, with low vapour pressure, nonflammability, high tuneability, and improved properties for application at process level. DESs are systems in which the charge delocalization occurring through hydrogen bonding between a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD) is responsible for decreasing the melting point of the mixture relatively to the individual components. Experimental studies regarding the solubility of refrigerants in DESs are scarce [95–98]. The solubility of R-134a in DES prepared by combining the IL $[C_2C_1Im][Cl]$ as hydrogen-bond acceptor (HBA) and 4-carbon perfluoroalkyl acids as hydrogen-bond donors (HBDs), was studied using both experimental solubility data and a theoretical model based on the soft-SAFT equation of state [89]. Additionally, the solubilization of F-gases was studied in DESs prepared by mixing high melting temperature FILs with perfluoropentanoic acid or nonafluoro-1-butanesulfonic acid (**Table 1**) [99]. The selected FILs were composed of different cations (cholinium, imidazolium, or a tetrabutylammonium cation) and anions with 4-carbon or

8-carbon perfluoroalkyl chains (**Table 1**). The melting temperatures of the prepared eutectic mixtures were significantly lower than the one of the neat FILs, which allowed to take advantage of the properties of FILs for the selective separation of F-gases, in a wider liquid range for F-gases solubilization [99].

4. Conclusions

In this chapter, the application of FILs as task-specific materials was fully described to be employed in both biomedical and engineering separation processes. The characteristic fluorinated domain and the different ions structural features prove to have a dominant effect on thermophysical and thermodynamic properties of FILs. Moreover, FILs have great surfactant behaviour and complete miscibility in water systems. The design of biocompatible and eco-friendly FILs without comprimising their surfactant behaviour was demonstrated which ultimate the applicability of FILs as enhanced materials comparing with PFCs and conventional fluorinated ILs.

The applicability of biocompatible FILs for biomedical applications was demonstrated by their great power to solubilize respiratory gases, supporting their use as artificial gas carriers. Additionally, the interaction and the encapsulation of different proteins in FIL aggregates, without comprimising the biological features of the biomolecules, also represents an advance in the application of FILs to pharmaceutical development. Finally, FILs exhibit great ability to be used individually, or in the development of materials to be further applied on the separation and recovery of F-gases, essentially due to their great free volume and gas-FIL enhanced interactions. To conclude, the discussion offered by this chapter highlights the identification of FILs as a novel and endless tool for the design of materials and processes whereas their fluorinated nanosegregated domain in combination with their ionic nature can provide unique features.

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Author details

Nicole S.M. Vieira, Margarida L. Ferreira, Paulo J. Castro, João M.M. Araújo and Ana B. Pereiro*
LAQV, REQUIMTE, Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Caparica, Portugal

*Address all correspondence to: anab@fct.unl.pt

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References

[1] Lindstrom AB, Strynar MJ, Libelo, EL. Polyfluorinated compounds: Past, present, and future. Environmental Science & Technology. 2011;45:7954–7961. DOI: 10.1021/es2011622

[2] Emerging chemical risks in europe – PFAS. European Environment Agency. 2019;DOI: 10.2800/486213

[3] Berger R, Resnati G, Metrangolo P, Weber E, Hulliger J. Organic fluorine compounds: a great opportunity for enhanced materials properties. Chemical Society Reviews. 2011;40:3496–3508. DOI: 10.1039/C0CS00221F

[4] Castro CI, Briceno JC. Perfluorocarbon-based oxygen carriers: review of products and trials. Artificial Organs. 2010;34:622–634. DOI: 10.1111/j.1525-1594.2009.00944.x

[5] Lindstrom AB, Strynar MJ, Libelo, EL, Field JA. Guest comment: Perfluoroalkyl acid focus issue. Environmental Science & Technology. 2011;45:7951–7953. DOI: 10.1021/es202963p

[6] Tsai W.-T, Chen H.-P, Hsien W.-Y. A review of uses, environmental hazards and recovery/recycle technologies of perfluorocarbons (PFCs) emissions from the semiconductor manufacturing processes. Journal of Loss Prevention in the Process Industries. 2002;15:65–75. DOI: 10.1016/S0950-4230(01)00067-5

[7] Melich R, Zorgani A, Padilla F, Charcosset C. Preparation of perfluorocarbon emulsions by premix membrane emulsification for Acoustic Droplet Vaporization (ADV) in biomedical applications. Biomedical Microdevices. 2020;22:62. DOI: 10.1007/s10544-020-00504-5

[8] Choi M, Park S, Park K, Jeong H, Hong J. Nitric oxide delivery using biocompatible perfluorocarbon microemulsion for antibacterial effect. ACS Biomaterials Science & Engineering. 2019;5:1378–1383. DOI: 10.1021/acsbiomaterials.9b00016

[9] Choi H, Choi W, Kim J, Kong WH, Kim KS, Kim C, Hahn, SK. Multifunctional nanodroplets encapsulating naphthalocyanine and perfluorohexane for bimodal image-guided therapy. Biomacromolecules. 2019;20:3767–3777. DOI: 10.1021/acs.biomac.9b00842

[10] Fernandes DA, Kolios MC. Near-infrared absorbing nanoemulsions as nonlinear ultrasound contrast agents for cancer theranostic. Journal of Molecular Liquids. 2019;287:110848. DOI: 10.1016/j.molliq.2019.04.125

[11] Badv M, Alonso-Cantu C, Shakeri A, Hosseinidoust Z, Weitz JI, Didar TF. Biofunctional Lubricant-infused vascular grafts functionalized with silanized bio-inks suppress thrombin generation and promote endothelialization. ACS Biomaterials Science & Engineering. 2019;5:6485–6496. DOI: 10.1021/acsbiomaterials.9b01062

[12] Kohlhauer M, Boissady E, Lidouren F, de Rochefort L, Nadeau M, Rambaud J, Hutin A, Dubuisson R.-M, Guillot G, Pey P, Bruneval P, Fortin-Pellerin E, Sage M, Walti H, Cariou A, Ricard J.-D, Berdeaux A, Mongardon N, Ghaleh B, Micheau P, Tissier R. A new paradigm for lung-conservative total liquid ventilation. EBioMedicine. 2020;50:102365. DOI: 10.1016/j.ebiom.2019.08.026

[13] Courrier HA, Vandamme TF, Krafft MP. Reverse water-in-fluorocarbon emulsions and microemulsions obtained with a fluorinated surfactant. Colloids and Surfaces A Physicochemical and Engineering Aspects. 2004;244:141–148. DOI: 10.1016/j.colsurfa.2004.06.003

[14] Zhu J, Wang Z, Xu X, Xu M, Yang X, Zhang C, Liu J, Zhang F, Shuai X, Wang W, Cao Z. Polydopamine-encapsulated perfluorocarbon for ultrasound contrast imaging and photothermal therapy. Molecular Pharmaceutics. 2020;17:817–826. DOI: 10.1021/acs.molpharmaceut.9b01070

[15] Bakker J, Reihlen A, Meura Lucie, Camboni M, Goldenman G, Lietzmann J. Study for the strategy for a non-toxic environment of the 7th Environment Action Programme. Publications Office of the European Union. 2017;DOI: 10.2779/025

[16] Gyllenhammar I, Berger U, Sundström, M, McCleaf P, Eurén K, Eriksson S, Ahlgren S, Lignell S, Aune M, Kotova N, Glynn A. Influence of contaminated drinking water on perfluoroalkyl acid levels in human serum – A case study from Uppsala, Sweden. Environmental Research. 2015; 140:673–683. DOI: 10.1016/j.envres.2015.05.019

[17] Naile JE, Khim JS, Wang T, Chen C, Luo W, Kwon B.-O, Park J, Koh C.-H, Jones PD, Lu Y, Giesy JP. Perfluorinated compounds in water, sediment, soil and biota from estuarine and coastal areas of Korea. Environmental Pollution. 2010;5: 1237–1244. DOI: 10.1016/j.envpol.2010.01.023

[18] Noorlander CW, van Leeuwen SPJ, te Biesebeek JD, Mengelers MJB, Zeilmaker MJ. Levels of perfluorinated compounds in food and dietary intake of PFOS and PFOA in The Netherlands. Journal of Agricultural and Food Chemistry. 2011;59:7496–7505. DOI: 10.1021/jf104943p

[19] Rogers RD, Seddon KR. Ionic liquids-Solvents of the future?. Science. 2003;302:792–793. DOI: 10.1126/science.1090313

[20] Qiao Y, Ma W, Theyssen N, Chen C, Hou Z. Temperature-responsive ionic liquids: Fundamental behaviors and catalytic applications. Chemical Reviews. 2017;117:6881–6928. DOI: 10.1021/acs.chemrev.6b00652

[21] Watanabe M, Thomas ML, Zhang S, Ueno K, Yasuda T, Dokko K. Application of ionic liquids to energy storage and conversion materials and devices. Chemical Reviews. 2017;117:7190–7239. DOI: 10.1021/acs.chemrev.6b00504

[22] Ventura SPM, A. e Silva F, Quental MV, Mondal D, Freire MG, Coutinho JAP. Ionic-liquid-mediated extraction and separation processes for bioactive compounds: Past, present, and future trends. Chemical Reviews. 2017; 117:6984–7052. DOI: 10.1021/acs.chemrev.6b00550

[23] Egorova KS, Gordeev EG, Ananikov VP. Biological activity of ionic liquids and their application in pharmaceutics and medicine. Chemical Reviews. 2017;117:7132–7189. DOI: 10.1021/acs.chemrev.6b00562

[24] Marrucho IM, Branco LC, Rebelo LPN. Ionic liquids in pharmaceutical applications. Annual Review of Chemical and Biomolecular Engineering. 2014;5:527–546. DOI: 10.1146/annurev-chembioeng-060713-040024

[25] Araújo JMM, Florindo C, Pereiro AB, Vieira NSM, Matia AA, Duarte CMM, Rebelo LPN, Marrucho IM. Cholinium-based ionic liquids with pharmaceutically active anions. RSC Advances. 2014;4:28126–28132. DOI: 10.1039/c3ra47615d

[26] Earle MJ, Esperança JMSS, Gilea MA, Canongia Lopes JN, Rebelo LPN, Magee JW, Seddon KR, Widegren JA. The distillation and volatility of ionic liquids. Nature. 2006; 439:831–834. DOI: 10.1038/nature04451

[27] Plechkova NV, Seddon KR. Applications of ionic liquids in the

chemical industry. Chemical Society Reviews. 2008;37:123–150. DOI: 10.1039/b006677j~

[28] Egorova KS, Ananikov VP. Toxicity of Ionic Liquids: Eco(cyto)activity as complicated, but unavoidable parameter for task-specific optimization. ChemSusChem. 2014;7:336–360. DOI: 10.1002/cssc.201300459

[29] Lei Z, Chen B, Koo Y.-M, MacFarlane DR. Introduction: Ionic liquids. Chemical Reviews. 2017;117: 6633–6635. DOI: 10.1021/acs.chemrev.7b00246

[30] Pereiro AB, Araújo JMM, Martinho S, Alves F, Nunes S, Matias, A, Duarte CMM, Rebelo, Rebelo LPN, Marrucho IM. Fluorinated ionic liquids: Properties and applications. ACS Sustainable Chemistry & Engineering. 2013;1:427–439. DOI: 10.1021/sc300163n

[31] Pereiro AB, Araújo JMM, Esperança JMSS, Rebelo LPN. Surfactant fluorinated ionic liquids. In: Eftekhari A editor. Ionic Liquid Devices. Smart Materials No. 28: Royal Society of Chemistry; 2018. p. 79–102. DOI: 10.1039/9781788011839

[32] Tindale JJ, Na C, Jennings MC, Ragogna PJ. Synthesis and characterization of fluorinated phosphonium ionic liquids. Canadian Journal of Chemistry. 2007;85:660–667. DOI: 10.1139/V07-035

[33] Pereiro AB, Pastoriza-Gallego MJ, Shimizu K, Marrucho IM, Canongia Lopes JN, Piñeiro MM, Rebelo LPN. On the Formation of a Third, Nanostructured Domain in Ionic Liquids. The Journal of Physical Chemistry B. 2013;117:10826–10833. DOI: 10.1021/jp402300c

[34] Pereiro AB, Araújo JMM, Teixeira FS, Marrucho IM, Piñeiro MM, Rebelo LPN. Aggregation behavior and total miscibility of fluorinated ionic liquids in water. Langmuir. 2015;31: 1283–1295. DOI: 10.1021/la503961h.

[35] Teixeira FS, Vieira NSM, Cortes OA, Araújo JMM, Marrucho IM, Rebelo LPN, Pereiro AB. Phase equilibria and surfactant behavior of fluorinated ionic liquids with water. The Journal of Chemical Thermodynamics. 2015;82:99–107. DOI: 10.1016/j.jct.2014.10.021

[36] Vieira NSM, Stolte S, Araújo JMM, Rebelo LPN, Pereiro AB, Markiewicz M. Acute aquatic toxicity and biodegradability of fluorinated ionic liquids. ACS Sustainable Chemistry & Engineering. 2019;7:3733–3741. DOI: 10.1021/acssuschemeng.8b03653

[37] Vieira NSM, Bastos JC, Rebelo LPN, Matias, A, Araújo JMM, Pereiro AB. Human cytotoxicity and octanol/water partition coefficients of fluorinated ionic liquids. Chemosphere. 2019;216: 576e586. DOI: 10.1016/j.chemosphere.2018.10.159

[38] Prikhod'ko SA, Shabalin AY, Shmakov MM, Bardin VV, Adonin NY. Ionic liquids with fluorine-containing anions as a new class of functional materials: features of the synthesis, physicochemical properties, and use. Russian Chemical Bulletin. 2020;69:17–31. DOI: 1066–5285/20/6901–0017

[39] Tong B, Chen X, Chen L, Zhou Z, Peng Z. Engineering solid electrolyte interphase in lithium metal batteries by employing an ionic liquid ether double-solvent electrolyte with Li[(CF_3SO_2)(n-$C_4F_9SO_2$)N] as the salt. ACS Applied Energy Materials. 2018;1:4426–4431. DOI: 10.1021/acsaem.8b00821.

[40] Lepre LF, Andre D, Denis-Quanquin S, Gautier A, Pádua AAH., Gomes MC. Ionic liquids can enable the recycling of fluorinated greenhouse gases. ACS Sustainable Chemistry & Engineering. 2019;7:16900–16906. DOI: 10.1021/acssuschemeng.9b04214

[41] Rufino-Felipe E, Valdes H, German-Acacio JM, Reyes-Marquez V, Morales-Morales D. Fluorinated N-Heterocyclic carbene complexes. Applications in catalysis. Journal of Organometallic Chemistry. 2020;921:121364. DOI: 10.1016/j.jorganchem.2020.121364

[42] Vieira NSM, Reis PM, Shimizu K, Cortes AO, Marrucho IM, Araújo JMM, Esperança JMSS, Canongia Lopes JN, Pereiro AB, Rebelo LPN. A thermophysical and structural characterization of ionic liquids with alkyl and perfluoroalkyl side chains. RSC Advances. 2015;5:65337–65350. DOI: 10.1039/C5RA13869H

[43] Luís A, Shimizu K, Araújo JMM, Carvalho PJ, Lopes-da-Silva JA, Canongia Lopes JN, Rebelo LPN, Coutinho JAP, Freire MG, Pereiro AB. Influence of nanosegregation on the surface tension of fluorinated ionic liquids. Langmuir. 2016;32:6130–6139. DOI: 10.1021/acs.langmuir.6b00209

[44] Teles ARR, Correia H, Maximo GJ, Rebelo LPN, Freire MG, Pereiro AB, Coutinho JAP. Solid–liquid equilibria of binary mixtures of fluorinated ionic liquids. Physical Chemistry Chemical Physics. 2016;18:25741–25750. DOI: 10.1039/C6CP05372F

[45] Vieira NSM, Luís A, Reis PM, Carvalho PJ, Lopes-da-Silva JA, Esperança JMSS, Araújo JMM, Rebelo LPN, Freire MG, Pereiro AB. Fluorination effects on the thermodynamic, thermophysical and surface properties of ionic liquids. The Journal of Chemical Thermodynamics. 2016;97:354–361. DOI: 10.1016/j.jct.2016.02.013

[46] Ferreira ML, Pastoriza-Gallego MJ, Araújo JMM, Canongia Lopes JN, Rebelo LPN, Piñeiro MM, Shimizu K, Pereiro AB. Influence of nanosegregation on the phase behavior of fluorinated ionic liquids. The Journal of Physical Chemistry C. 2017;121:5415–5427. DOI: 10.1021/acs.jpcc.7b00516

[47] Pereiro AB, Llovell F, Araújo JMM, Santos ASS, Rebelo LPN, Piñeiro MM, Vega LF. Thermophysical Characterization of ionic liquids based on the perfluorobutanesulfonate anion: experimental and soft-SAFT modeling results. ChemPhysChem. 2017;18:1–13. DOI: 10.1002/cphc.201700327

[48] Ferreira ML, Araújo JMM, Pereiro AB, Vega LF. Insights into the influence of the molecular structures of fluorinated ionic liquids on their thermophysical properties. A soft-SAFT based approach. Physical Chemistry Chemical Physics. 2019;21:6362–6380. DOI: 10.1039/C8CP07522K

[49] Ferreira ML, Llovell F, Vega LF, Pereiro AB, Araújo JMM. Systematic study of the influence of the molecular structure of fluorinated ionic liquids on the solubilization of atmospheric gases using a soft-SAFT based approach. Journal of Molecular Liquids. 2019;294:111645. DOI: 10.1016/j.molliq.2019.111645

[50] Ferreira ML, Araújo JMM, Vega LF, Llovell F, Pereiro AB. Functionalization of fluorinated ionic liquids: A combined experimental-theoretical study. Journal of Molecular Liquids. 2020;302:112489. DOI: 10.1016/j.molliq.2020.112489

[51] Bastos JC, Carvalho SF, Welton T, Canongia Lopes JN, Rebelo LPN, Shimizu K, Araújo JMM, Pereiro AB. Design of task-specific fluorinated ionic liquids: nanosegregation versus hydrogen-bonding ability in aqueous solutions. Chemical Communications. 2018;54:3524–3527. DOI: 10.1039/C8CC00361K

[52] Vieira NSM, Bastos JC, Hermida-Merino C, Pastoriza-Gallego MJ, Rebelo LPN, Piñeiro MM, Araújo JMM, Pereiro AB. Aggregation and phase equilibria of fluorinated ionic liquids.

Journal of Molecular Liquids. 2019;285: 386–396. DOI: 10.1016/j.molliq.2019.04.086

[53] Gupta S, Olson JD. Industrial needs in physical properties. Industrial & Engineering Chemistry Research. 2003;42:6359–6374. DOI: 10.1021/ie030170v

[54] Ueno K, Tokuda H, Watanabe M. Ionicity in ionic liquids: correlation with ionic structure and physicochemical properties. Physical Chemistry Chemical Physics. 2010;12:1649–1658. DOI: 10.1039/B921462N

[55] Tariq M, Forte PAS, Costa Gomes MF, Canongia Lopes JN, Rebelo LPN. Densities and refractive indices of imidazolium- and phosphonium-based ionic liquids: Effect of temperature, alkyl chain length, and anion. The Journal of Chemical Thermodynamics. 2009;41:790–798. DOI: 10.1016/j.jct.2009.01.012

[56] Santos CS, Baldelli S, Gas-liquid interface of room-temperature ionic liquids. Chemical Society Reviews. 2010;39:2136–2145. DOI: 10.1039/b921580h.

[57] Szajdzinska-Pietek E, Wolszczak M. Time-resolved fluorescence quenching study of aqueous solutions of perfluorinated surfactants with the use of protiated luminophore and quencher. Langmuir. 2000;16:1675–1680. DOI: 10.1021/LA990981X

[58] González-Pérez A, Ruso JM, Prieto G, Sarmiento F. Apparent molar quantities of sodium octanoate in aqueous solutions. Colloid and Polymer Science. 2004;282:1133–1139. DOI: 10.1007/s00396-003-1047-2

[59] López-Fontán JL, Sarmiento F, Schulz PC. The aggregation of sodium perfluorooctanoate in water. Colloid and Polymer Science. 2004;283:862–871. DOI: 10.1007/s00396-004-1228-7

[60] Ventura SPM, Gonçalves AMM, Sintra T, Pereira JL, Gonçalves F, Coutinho JAP. Designing ionic liquids: the chemical structure role in the toxicity. Ecotoxicology. 2013;22:1–12. DOI: 10.1007/s10646-012-0997-x

[61] Petkovic M, Ferguson JL, Gunaratne HQN, Ferreira R, Leitão MC, Seddon KR, Rebelo LPN, Pereira CS. Novel biocompatible cholinium-based ionic liquids-toxicity and biodegradability. Green Chemistry. 2010;12:643–649. DOI: 10.1039/B922247B

[62] Patinha DJS, Tomé LC, Florindo C, Soares HR, Coroadinha AS, Marrucho IM. New low-toxicity cholinium-based ionic liquids with perfluoroalkanoate anions for aqueous biphasic system implementation. ACS Sustainable Chemistry & Engineering. 2016;4:2670–2679. DOI: 10.1021/acssuschemeng.6b00171

[63] Gal N, Malferarri D, Kolusheva S, Galletti P, Tagliavini E, Jelinek R. Membrane interactions of ionic liquids: possible determinants for biological activity and toxicity. Biochimica et Biophysica Acta (BBA) – Biomembranes. 2012;1818:2967–2974. DOI: 10.1016/j.bbamem.2012.07.025

[64] Kumar RA, Papaïconomou N, Lee J, Salminen J, Clark DS, Prausnitz JM. In vitro cytotoxicities of ionic liquids: effect of cation rings, functional groups, and anions. Environmental Toxicology. 2008;24:388–395. DOI: 10.1002/tox

[65] Lungwitz R, Strehmel V, Spange S. The dipolarity/polarisability of 1-alkyl-3-methylimidazolium ionic liquids as function of anion structure and the alkyl chain length. New Journal of Chemistry. 2010;34:1135–1140. DOI: 10.1039/B9NJ00751B

[66] Kim, M., Li, L.Y., Grace, J.R., Yue, C., Selecting reliable physicochemical properties of perfluoroalkyl and

polyfluoroalkyl substances (PFASs) based on molecular descriptors. Environmental Pollution. 2015;196:462–472. DOI: 10.1016/j.envpol.2014.11.008

[67] Docherty KM, Dixon JK., Kulpa CF. Biodegradability of imidazolium and pyridinium ionic liquids by an activated sludge microbial community. Biodegradation. 2007;18:481–493. DOI: 10.1007/s10532-006-9081-7

[68] Zhang C, Wang H, Malhotra SV, Dodge CJ, Francis AJ. Biodegradation of pyridinium-based ionic liquids by an axenic culture of soil Corynebacteria. Green Chemistry. 2010;12:851–858. DOI: 10.1039/B924264C

[69] Busch MP, Kleinman SH, Nemo GJ. Current and emerging infectious risks of blood transfusions. The Journal of the American Medical Association. 2003;289: 959–962. DOI: 10.1001/jama.289.8.959

[70] Martinho S, Araújo JMM, Rebelo LPN, Pereiro AB, Marrucho IM. The Journal of Chemical Thermodynamics. 2013;64:71. DOI: 10.1016/j.jct.2013.04.019

[71] Pereiro AB, Tomé LC, Martinho S, Rebelo LPN, Marrucho IM. Industrial & Engineering Chemistry Research. 2013; 52:4994–5001. DOI: 10.1021/ie4002469

[72] Fujita K, MacFarlane DR, Forsyth M, Yoshizawa-Fujita M, Murata K, Nakamura N, Ohno H. Solubility and stability of cytochrome c in hydrated ionic Liquids: effect of oxo acid residues and kosmotropicity. Biomacromolecules.2007;8:2080–2086. DOI: 10.1021/bm070041o

[73] Moniruzzaman M, Tamura M, Tahara Y, Kamiya N, Goto M. Ionic liquid- in-oil microemulsion as a potential carrier of sparingly soluble drug: characterization and cytotoxicity evaluation. International Journal of Pharmaceutics. 2010;400:243–250. DOI: 10.1016/j.ijpharm.2010.08.034

[74] Alves M, Vieira NSM, Rebelo LPN, Araújo JMM, Pereiro AB, Archer, M. Fluorinated ionic liquids for protein drug delivery systems: Investigating their impact on the structure and function of lysozyme. International Journal of Pharmaceutics. 2017;526:309–320. DOI: 10.1016/j.ijpharm.2017.05.002

[75] Alves M, Araújo JMM, Martins IC, Pereiro AB, Archer, M. Insights into the interaction of bovine serum albumin with surface-active ionic liquids in aqueous solution. Journal of Molecular Liquids. 2020;114537. DOI: 10.1016/j.molliq.2020.114537

[76] Vieira NSM, Castro PJ, Marques DF, Araújo JMM, Pereiro AB. Tailor-made fluorinated ionic liquids for protein delivery. Nanomaterials. 2020;10:1594. Doi:10.3390/nano10081594

[77] Ibraheem D, Elaissari A, Fessi H. Administration strategies for proteins and peptides. International Journal of Pharmaceutics. 2014;477:578–589. DOI: 10.1016/j.ijpharm.2014.10.059

[78] Dai C, Wanga B, Zhao H. Microencapsulation peptide and protein drugs delivery system. Colloids and Surfaces B: Biointerfaces. 2005;41:117–120. DOI: 10.1016/j.colsurfb.2004.10.032

[79] Mishra H, Chauhan V, Kumar K, Teotia D. A comprehensive review on liposomes: A novel drug delivery system. Journal of Drug Delivery and Therapeutics. 2018;8:400–404. DOI: 10.22270

[80] Abeyrathne EDNS, Lee HY, Ahn DU. Egg white proteins and their potential use in food processing or as nutraceutical and pharmaceutical agents —A review. Poultry Science. 2013;92: 3292–3299. DOI: 10.3382/ps.2013-03391

[81] Bujacz A. Structures of bovine, equine and leporine serum albumin.

Acta Crystallographica Section D. 2012; 68:1278–1289. DOI: 10.1107/S0907444912027047

[82] F. Geng, L. Zheng, J. Liu, L. Yu, C. Tung, Interactions between a surface active imidazolium ionic liquid and BSA. Colloid and Polymer Science. 2009;287:1253–1259. DOI: 10.1007/s00396-009-2085-1

[83] Sosa JE, Ribeiro RPPL, Castro PJ, Mota JPB, Araújo JMM, Pereiro AB. Absorption of fluorinated greenhouse gases using fluorinated ionic liquids. Industrial & Engineering Chemistry Research. 2019;58:20769–20778. DOI: 10.1021/acs.iecr.9b04648

[84] Shiflett MB, Yokozeki A. Solubility and diffusivity of hydrofluorocarbons in room-temperature ionic liquids. AIChE Journal. 2006;52:1205–1219. DOI: 10.1002/aic.10685

[85] Shiflett MB, Yokozeki A. Binary vapor-liquid and vapor- liquid-liquid equilibria of hydrofluorocarbons (HFC-125 and HFC-143a) and hydrofluoroethers (HFE-125 and HFE-143a) with ionic liquid [Emim][Tf2N]. Journal of Chemical & Engineering Data. 2008;53:492–497. DOI: 10.1021/je700588d

[86] Shiflett, M. B.; Yokozeki, A. vapor-liquid-liquid equilibria of pentafluoroethane and ionic liquid [Bmim][PF6] mixtures studied with the volumetric method. The Journal of Physical Chemistry B. 2006;110:14436–14443. DOI: 10.1021/jp062437k

[87] Shiflett MB, Harmer MA, Junk CP, Yokozeki A. solubility and diffusivity of difluoromethane in room-temperature ionic liquids. Journal of Chemical & Engineering Data. 2006;51:483–495. DOI: 10.1021/je050386z

[88] Ren W, Scurto AM. Phase equilibria of imidazolium ionic liquids and the refrigerant gas, 1,1,1,2-Tetrafluoroethane (R-134a). Fluid Phase Equilibria. 2009;286:1–7. DOI: 10.1016/j.fluid.2009.07.007

[89] Lepre LF, Pison L, Otero I, Gautier A, Dévemy J, Husson P, Pádua AAH, Gomes MC. Using hydrogenated and perfluorinated gases to probe the interactions and structure of fluorinated ionic liquids. Physical Chemistry Chemical Physics. 2019;21: 8865–8873. DOI:10.1039/c9cp00593e

[90] Lepre LF, Andre D, Denis-Quanquin S, Gautier A, Pádua AAH, Gomes MC. Ionic liquids can enable the recycling of fluorinated greenhouse gases. ACS Sustainable Chemistry & Engineering. 2019;7:16900–16906. DOI: 10.1021/acssuschemeng.9b04214

[91] Jovell D, Gómez SB, Zakrzewska ME, Nunes AVM, Araújo JMM. Pereiro AB, Llovell F. Insight on the solubility of R134a in fluorinated ionic liquids and deep eutectic solvents. Journal of Chemical & Engineering Data. 2020;65:4956–4969. DOI: 10.1021/acs.jced.0c00588

[92] Liu X, He M, Lv N, Qi X, Su C. Vapor-liquid equilibrium of three hydrofluorocarbons with [HMIM][Tf2N]. Journal of Chemical & Engineering Data. 2015;60:1354–1361. DOI: 10.1021/je501069b

[93] Dong L, Zheng D, Sun G, Wu X. Vapor−liquid equilibrium measurements of difluoromethane + [Emim]OTf,difluoromethane + [Bmim]OTf, difluoroethane + [Emim]OTf, and difluoroethane + [Bmim]OTf systems. Journal of Chemical & Engineering Data. 2011;56:3663–3668. DOI: 10.1021/je2005566

[94] Sosa JE, Santiago R, Hospital-Benito D, Gomes MC, Araújo JMM, Pereiro AB, Palomar J. Process evaluation of fluorinated ionic liquids as F-gas absorbents. Environmental Science & Technology. 2020;54:12784–12794. DOI: 10.1021/acs.est.0c05305

[95] Leron RB, Li M. Solubility of carbon dioxide in a choline chloride-ethylene glycol based deep eutectic solvent. Thermochimica Acta. 2013;551:14–19. DOI: 10.1016/j.tca.2012.09.041

[96] Leron RB, Caparanga A, Li M. Carbon dioxide solubility in a deep eutectic solvent based on choline chloride and urea at T = 303.15–343.15K and moderate pressures. Journal of the Taiwan Institute of Chemical Engineers. 2013;44:879–885. DOI: 10.1016/j.jtice.2013.02.005

[97] Francisco M, van den Bruinhorst A, Zubeir LF, Peters CJ, Kroon MCA. New low transition temperature mixture (LTTM) formed by choline chloride +lactic acid: Characterization as solvent for CO2 capture. Fluid Phase Equilibria. 2013;340:77–84. DOI: 10.1016/j.fluid.2012.12.001

[98] Yang D, Hou M, Ning H, Zhang J, Ma J, Yang G, Han B. Efficient SO2 Absorption by renewable choline chloride−glycerol deep eutectic solvents. Green Chemistry. 2013;15:2261–2265. DOI: 10.1039/C3GC40815A

[99] Castro PJ, Redondo AE, Sosa JE, Zakrzewska ME, Nunes AVM, Araújo JMM, Pereiro AB. Absorption of fluorinated greenhouse gases in deep eutectic solvents. Industrial & Engineering Chemistry Research. 2020;59:13246–13259. DOI: 10.1021/acs.iecr.0c01893