

Editorial

# Recent Advances on Ionic Liquid Uses in Separation Techniques

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## 1. Introduction

Ionic liquids (ILs) are non-molecular solvents; specifically, molten salts with low melting points, often below 100 °C and even below room temperature, thus allowing these solvents to remain liquid [1–3]. Chemically, they are formed by a bulky organic cation and a variety of usually smaller inorganic/organic anions to achieve electrical neutrality. Therefore, the number of combinations of cations and anions with substituted head-groups is unlimited, whereas the hydrophobicity range is guaranteed by the alkyl chain length of the organic moieties [4]. The physico-chemical properties of ILs include volatility, flammability, thermal stability, viscosity, solvation ability, an electrochemical window and relatively low toxicity, among others [1,2]. All of them can be tuned and modulated by the appropriate selection of both IL cation and anion—but *what makes ILs so attractive?* The main reason for their popularity is that they are considered a greener alternative to pollutant organic solvents, traditionally used in many technical and scientific fields, to decrease the environmental impact and overall risk of chemical exposure. Consequently, the scientific interest in ILs has been extended to different fields of chemistry with a high impact. In analytical chemistry, ILs have attracted special attention in separation techniques, where new ILs with specific properties, such as amphiphilic, magnetic and chiral properties, among others, are continuously being developed for new applications [3]. All this research has resulted in a rapid growth of the literature on the development and use of ILs, with an almost exponential increase, which usually involves books and Special Issues, such as the one we presented in *Separations* in 2019–2020.

The Special Issue (SI), entitled “Recent Advances on Ionic Liquid Uses in Separation Techniques”, was devoted to applications of ILs in chromatography, extraction for sample preparation and related techniques. The scope was extended to deep eutectic solvents (DES), which are a promising class of solvents with similar properties to ILs [5]. The SI gathered the collaborations of different authors with wide experience in the IL or DES fields that discussed the state-of-the-art preparation and application of IL-based composites and hydrophobic DES in analytical sample preparation, or presented new results in different HPLC modes for the analysis of basic compounds.

## 2. Summary of the Special Issue

Two reviews and two original research papers dealing with the use of ILs or DES in liquid chromatography and extraction techniques were published in the SI after the corresponding peer-review process. The topics and the nature of the related papers are described here.

Complex samples are difficult to directly analyze due to the presence of target analytes at trace concentration levels in an environment containing high contents of certain sample matrix components, which can act as interfering species and give rise to an undesirable matrix effect. In this context, sample preparation, referring to all steps carried out in the laboratory before the final measurement with the analytical instruments, plays an essential



**Citation:** Ruiz-Ángel, M.J.; Carda-Broch, S. Recent Advances on Ionic Liquid Uses in Separation Techniques. *Separations* **2022**, *9*, 96. <https://doi.org/10.3390/separations9040096>

Received: 5 April 2022

Accepted: 8 April 2022

Published: 11 April 2022

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role to ensure the maximum quality of the results. Conventional extraction methods, both in their liquid and solid-phase modes, are extensively used for sample preparation [6,7]. It should be indicated that sorbent-based extraction methods are preferred over liquid-based in terms of simplicity, cost effectiveness, and robustness. Among sorbent-based analytical sample clean-up procedures, solid-phase extraction (SPE) is the most used preparation method worldwide, with a wide variety of commercially available SPE sorbents for different applications [7,8]. However, drawbacks related to the reusability of SPE devices, and low selectivity and extraction efficiency, still persist. In this context, ILs have been revealed as excellent sorbent or sorbent dopant materials to overcome these problems.

The review presented by Gutiérrez-Serpa et al. [9] gives an overview of the incorporation of ILs, such as polymeric ILs, and the combination of ILs with other materials (magnetic particles, carbon, silica and metal–organic frameworks) to prepare solid IL-based composites, in different SPE devices. In these cases, the IL strongly modifies the final characteristics of the composite materials, which are more homogeneous, porous and permeable, and also participates in the extraction of the substances of interest. It should be noted that imidazolium-based ILs, mainly methyl and alkyl chains between 4 and 16 atoms, were selected in practically all the applications described. The effect of different lengths of the alkyl chain and different anions was frequently explored, as opposed to the tunability of ILs. The authors concluded that selective sorbents with specific properties for certain applications should be prepared and rigorously investigated.

It should be noted that the most studied imidazolium-based ILs, and especially those associated with fluorinated anions, show low biodegradability and biocompatibility, and high toxicity and cost [10,11]. To address this problem, DES are an alternative that share most of the properties of ILs, but unlike ILs, they comprise mixtures of at least two compounds [12], which may limit the reproducibility and accuracy of analyses. Dwamena reviewed the recent advances in a specific type of DES, hydrophobic DES (HDES), focusing on their synthesis, applications, challenges, and future perspectives [13]. The concept of HDES was introduced by van Osch and co-workers in 2015 from the combination of diverse quaternary ammonium salts with decanoic acid [14]. The simple preparation of HDES, together with their low toxicity and water-accessible nature, makes them promising in the liquid–liquid extraction of non-polar analytes and transition metals from an aqueous environment over hydrophobic ILs or conventional organic solvents, although drawbacks related to their high viscosity have been addressed. Nevertheless, as indicated by the author, most research has concentrated mainly on hydrophilic DES. Therefore, the use of HDES is still in its infancy, and extensive work is still required.

In reversed-phase liquid chromatography (RPLC), solutes are retained using conventional alkyl-bonded silica phase columns (octyl or octadecyl) according to their hydrophobicity [15]. However, residual silanols present on these stationary phases are negatively charged at the typical working pH range (between 2 and 8), and are able to establish additional ion-exchange interactions with cationic compounds, increasing their retention and giving rise to broad and asymmetrical peaks [16,17]. The reduction of this process, known as the “silanol effect”, is of great importance in the analysis of basic compounds, which are usually of pharmaceutical interest [18]. The most practical approach to minimize or suppress the undesirable influence of silanols on the chromatographic performance of basic drugs is the addition of different types of additives to the hydro-organic mobile phase [19,20]. Among the common reagents traditionally used to mask the silanophilic activity (i.e., amines, surfactants, etc.), ILs have become a serious alternative due to the significant improvement in peak performance observed with their use [21]. The two research articles included in the SI involved the use of imidazolium ILs differing in their cations/anions as modifiers of the chromatographic behavior of  $\beta$ -adrenoceptor antagonists.

Ruiz-Angel [22] applied a mathematical model based on two chemical equilibria to estimate the association constants between the solutes and alkyl-bonded stationary phase, as well as those between solutes and the additive in the mobile phase. The constant values,

together with the changes in retention and peak shape, revealed information about the retention mechanism and reducing the “silanol effect”.

Peris-García et al. compared the chromatographic performance obtained by the addition of ILs with the mobile phase in RPLC for the analysis of a group of  $\beta$ -adrenoceptor antagonists, with the results obtained by hydrophilic interaction liquid chromatography (HILIC) [23]. ILs are able to adsorb on alkyl-bonded stationary phases, changing their behavior, whereas in HILIC, water forms an adsorbed layer on the surface of the polar stationary phase, which modifies the selectivity with regard to RPLC [24]. In both chromatographic modes, RPLC with added IL and HILIC, the variety of interactions gave rise to complex retention mechanisms, but they were a viable solution to the problem of poor peak shape for basic compounds. However, the use of HILIC is limited by the polarity range of the solutes.

Further topics related to the use of ILs in analytical chemistry remain to be dealt with. New findings and applications are frequently reported, and more research is still needed involving separation techniques and ILs.

**Author Contributions:** Writing—original draft preparation and review, M.J.R.-Á.; writing—review and editing, S.C.-B. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was supported by grant PID2019-106708GB-I00 funded by MCIN (Ministry of Science and Innovation of Spain)/AEI/10.13039/501100011033.

**Acknowledgments:** Thank you to all the authors that made this Special Issue possible, and the Separations editorial team for their trust and support.

**Conflicts of Interest:** The authors declare no conflict of interest.

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