

Potential Threats of Ionic Liquids to the Environment and Ecosphere



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Introduction

“Sustainability” is a concept guiding contemporary scientific research in the design, manufacture, and use of more efficient, effective and safer, more benign, and environmentally friendly products and processes [1]. Within this concept, the design of environmentally friendly solvents that could replace the volatile organic solvents currently used has been developed [2]. Ionic liquids (ILs) are an example of designer solvents that have been attracting increased attention for the preparation of greener solvents [3]. By changing the cation or the anion, through the addition of alkyl chains, functional groups, or aromatic rings, ILs can be designed to possess certain features, and the possibilities are almost endless [4]. This designer-like feature is attractive in many fields but creates

difficulties in the assessment of their environmental impact and fate.

Low flammability, stability against air and moisture, high solvation potential, low water content, chemical and thermal stability, high heat capacity, density, and conductivity are common characteristics of ILs, its nonvolatility being the argument most often used to support their “greenness” [5]. Due to their ionic character, almost all ILs are soluble in water [6], which can represent an environmental problem. This means that although ILs may not be hazardous for manipulators (concerning inhalation), their potential impact on water and soils, as well as in the associated biota, could not be neglected. Several studies showed that ILs have, as expected, some toxicity and environmental impact [7–14]. Although ILs are not yet used massively in industrial applications, this may happen in the near future, rendering discharge and contamination of soils and waters a likely scenario and their environmental toxicity being a regulatory variable constraining marketing and license use, for example, in Europe under the scope of REACH regulation [15].

Several biological systems were already used for the evaluation of ILs toxicity, such as bacteria [e.g., 16], green microalgae, crustaceans [e.g., 17], fishes [e.g., 18], amphibians [e.g., 19] plants [e.g., 9], vertebrates [e.g., 20], or cell cultures [e.g., 21]. However, despite the increasing number of studies that attempts to assess their toxic effects, knowledge of their ecotoxicity, and biodegradability is still limited and not completely

clarified, [9] and the feasible prediction of their actual ecological impact is a herculean task due to the countless number of ILs that can be synthesized [22].

This chapter focuses on the existent knowledge on the ecological impact of ILs in soil chemistry and the associated biota, as well as on the general trends that have been established specifically regarding toxicity and biodegradability. The water compartment will not be here discussed since many dedicated reviews are available containing up-to-date information [23–27]. Herein, we will first address how ILs can affect the environment and the main factors that contribute to their impact, toxicity, and biodegradability; then, brief notes on predictive models to assess toxicity and their importance are reported; finally, we will discuss the general trends known regarding IL toxicity and biodegradability and on how to design better IL structures to potentiate environmental safety.

The Path of ILs Toward Threatening the Soil Ecosphere

Sources and Transport

ILs, as essentially all xenobiotics, have the potential to negatively affect the environment and the ecosphere depending on the dose, as they can enter in different compartments, e.g., lithosphere, hydrosphere, and biosphere (so, the ecosphere), and exert toxicity following the onset of alterations in the chemical and physical properties of the compartments. In spite of their low potential as atmospheric contaminants (negligible vapor pressure), ILs can act as environmental pollutants originating in postproduction waste, as well as industrial wastewater discharge or accidents during processing or transportation [27]. Once in the environment, ILs can distribute through the different compartments depending on their physicochemical properties. Water solubility strongly affects the distribution of chemicals through the environment, as well as their toxicity [28], bioavailability, and bioaccumulation potential [6]. Other important features determining environment partitioning are the boiling point, melting point, gas and liquid densities, surface tension,

vapor pressure, air-water partition coefficient, sorption coefficient for soil and sediment, bioconcentration factor, diffusivity in air and water, and phase transfer coefficient for air-soil and air-water [29].

The chemical structure of ILs is a crucial variable on its environmental transport as it is regarding their toxicity (e.g., functional groups, shape, and charge density) [30, 31]. Besides the chemical structure, physical processes like solubility, advection, dispersion, formation, diffusion, sorption on immobile solid phases (soils, sediments, biota), and aggregation also affect the transport of ILs. Finally, the fate of ILs is also dependent on several reactions of oxidation, reduction, complex formation, and biological processes like biotransformation and biodegradation [32].

Bioavailability in the Soil Matrix

Ionic liquids can affect the soil through their tendency to be sorbed into particles of the soil matrix or to dissolve in soil water. Bioavailability of ILs is dependent on sorption processes that affect their retention/mobility, on soil features, and on their physicochemical properties [33]. Adsorption is influenced by both the properties of the soil and the properties of the compound, i.e., size, shape, configuration, molecular structure, solubility, polarity, polarizability, charge distribution of interacting species, and the acid-base nature of the molecule [34, 35]. The molecular transference is of major importance because it constrains the uptake by different organisms, thus necessarily constraining bioavailability and biotransformation [36]. The binding of xenobiotics to soil or sediment normally reduces their overall toxic potential since this process generally decreases the availability of the compound to interact with organisms, also reducing the likelihood of transport, e.g., by leaching [37].

Briefly, hydrophilic ILs dissolve in water but may also sorb into soils; lipophilic ILs can also sorb to soil particles depending on their composition, and in such a case, these will be less bioavailable. Soils with a large fraction of clay particles and organic matter are more prone to sustain higher sorption [38], and electrostatic and hydrophobic interactions [39], hydrogen

bonding [40], and the length of the alkyl chain [36] are major features of ILs ruling sorption onto soil and sediments. ILs with longer alkyl chains are more strongly adsorbed into soils, which naturally links to decreased uptake by the soil biota (e.g., Pawlowska et al. [41] showed that uptake by plant roots is lower from ILs with larger alkyl chains).

IL cations like imidazolium and pyridinium are more prone to be adsorbed in soil, and this reduces their mobility. On the contrary, anions normally are not retained in soil colloids [33]. Since soils are normally negatively charged matrices [33], limited interactions between IL anions and soil colloids are expected, which may translate into to a higher relative bioavailability [42].

Interaction of ILs with the Biota

Following uptake, which can be through ingestion or passive diffusion, ILs can affect the biota through different pathways, primarily depending on their lipophilicity/hydrophilicity. They can then bioaccumulate [43] or degrade into metabolites that can eventually be more toxic than the initial compound [44]. A key feature that constrains passive diffusion of ILs across biological membranes is IL solubility in water versus lipids, conventionally given by the octanol-water partition coefficient (K_{ow}). The higher the K_{ow} , the more lipophilic the IL, which, following uptake, can associate to lipoproteins and membranes, becoming more difficult to excrete. For example, longer alkyl chains, mostly in the cation, increase the IL lipophilicity, facilitating its transport across the cell membrane and thus promoting the accumulation of the molecule in the cytoplasm, which exacerbates toxicity [45]. The correlation between long alkyl chains and toxicity was already described in many test organisms such as *Caenorhabditis elegans* [46], *Staphylococcus aureus*, *Pseudomonas aeruginosa* [47], *Scenedesmus quadricauda*, and *Chlamydomonas reinhardtii* [48], *Aliivibrio fischeri*, and *Daphnia magna* [45]. On the other hand, hydrophilic ILs mainly dissolve in blood and are more readily excreted in feces and urine [49].

The primary toxicity mechanism of ILs involves cell membrane damaging and/or reactive

oxygen species (ROS) production. These change the physiological functions of the membrane and can lead to the liberation of cellular content and cell death [50]. In this context, Petkovic et al. [51] studied the membrane integrity of the fungus *Aspergillus nidulans* after exposure to alkyltributylphosphonium chlorides, finding that systematic elongation of the alkyl chain on the cation side caused increased (by 25 up to 90%) cell damage. Kulacki and Lamberti [48] showed the same trend for other organisms such as microalgae. However, differences in cell wall structure may play an important role in protecting organisms from toxic effects. Latala et al. [52] suggest that organisms with siliceous cell walls (e.g., diatoms) are more sensitive to disruption by ILs, followed by cellulose- and glycoprotein-based cell walls. This example of compositional-dependent sensitivity highlights the need to cover for different organisms when attempting to broadly understand the effects of ILs [50].

Studies at molecular level have been dissecting these interactions of ILs with biological systems. Cornmell et al. [43] showed that trihexyltetradecylphosphonium bis(trifluoromethylsulfonyl)imide restrictively accumulates in the cell membrane of *Escherichia coli*, evidencing that the toxicity mechanism is directly related to the lipophilic profile of ILs and based on membrane damage. Apart from direct membrane damage, ILs can induce ROS production, including $O_2^{\cdot-}$, OH^{\cdot} , and H_2O_2 , as shown by Du et al. [53] by exposing the zebra fish to 1-methyl-3-octylimidazolium bromide. ROS are crucial in apoptosis and signal transmission; however, their accumulation leads to DNA damage (e.g., genotoxicity) and lipid peroxidation whenever the antioxidant defense of the affected cells is overcome [54]. In a study conducted with earthworms (*Eisenia fetida*) exposed to 1-butyl-3-methylimidazolium tetrafluoroborate, lipid peroxidation and DNA damage were evidenced; the authors additionally showed that induced DNA damage was time- and dose-dependent [55]. Also in the plant *Vicia faba*, the increase in ROS and DNA damage promoted by ILs was described Liu et al. [56]. Recent research with the microalgae *Scenedesmus obliquus* correlates oxidative stress

with effects at higher levels of biological organization, namely, population growth, by four different types of ILs, 1-hexyl-3-methylimidazolium nitrate, 1-hexyl-3-methylimidazolium chloride, N-hexyl-3-methylpyridinium bromide, and N-hexyl-3-methylpyridinium chloride [57]. In all cases (although more prominently for imidazolium-compared to pyridinium-based ILs or for nitrate and bromide anions compared to chloride), ROS content increased with IL concentration, and as the cell antioxidant system cannot withstand high ROS levels, oxidative damage occurs and ultimately translates into cell death, which reflects in growth inhibition.

It was recently found that ILs may also cause structural changes in organelles like chloroplasts, nucleus, mitochondria, and rough endoplasmic reticulum [58].

IL Toxicity

Commonly, studies addressing IL environmental toxicity only considered short-term exposure and acute toxicity. Several organisms have been used for the purpose such as bacteria and fungi (e.g., *Aliivibrio fischeri*), algae (e.g., *Raphidocelis subcapitata*), plants (e.g., *Triticum aestivum*), invertebrates (e.g., *Daphnia* sp., *Eisinia fetida*), and vertebrates (e.g., fish). However, few studies considered IL toxicity toward multiple functionally relevant models (see, e.g., Santos et al. [17]) or through community approaches (see, e.g., Maltby and Naylor [59]). These studies are a keystone because they demonstrate that toxicity trends of ILs are species-dependent. In general, most studies showed relatively high toxicity and low biodegradability of ILs with long alkyl chain-based cations, due to their lipophilicity. To reduce the toxicity, functionalization of the IL structure by adding oxygenated groups can be recommended. The counteranion has little or no effect. Below, studies concerning the main groups of organisms (Tables 1 and 2 summarize the most significant knowledge on IL toxicity focusing the soil compartment) and main trends observed in IL toxicity patterns will be discussed, while more complete view on these aspects can be found, e.g., in Pham

et al. [23] or Gomes et al. [68]. Data on toxicity to soil bacteria and fungi were not compiled in a similar table since most studies addressing IL effects in such organisms use species such as *Escherichia coli*, *Staphylococcus aureus*, or *Candida albicans*, which are models for human health risk assessment and biotechnological applications. All search hits were carefully analyzed, and these prominent focuses were confirmed, highlighting the scarcity of information regarding the toxicity of ILs to environmentally relevant soil microorganisms, e.g., *Actinomycetes* or *Firmicutes*.

Still, ILs proved to have antimicrobial and antifungal activity [69–72]. Increasing toxicity follows the increase of the alkyl chain substituent in the pyridinium, imidazolium, and quaternary ammonium salts, and the anion has little influence in microbial toxicity [73–75]. Gram-positive bacteria seem to be more sensitive to ILs, possibly due to their cell wall composition [75, 76]. Considering specifically environmental assessment, the most tested species of bacteria is *Aliivibrio fischeri*, which is an ecotoxicological model [77] showing that anions have little influence and cations play the major role in IL toxicity [45]. Fungi are more tolerant to ILs than bacteria, as shown by Deive et al. [76] with cholinium chloride, 1-ethyl-3-methylimidazolium chloride, and 1-ethyl-3-methylimidazolium ethyl sulfate. These authors remark that at high concentrations, even the most benign ILs like the ones derived from cholinium cation [78] can significantly affect the microbial fauna of the soil.

Several studies also addressed the toxicity of ILs in plants, especially edible species, agreeing that IL toxicity is species-dependent [9, 62, 79, 80] and dose-dependent [56, 58, 61, 81]. In plants, photosynthesis, oxidative stress [62], root and shoot growth [62, 80], and germination [9, 79, 81] are negatively affected by ILs. However, Tot et al. [80] found conflicting results (no effects in photosynthesis and oxidative stress) with 1-(2-oxybutyl)-3-methylimidazolium chloride, 1-(2-oxypropyl)-3-methylimidazolium chloride, 1-(3-hydroxypropyl)-3-ethylimidazolium chloride, 1-(3-hydroxypropyl)-3-methylimidazolium chloride, 1-(2-hydroxyethyl)-3-methylimidazolium chloride, 1-butyl-3-methylimidazolium

Potential Threats of Ionic Liquids to the Environment and Ecosphere, Table 1 Summary of the toxicity of ILs and their precursors to plants. Wheat (*Triticum aestivum*), the water cress (*Lepidium sativum*), and the spring barley (*Hordeum vulgare*) were selected as the most commonly tested plants in this context (a systematic search on Web of Science[®], by Clarivate Analytics,

supported this restriction criterion), thus the collection with broader IL coverage for a non-exhaustive compilation. Only studies providing median effect concentration (EC₅₀) estimates based on feasible concentration-response models were included. The values of EC₅₀ are reported exactly as the authors reported regarding the units associated

| ILs | EC ₅₀ | | | Endpoint | Reference | |
|--|----------------------------|----------------------------|----------------------------|--------------|-----------|--------------|
| | Wheat | Water cress | Spring barley | | | |
| 1-Butyl-3-methylimidazolium tetrafluoroborate | 1700 µmol.L ⁻¹ | 1900 µmol.L ⁻¹ | | Growth | [42] | |
| 1-Methyl-3-octylimidazolium tetrafluoroborate | 290 µmol.L ⁻¹ | 300 µmol.L ⁻¹ | | | | |
| Sodium tetrafluoroborate | 4500 µmol.L ⁻¹ | | | | | |
| Lithium bis (trifluoromethylsulfonyl)imide | 100 µmol.L ⁻¹ | 1200 µmol.L ⁻¹ | | | | |
| 1-Butyl-3-methylimidazolium chloride | >3000 µmol.L ⁻¹ | >3000 µmol.L ⁻¹ | | | | |
| 1-Butyl-3-methylimidazolium octylsulfate | >3000 µmol.L ⁻¹ | >3000 µmol.L ⁻¹ | | | | |
| 1-Butyl-3-methylimidazolium bis(trifluoromethylsulfonyl) imide | 110 µmol.L ⁻¹ | 400 µmol.L ⁻¹ | | | | |
| 1-Butyl-3-methyl-imidazolium bis(trifluoromethyl)imide | >3500 µmol.L ⁻¹ | >3500 µmol.L ⁻¹ | | Germination | [60] | |
| 1-Ethyl-3-methylimidazolium chloride | | 0.1046 mg.mL ⁻¹ | | | | |
| 1-Butyl-3-methylimidazolium chloride | | 0.0510 mg.mL ⁻¹ | | | | |
| 1-Hexyl-3-methylimidazolium chloride | | 0.0122 mg/mL ⁻¹ | | Root length | [61] | |
| 1-[(1R,2S,5R)-(-)-menthoxyethyl]-3-methylimidazolium hexafluorophosphate | | | 42.48 mg. Kg ⁻¹ | | | Shoot length |
| | | | 9.993 mg. Kg ⁻¹ | | | Fresh weight |
| | | | 9.844 mg. Kg ⁻¹ | | | |
| 1-[(1R,2S,5R)-(-)-menthoxyethyl]-3-methylimidazolium trifluoroacetate | | | 132.6 mg. Kg ⁻¹ | Root length | | |
| | | | 60.33 mg. Kg ⁻¹ | Shoot length | | |
| | | | 50.38 mg. Kg ⁻¹ | Fresh weight | | |

(continued)

Potential Threats of Ionic Liquids to the Environment and Ecosphere, Table 1 (continued)

| ILs | EC ₅₀ | | | Endpoint | Reference |
|---|-------------------------|-------------|----------------------------|--------------|-----------|
| | Wheat | Water cress | Spring barley | | |
| 1-Butyl-1-methylpyrrolidinium hexafluorophosphate | | | 88.97 mg. Kg ⁻¹ | Root length | [62] |
| | | | 10.16 mg. Kg ⁻¹ | Shoot length | |
| | | | 10.04 mg. Kg ⁻¹ | Fresh weight | |
| 1-Butyl-1-methylpiperidinium hexafluorophosphate | | | 114.9 mg. Kg ⁻¹ | Root length | |
| | | | 19.86 mg. Kg ⁻¹ | Shoot length | |
| | | | 11.40 mg. Kg ⁻¹ | Fresh weight | |
| 1-Butyl-4-methylpyridinium hexafluorophosphate | | | 97.78 mg. Kg ⁻¹ | Root length | |
| | | | 14.49 mg. Kg ⁻¹ | Shoot length | |
| | | | 10.31 mg. Kg ⁻¹ | Fresh weight | |
| 1-Methyl-3-octylimidazolium chloride | 12.9 mg.L ⁻¹ | | | Germination | [63] |
| | 7.33 mg.L ⁻¹ | | | Shoot length | |
| | 3.89 mg.L ⁻¹ | | | Root length | |
| | 9.32 mg.L ⁻¹ | | | Dry weight | |
| 1-Methyl-3-octylimidazolium bromide | 12.4 mg.L ⁻¹ | | | Germination | |
| | 7.14 mg.L ⁻¹ | | | Shoot length | |
| | 3.56 mg.L ⁻¹ | | | Root length | |
| | 7.25 mg.L ⁻¹ | | | Dry weight | |
| Benzyltrimethylammonium chloride | | | 654.7 mg. Kg ⁻¹ | Root length | [64] |
| | | | 1008 mg. Kg ⁻¹ | Shoot length | |
| | | | 735.6 mg. Kg ⁻¹ | Fresh weight | |
| Benzyltriethylammonium chloride | | | 2120 mg. Kg ⁻¹ | Root length | |
| | | | 2798 mg. Kg ⁻¹ | Shoot length | |
| | | | 907.5 mg. Kg ⁻¹ | Fresh weight | |

chloride, and imidazolium chloride in cucumber. While some studies found that IL phytotoxicity depends on the cation structure [81] and less on the anion [63, 81], others showed cations playing a minor role [62] and anions influencing more significantly toxicity [58, 79]. Again, an increase in the alkyl chain generally translates into

increasing toxicity (see Bubalo et al. [81] and Peric et al. [79] for imidazolium-based ILs; Oliveira et al. [71] for protic ILs), but this tendency does not always apply (Tot et al. [80] and Table 1).

Regarding ecotoxicological studies with invertebrates, *Daphnia magna* is the most used model,

Potential Threats of Ionic Liquids to the Environment and Ecosphere, Table 2 Summary of the toxicity of ILs and their precursors to animals. Springtails (*Folsomia candida*), earthworms (*Eisenia foetida*), and nematodes (*nematode*) were selected as the most commonly tested animals in this context (a systematic search on Web of Science[®], by Clarivate Analytics, supported this

restriction criterion), thus the collection with broader IL coverage for a non-exhaustive compilation. Only studies providing median effect concentration (EC_{50}) estimates based on feasible concentration-response models were included. The values of EC_{50} are reported exactly as the authors reported regarding the units associated

| ILs | EC_{50} | | | Endpoint | Reference |
|---|--------------------------------|-----------|---|--------------|-----------|
| | Springtail | Earthworm | <i>nematode</i> | | |
| 1-Methyl-3-octylimidazolium tetrafluoroborate | 100 $\mu\text{mol. Kg}^{-1}$ | | | Reproduction | [42] |
| Lithium bis(trifluoromethylsulfonyl) imide | 18 $\mu\text{mol. Kg}^{-1}$ | | | Reproduction | |
| 1-Butyl-3-methylimidazolium octylsulfate | 1100 $\mu\text{mol. Kg}^{-1}$ | | | Reproduction | |
| 1-Butyl-3-methylimidazolium bis (trifluoro-methylsulfonyl)imide | 30 $\mu\text{mol. Kg}^{-1}$ | | | Reproduction | |
| 1-Ethyl-3-methylimidazolium bromide | | | $2.23 \times 10^{-1} \text{Mol.L}^{-1}$ | Mortality | [46] |
| 1-Butyl-3-methylimidazolium bromide | | | $4.10 \times 10^{-2} \text{Mol.L}^{-1}$ | Mortality | |
| | | | 6.62 mg. mL^{-1} | Mortality | [65] |
| 1-Hexyl-3-methylimidazolium bromide | | | $1.88 \times 10^{-2} \text{Mol.L}^{-1}$ | Mortality | [46] |
| 1-Methyl-3-octylimidazolium bromide | | | $1.08 \times 10^{-2} \text{Mol.L}^{-1}$ | Mortality | |
| | | | 1.33 mg. mL^{-1} | Mortality | [65] |
| 1-Dodecyl-3-methylimidazolium bromide | | | $5.31 \times 10^{-4} \text{Mol.L}^{-1}$ | Mortality | [46] |
| | | | 0.11 mg. mL^{-1} | Mortality | [65] |
| 1-Tetradecyl-3-methylimidazolium bromide | | | $6.48 \times 10^{-5} \text{Mol.L}^{-1}$ | Mortality | [46] |
| 1-Hexadecyl-3-methylimidazolium bromide | | | $4.85 \times 10^{-5} \text{Mol.L}^{-1}$ | Mortality | |
| 1-Propenyl-3-methylimidazolium chloride | | | $1.77 \times 10^{-1} \text{Mol.L}^{-1}$ | Mortality | |
| 1-Butyl-3-methylimidazolium chloride | | | $8.85 \times 10^{-2} \text{Mol.L}^{-1}$ | Mortality | |
| | >3000 $\mu\text{mol. Kg}^{-1}$ | | | Reproduction | [42] |

(continued)

Potential Threats of Ionic Liquids to the Environment and Ecosphere, Table 2 (continued)

| ILs | EC ₅₀ | | | Endpoint | Reference |
|--|------------------|---------------------------------|--|---------------------|-----------|
| | Springtail | Earthworm | <i>nematode</i> | | |
| 1-Pentyl-3-methylimidazolium chloride | | | 6.65×10^{-2} Mol.L ⁻¹ | Mortality | [46] |
| 1-Methyl-3-octylimidazolium chloride | | | 1.09×10^{-4} Mol.L ⁻¹ | Mortality | |
| 1-Decyl-3-methylimidazolium chloride | | | 2.68×10^{-3} Mol.L ⁻¹ | Mortality | |
| 1-Tetradecyl-3-methylimidazolium chloride | | | 1.06×10^{-4} Mol.L ⁻¹ | Mortality | |
| 1-Hexadecyl-3-methylimidazolium chloride | | | 2.35×10^{-5} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium acetate | | | 8.38×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium dibutyl phosphate | | | 2.71×10^{-3} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium nitrate | | | 5.27×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium iodide | | | 8.71×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium tetrafluoroborate | | | 1.13×10^{-3} Mol.L ⁻¹ | Mortality | |
| | | 744–870 mg. Kg ⁻¹ | | Mortality (7 d) | [55] |
| | | 489–678 mg. Kg | | Mortality (14 d) | [55] |
| | | >4400 μmol. Kg ⁻¹ | | Reproduction | [42] |
| 1-Butyl-3-methylimidazolium dicyanamide | | | 3.54×10^{-2} Mol.L ⁻¹ | Mortality | [46] |
| 1-Butyl-3-methylimidazolium trifluoromethanesulfonate | | | 2.79×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium tosylate | | | 9.97×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium thiocyanate | | | 5.33×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium bis (trifluoromethylsulfonyl)imide | | | 1.68×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium perchlorate | | | 4.44×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Butyl-3-methylimidazolium trifluoroacetate | | | 3.11×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Propenyl-3-methylimidazolium bromide | | | 1.39×10^{-1} Mol.L ⁻¹ | Mortality | |
| 1-Pentyl-3-methylimidazolium bromide | | | 3.35×10^{-2} Mol.L ⁻¹ | Mortality | |
| 1-Ethyl-3-methylimidazolium chloride | | | 2.89×10^{-1} Mol.L ⁻¹ | Mortality | |
| 1-Hexyl-3-methylimidazolium chloride | | | 2.87×10^{-2} Mol.L ⁻¹ | Mortality | |

(continued)

Potential Threats of Ionic Liquids to the Environment and Ecosphere, Table 2 (continued)

| ILs | EC ₅₀ | | | Endpoint | Reference |
|--|------------------|------------------------------|------------------------------|---------------------|-----------|
| | Springtail | Earthworm | nematode | | |
| 1-Decyl-3-methylimidazolium bromide | | | 0.42 mg. mL ⁻¹ | Mortality | [65] |
| 1-Butyl-2-methyl-3-methylimidazolium bromide | | | 6.64 mg. mL ⁻¹ | Mortality | |
| 1-Methyl-3-n-octylimidazolium bromide | | | 1.54 mg. mL ⁻¹ | Mortality | |
| 1-Decyl-2,3-methylimidazolium bromide | | | 0.39 mg. mL ⁻¹ | Mortality | |
| 1-Dodecyl-2,3-methylimidazolium bromide | | | 0.09 mg. mL ⁻¹ | Mortality | |
| 1-Ethyl-3-methylimidazolium bromide | | | | Mortality (48 h) | [66] |
| | | 1441 mg. Kg ⁻¹ | | Mortality (14 d) | |
| 1-Butyl-3-methylimidazolium bromide | | | | Mortality (48 h) | [67] |
| | | 358 mg. Kg ⁻¹ | | Mortality (14 d) | [66] |
| 1-Hexyl-3-methylimidazolium bromide | | | | Mortality (48 h) | [67] |
| | | 306 mg. Kg ⁻¹ | | Mortality (14 d) | [66] |
| 1-Methyl-3-octylimidazolium bromide | | | | Mortality (48 h) | [67] |
| | | 159 mg. Kg ⁻¹ | | Mortality (14 d) | |
| 1-Decyl-3-methylimidazolium bromide | | | | Mortality (48 h) | |
| | | 153 mg. Kg ⁻¹ | | Mortality (14 d) | [66] |
| 1-Dodecyl-3-methylimidazolium bromide | | | | Mortality (48 h) | [67] |
| | | 160 mg. Kg ⁻¹ | | Mortality (14 d) | [66] |

but it represents the aquatic compartment. The most used species to assess IL effects in the soil compartment are the springtail *Folsomia candida*, the earthworm *Eisenia fetida*, and the nematode *Caenorhabditis elegans*, yet the latter is very frequently explored as a human health model. Although scarcer, these studies showed that IL toxicity follows the same trend already described for plants: it is dose- and species-dependent [42, 65] and it increases with the elongation of alkyl chains [65, 66]. At the subcellular level, Shao et al. [55, 66] also confirmed that exposure of *Eisenia fetida* to imidazolium bromide ionic

liquids increased the ROS content and caused DNA damage. The number of studies with vertebrates is considerably smaller mostly due to ethical concerns. Zebra fish (*Danio rerio*) [18], amphibians (e.g., *Rana nigromaculata*) [19], rats, and mice [20] are among the most used animals to assess IL toxicity. These studies showed that ILs can promote embryonic mortality and malformations in *Rana nigromaculata* (see Li et al. [19] for 1-methyl-3-octylimidazolium bromide), as well as reduction of fetal weight and malformations in rats, suggested teratogenicity (see Bailey et al. [20] with 1-butyl-3-methylimidazolium chloride).

IL Biodegradability

The biodegradability of ILs, as for any other contaminant, modulates its environmental toxicity. The term biodegradability is related with the degradation/transformation of chemicals by microorganisms, plants, and animals. If chemicals are biodegradable, complete transformation into carbon dioxide, water, and mineral salts (i.e., mineralization) may occur [82]. In other cases, chemicals can be transformed into degradation products (also designed as metabolites) that can be more or less toxic and more or less persistent than the original chemical [44, 83].

The chemical structure of ILs strongly affects their biodegradability, and detailed reviews are available in this topic (Boethling et al. [84], Coleman and Gathergood [85], Jordan et al. [86]). However, the actual environmental conditions of IL biodegradation have a tremendous influence on their biodegradability, this being a scenario mostly uncovered in laboratory studies. The appropriate microorganisms need to be present, as well as the appropriate nutrients; also important are the conditions of temperature, pH or pO_2 , the concentration, and composition of the substrate [87].

The imidazolium family is the most often studied, with 1-alkyl-3-methylimidazolium-based ILs being the most scrutinized. Studies suggest that shorter alkyl side chains ($< C_6$) lead to low biodegradability, while longer alkyl side chains ($> C_6$) of the cations are more easily biodegradable [88]. Unfortunately for the design of greener ILs, this is not in agreement with the general trends found for environmental toxicity, where longer alkyl chains are more prone to be more toxic [50, 73–75, 79]. Biodegradability could be improved by increasing IL lipophilicity to facilitate uptake by biodegradation agents [88]. Also, the introduction of an ester group in the side alkyl chain also improves biodegradability of imidazolium-based ILs, compared to the corresponding non-functionalized ILs [89]. The anion shows poorer influence than the cation in biodegradability [89, 90]. Harjani et al. [89] showed that the functionalization of the *N*-substituent of the imidazolium ions affects biodegradability as well as alkylsulfate ions,

saccharin, and lactate. Morrissey et al. [91] observed that ILs with butoxy and propoxy-terminus are readily biodegradable, while ILs with methoxy- or ethoxy-terminal substitution are less biodegradable ($< 60\%$, which is the threshold for readily biodegradable).

Pyridinium-based ILs are normally more easily biodegraded than imidazolium-based ILs [44], the cleavage of pyridinium and imidazolium ring being the constraints [44, 83]. Consistently, an increase in the alkyl chain increases biodegradability of pyridinium-based ILs [44], e.g., the increase in alkyl chains from C_4 to C_{11} improves biodegradability considering both cation and anion sites [92]. The introduction of a 1-(2-hydroxyethyl) group in the pyridinium cation was suggested to be a driver of a higher biodegradability nature [93]. In pyridinium-based ILs, the cation is more influential than the anion, although the presence of an amide group in pyridinium rings does not improve biodegradability [90]. Methyl or ethyl ether groups seem not to represent significant functionalization in this context [93].

Docherty et al. [83] found that the degradation products of 1-butyl-3-methylpyridinium bromide, 1-hexyl-3-methylpyridinium bromide, and 1-octyl-3-methylpyridinium bromide are less toxic than the initial compounds to *Daphnia magna*, suggesting that the biodegradation in the aquatic compartment could decrease the toxicity. However, this is not always true as demonstrated before by the same authors [44]. A final relevant remark is worth making regarding the use of renewable materials, which does not necessarily improve IL biodegradability: several mandelic acid-based ILs did not reach $>60\%$ biodegradation in 28 days and cannot be considered as readily biodegradable [94].

Predictive Methods as a Tool for IL Design

IL designer nature makes the study of their environmental impact a daunting task. In this sense, the use of predictive models like quantitative structure-activity relationships (QSAR) is a powerful tool in the study of their environmental impact and fate. These models are an alternative to experimental

assessment, with positive economic implications and improving animal welfare [95]. However, they should be fed and corroborated by experimental data to ensure feasibility. QSAR models are seen as reliable by the Organization for Economic Co-operation and Development [96] and are accepted and encouraged to be used by several regulatory authorities, e.g., the European Chemicals Agency [97]. A specific note is worth making here regarding *Kow* since this is a variable used (both as a predictor and as the estimate) in QSAR models within environmental risk assessment protocols [98]. Log *Kow* values lower than 4.5 (hydrophilic compounds) indicate that the lipophilicity of the compounds is insufficient to exceed bioaccumulation benchmarks [99]. For example, the studies of Montálban et al. [100] and Ventura et al. [101] show that imidazolium- and pyridinium-based ILs have lower *Kow* values than traditional organic solvents, thus lower likelihood of bioaccumulation.

QSAR models are generally applied to predict how the activity (QSAR), properties (QSPR), or toxicity (QSTR) of a group of compounds varies with structural variation [102]. This could be applied also to chemicals that are not yet synthesized and also to chemicals that, due to its extremely hazardous nature, are difficult to test experimentally [103]. *Aliivibrio fischeri* and *Daphnia magna* are the most studied organisms in the QSAR context considering ILs [e.g., 104–107]. Among the most widely studied cations are imidazolium, pyridinium, pyrrolidinium, quaternary ammonium, and piperidinium. Regarding the anions, monovalent halides, tetrafluoroborates, fluorophosphates, trifluoromethanesulfonylimide (trifluoromethyl)sulfonyl, alkyl sulfates, and dicyanamide are the most studied [102]. These QSAR studies showed that the lipophilicity and its contributing factors, e.g., molecular size, branching, and hydroxyl groups, are all important variables modulating the toxicity in *Aliivibrio fischeri*. Also important is the presence of positively charged atoms in anions and nitrogen in cationic aromatic rings, as demonstrated to both *Aliivibrio fischeri* and *Daphnia magna*.

Summary of Trends in IL Toxicity and Biodegradability Ruling the Application of QSAR

It is known that the toxicity and biodegradability of ILs strongly depend on their structure; however, there are contradictory results preventing the establishment of heuristic rules in this context. Still, some general assumptions can be made, including for the development of feasible QSAR models, always keeping in mind that toxicity is species-dependent and that biodegradability is strongly affected by the environmental context. These assumptions are synthesized in Box 1 from several studies [8, 9, 23, 44, 45, 50, 58, 62, 73–76, 79, 80, 84, 88], explored in detail previously in this chapter.

Box 1 Summary of trends for designing ILs toward a better performance regarding environmental toxicity and biodegradability

1. Toxicity of ILs is species-dependent

Importantly, this means that predictions made considering one species may not apply to other species, thus may not adequately inform *per se* on the noxious potential toward the biota.

2. Biodegradability is strongly dependent on the environmental context

The specific microorganism communities standing in each threatened environmental compartment as well as physicochemical properties of each environmental matrix (e.g., organic matter content and type and amount of clay minerals in soils) constrain biodegradation; thus, rates assessed under standard conditions may not represent actual scenarios.

3. Longer alkyl chains increase ILs' toxic potential

(continued)

Box 1 Summary of trends for designing ILs toward a better performance regarding environmental toxicity and biodegradability (continued)

ILs with longer alkyl chains are more lipophilic, which means that they have better ability to interact with or permeate through cell membrane and onset a toxic challenge.

4. Longer alkyl chains turn ILs more biodegradable

This may pose a design conflict since to lower toxicity, alkyl chains should be shorter, but by this shortening one impairs the IL biodegradability. This is a problem depending on rates and the extents of biodegradation that can be achieved in one or the other configuration, as well as on the magnitude of the change in toxicity observed when the structure changes.

5. Cations play a stronger role in ILs' toxicity than anions

Meaning that by engineering the cation, one can achieve toxicity changes of a larger magnitude than by focusing on the anion.

6. The pyridinium cation is less toxic than imidazolium and also more easily biodegradable

If performing equally well in the focused application, selection among different IL families can be the simplest way to conform with environmental protection requirements.

7. Introduction of functional polar groups to the alkyl chain could reduce the toxicity

Polar groups can reduce hydrophobicity, inherently decreasing the affinity toward cell membranes.

Searching for the Ideal IL, the Least Environmentally Hazardous, Still Up to the Function

An ideal IL needs to meet the requirements of its application, but it also needs to be nontoxic, biodegradable, and ideally renewable. In this sense, several studies focused on recycling ILs [e.g., 108, 109], and techniques of distillation and extraction are among the most focused for the purposes. Volatile products can be isolated from ILs by distillation under mild conditions, while low-volatility products can be separated by extraction or membrane processes, such as nanofiltration and evaporation [110]. The development of a new generation of ILs is another route toward environmental sustainability where synthetic quaternary cations (e.g., ammonium, imidazolium, and pyridinium) are replaced by naturally occurring cations such as cholinium chloride and harmful fluorinate anions (e.g., tetrafluoroborate and hexafluorophosphate) by anions from natural sources, such as amino acids or organic acids. There are studies exploring lactates [111], sugar substitutes [112], or amino acids [14]. These new ILs are expected to be less toxic and less expensive compared to conventional ILs [50]. However, the use of nontoxic materials does not always guarantee that the synthesized IL is nontoxic. Parajó et al. [14] tested analogues of glycine-betaine-based ILs and glycine-betaine-based ILs with the bacteria *Aliivibrio fischeri* and the microalgae *Raphidocelis subcapitata*, and all ILs were found hazardous for the aquatic environment. Oppositely, Hou et al. [113] tested cholinium-based ILs with different amino acids and observed their low toxicity regarding acetylcholinesterase activity in different bacteria. Radošević et al. [114] also found low toxicity of cholinium-based ILs using amino/organic acids as anions on channel catfish ovary cells.

A final note is worth making here re-highlighting the essentials of the previous section given its relevance in the search for the ideal IL: the conflict between structural features that cause toxicity and features that increase biodegradability is the main barrier (Box 1). For example, the elongation of alkyl chains or the introduction of functional

polar groups was shown to reduce the toxicity of ILs but also to increase biodegradability. Non-conflicting scenarios can also be highlighted: pyridinium has been found to be more environmentally friendly than imidazolium, which is valid for toxicity as well as for biodegradability (Box 1). Despite the efforts and data obtained so far, aiming to establish appropriate heuristic rules, it seems that the main question remains on what the best solution is to deal with the duality toxicity versus biodegradability.

Cross-References

- ▶ Abiotic Degradation of Ionic Liquids (ILs)
- ▶ Aquatic Toxicology of Ionic Liquids (ILs)
- ▶ Biodegradability of Ionic Liquids (ILs) under Aerobic and Anaerobic Conditions
- ▶ Methods for Biodegradability and Toxicity Assessment of Ionic Liquid
- ▶ Terrestrial Toxicity of Ionic Liquids

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