Recovery of Syringic Acid from Industrial Food Waste with Aqueous Solutions of Ionic Liquids

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[S] *Supporting Information*

ABSTRACT: Phenolic acids present in industrial food waste display a broad range of biological activities and related health benefits, among which their strong antioxidant and free-radical scavenger activities are the most investigated. However, food waste is still scarcely considered as an alternative source for these compounds, and volatile organic solvents for their extraction are still the preferred choice. In this work, aqueous solutions of ionic liquids (ILs) with hydrotropic or surfactant character were investigated to improve the solubility and effectively extract syringic acid from Rocha pear peels, a relevant waste of the food industry. The solubility of syringic acid in aqueous solutions of a wide variety of ILs at different concentrations at 30 °C was first ascertained. The results obtained show that ILs that behave as cationic hydrotropes are the best option to enhance the solubility of syringic acid in aqueous media, with increases in solubility of up to 84-fold when compared with water. After identifying the most promising IL aqueous solutions, a response surface methodology was used to optimize operational extraction conditions (extraction time, solid−liquid (biomass−solvent) ratio, and temperature), leading to a maximum extraction yield of syringic acid of 1.05 wt % from pear peels. Both the solvent and biomass reuse were additionally investigated, allowing to overcome the biomass−solvent ratio constraints and mass-transfer effects and leading to extraction yields of 2.04 and 2.22 wt %. Although other methods for the recovery of syringic acid can be applied, taking advantage of the hydrotropy phenomenon and the solubility of syringic acid dependency with the IL concentration, water was used as an antisolvent, allowing to obtain 77% of the extracted phenolic acid. A continuous countercurrent process conceptualized for large-scale applications and that further allows the solvent recycling after the recovery of syringic acid is finally proposed.

KEYWORDS: Food industrial wastes, Syringic acid, Extraction, Recovery, Ionic liquids
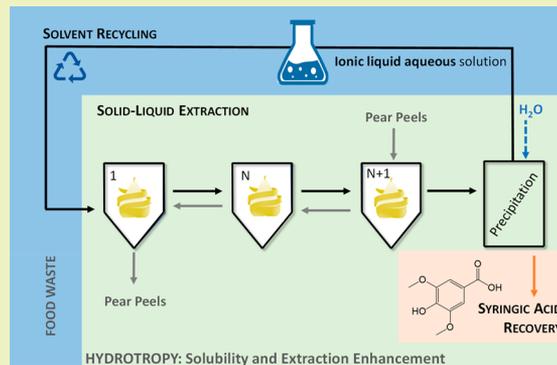
INTRODUCTION

Biomass is a source of high-value compounds with relevant biological activities such as phenolic compounds, one of the most abundant families of secondary metabolites in plants.[1] The interest in phenolic compounds results from their broad range of biological activities and related health benefits, among which the strong antioxidant and free-radical scavenger activities are well-established.[2] These properties are responsible for their application in the food, nutraceutical, cosmetic, and pharmaceutical industries.[3] Examples of phenolic compounds present in biomass are, among others, vanillic, gallic, protocatechuic, ellagic, and syringic acids, quercetin, vanillin, and resveratrol.[1]

Most of these compounds can be obtained from waste generated by agroforest and agrofood industries, thus contributing to the full valorization of feedstocks in an integrated biorefinery perspective and, ultimately, contributing to a circular economy.[4] Accordingly, the development of sustainable extraction, purification, and recovery processes of high-value compounds from food industry waste, suitable for industrial implementation, is nowadays a crucial need and in line with the United Nations Sustainable Development Goals.[5,6]

Most of these compounds, and particularly those with recognized health benefits, are of high cost due to the complex and multistep methods required for their extraction, purification, and recovery. The extraction of these compounds from biomass is commonly carried out using volatile organic solvents,[7] which recently have been combined with microwave- and ultrasound-assisted methods to improve the extraction efficiency.[8] Supercritical CO_2 extraction and alternative solvents, such as ionic liquids (ILs) and deep eutectic solvents, have also been investigated.[8−10] In addition to the extraction step, further purification steps are required, typically carried
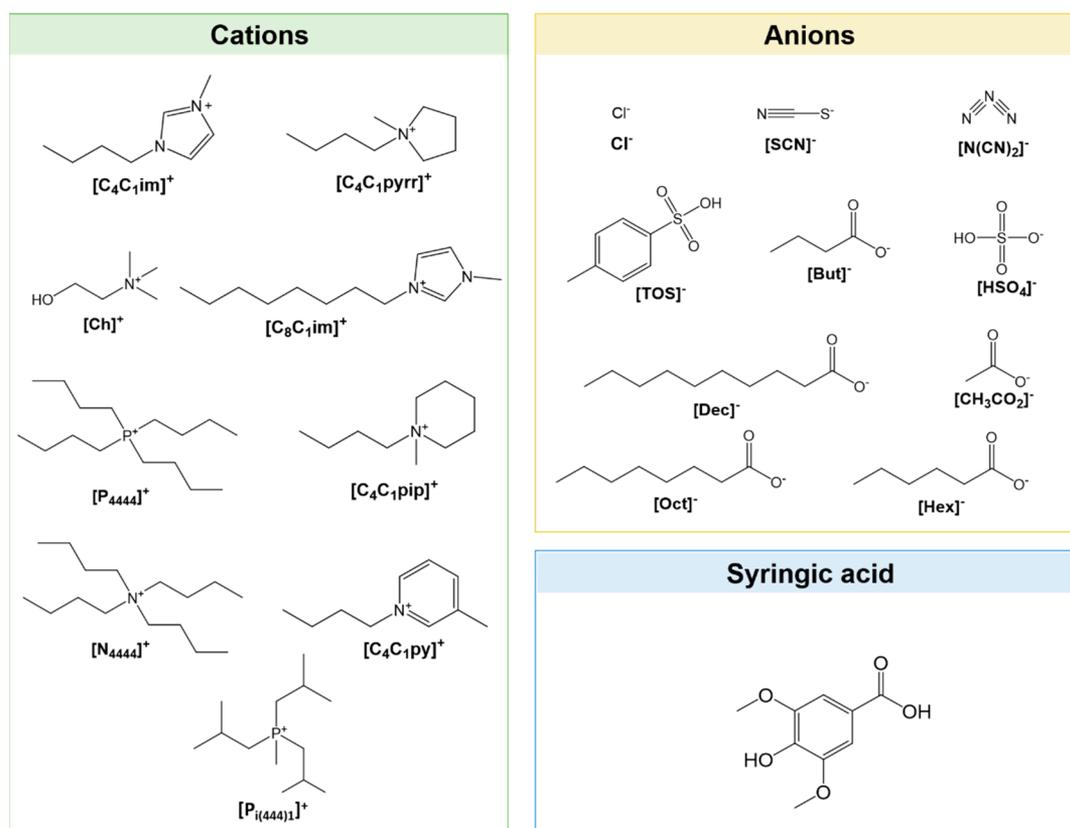
Figure 1. Chemical structures of syringic acid and cations/anions of the ionic liquids investigated.

out by solid-phase extraction, back-extraction with organic solvents, evaporation of the solvents or compounds (when applicable), and induced precipitation.[9]

Among the several solvents that can be used for the extraction of bioactive compounds from food industry waste and taking into account their envisioned consumption by humans, water certainly corresponds to the most benign solvent and preferred choice. Nevertheless, many bioactive compounds display a limited solubility in water,[11] restricting its use for their effective extraction from biomass. To increase the solubility of bioactive compounds in aqueous solutions, additives such as surfactants or hydrotropes can be used.[12,13] Surfactants have long alkyl side chains, have well-defined critical micelle concentration (CMC) values, and are able to form micelles. Therefore, surfactants may be used in micelle-mediated extraction processes, which are particularly relevant to enhance the solubility and to extract highly hydrophobic compounds, such as triterpenic acids.[14,15] On the contrary, hydrotropes do not have a CMC or form micelles but can increase the solubility of given solutes in aqueous media by the formation of hydrotrope−solute aggregates.[14] The aggregation of a target solute with a given hydrotrope occurs above a minimum hydrotrope concentration and is due to the establishment of favorable interactions between the two species, including dispersion forces between less polar moieties and other specific interactions such as hydrogen bonding and $\pi-\pi$ interactions. Hydrotropes are usually anionic or cationic aromatic-ring-functionalized compounds with a sulfate, sulfonate, or carboxylate group.[16,17] Besides enhancing the solubility of target compounds in aqueous media, hydrotropes play an important role in the stabilization of aqueous solutions and in tailoring their viscosity.[18,19] Furthermore, because the

solubility of a given solute in aqueous media depends on the hydrotrope concentration, it is possible to design strategies for the solute recovery using water as an antisolvent. In addition to the well-known ability of designed ILs to act as surfactants, it was recently demonstrated that some ILs in aqueous media behave as hydrotropes.[14,20,21] This was shown by determining the solubility of vanillin and gallic acid in aqueous solutions of a wide range of IL aqueous solutions, where an increase in the solubility of up to 40-fold was observed when using ILs with hydrotropic character.[13,14] Dynamic light scattering, nuclear magnetic resonance, and molecular dynamics simulations studies were additionally employed, allowing confirmation of the presence of IL−biomolecule aggregates.[13,14,22−25]

On the basis of the need of developing cost-effective and sustainable processes to extract and recover bioactive compounds from industry waste, in this work, we investigated a series of ILs to improve the solubility of syringic acid in aqueous media and for its extraction from Rocha pear peels. The interest in syringic acid is related to its bioactive properties, namely, antioxidant, antiproliferative, antiendotoxic, antimicrobial, anti-inflammatory, and anticancer activities.[26] Pears, in general, are rich in phenolic compounds, such as syringic, chlorogenic, ferulic, and coumaric acids.[27−30] Among these, syringic acid is one of the phenolic compounds present at higher concentrations in pears (9.5−21.26 mg/100 g fresh pears).[27−30] The Rocha pear was chosen because of its economic importance for the agrofood industry in Portugal, with an average annual production of 173 000 tons.[31] The Rocha pear is used to produce juices, jams, and other food products, generating vast amounts of peel residues.

We first determined the solubility of syringic acid in aqueous solutions of a wide range of ILs and concentrations to identify

the most promising ILs and then applied the best IL aqueous solutions to extract the target phenolic acid from pear peels. To optimize the extraction operational conditions, namely, temperature, solid—liquid (biomass—solvent) ratio, and time of extraction, a factorial planning was applied. Both the solvent and biomass reuse have been investigated, allowing us to propose a continuous countercurrent process conceptualized for large-scale applications, which further allows the solvent recycling after the recovery of syringic acid by the addition of water that acts as antisolvent. Combined solubility data and extractions from biomass are applied to demonstrate the relevance of the hydrotropy phenomenon displayed by ILs.

■ EXPERIMENTAL SECTION

Materials. Syringic acid (>99% pure), whose chemical structure is shown in Figure 1, was purchased from Sigma-Aldrich and was used as received. The water employed was double-distilled, passed across a reverse osmosis system, and further treated with a Milli-Q plus 185 water purification apparatus. A large variety of ILs with hydrotropic or surfactant character were investigated in aqueous solutions, aiming at improving the solubility and extraction of syringic acid from pear peels. The chemical structures of the investigated ILs are depicted in Figure 1. The ILs investigated were 1-butyl-3-methylimidazolium tosylate ($[C_4C_1im][TOS]$, 98% pure), 1-butyl-3-methylimidazolium thiocyanate ($[C_4C_1im][SCN]$, >98% pure), 1-butyl-3-methylimidazolium hydrogensulfate ($[C_4C_1im][HSO_4]$, >98% pure), 1-butyl-3-methylimidazolium chloride ($[C_4C_1im]Cl$, 99% pure), 1-butyl-3-methylimidazolium dicyanamide ($[C_4C_1im][N(CN)_2]$, >98% pure), 1-butyl-3-methylimidazolium acetate ($[C_4C_1im][Ac]$, >98% pure), 1-methyl-3-octylimidazolium chloride ($[C_8C_1im]Cl$, 99% pure), 1-butyl-3-methylpyridinium chloride ($[C_4C_1py]Cl$, 99% pure), 1-butyl-1-methylpiperidinium chloride ($[C_4C_1pip]Cl$, 99% pure), 1-butyl-1-methylpyrrolidinium chloride ($[C_4C_1pyrr]Cl$, 99% pure), tetrabutylammonium chloride ($[N_{4444}]Cl$, ≥97% pure), tetrabutylphosphonium chloride ($[P_{4444}]Cl$, 96% pure), triisobutyl(methyl)phosphonium tosylate ($[P_{i(444)1}][TOS]$, 98% pure), cholinium chloride $[Ch]Cl$, ≥99% pure), cholinium acetate ($[Ch][Ac]$, 98% pure), cholinium butanoate ($Ch][But]$, >97 wt % pure), cholinium hexanoate ($[Ch][Hex]$, >97 wt % pure), cholinium octanoate ($[Ch][Oct]$, >97 wt % pure), and cholinium decanoate ($[Ch][Dec]$, >97 wt % pure). The imidazolium-, pyridinium-, piperidinium-, and pyrrolidinium-based ILs were purchased from Iolitec. The tetrabutylphosphonium chloride and triisobutyl(methyl)phosphonium tosylate were kindly supplied by Cytec Industries. Tetrabutylammonium chloride and cholinium chloride were acquired from Sigma-Aldrich. With the exception of cholinium acetate, which was purchased from Iolitec, the remaining cholinium carboxylate ILs were synthesized by us using the previously published protocol.[32] Before use, all ILs were dried under vacuum (10^{-2} Pa) at 30 °C for a minimum of 48 h.

Solubility of Syringic Acid in Ionic Liquid Aqueous Solutions. IL aqueous solutions were prepared with concentrations ranging from 0.1 to 4.0 mol·L^{-1}. Syringic acid was added in excess to each IL aqueous solution and equilibrated under constant stirring and fixed temperature using Eppendorf Thermomixer Comfort equipment. Solubility data were determined at 30 °C using optimized equilibration conditions, namely, a stirring velocity of 750 rpm and an equilibration time of at least 72 h. Samples were then centrifuged in a Hettich Mikro 120 centrifuge, for 20 min at 4500 rpm, to separate the macroscopic solid (syringic acid) and liquid (IL aqueous solution saturated with syringic acid) phases. After centrifugation, samples were placed in an air bath equipped with a Pt 100 probe and a proportional—integral—derivative (PID) controller at the temperature used in equilibrium assays for >2 h. Samples of the liquid phase were collected and diluted in ultrapure water, and the amount of syringic acid was quantified through UV spectroscopy using a Shimadzu UV-1700 Pharma-Spec spectrometer at a wavelength of 271 nm using an established calibration curve. Controls containing each IL at the same concentration were used in all experiments. At least three individual

samples were prepared and quantified. The same procedure was applied to determine the solubility of syringic acid in pure water.

Extraction of Syringic Acid from Pear Peels Using Ionic Liquid Aqueous Solutions. Peels from fresh Portuguese Rocha pears, purchased in a local supermarket, were manually removed, dried at 25 °C for 2 days, and ground with a commercial coffee grinder. Weighted amounts ($\pm 10^{-4}$ g) of ground pear peels were added to $[C_4C_1im]Cl$ aqueous solutions. This IL was used on this set of experiments due to its significant hydrotropic effect and its ability to improve the solubility of syringic acid in aqueous media, as identified in the previous set of experiments. Operational conditions, namely, temperature, solid—liquid (biomass-solvent) ratio, and time of extraction, were optimized by a 2^3 factorial planning to simultaneously analyze various operational conditions and to identify the most significant parameters that enhance the syringic acid extraction yield.[33] The Student's t test was used to evaluate the statistical significance of the adjusted data. The suitability of the model was determined by evaluating the lack of fit, the regression coefficient (R^2), and the F value obtained from the analysis of variance (ANOVA). In the factorial planning, the central point was experimentally considered at least in triplicate. Additional 12—20 experiments per factorial planning were carried out, for which several operational conditions were repeated to guarantee the accuracy of the data. The StatSoft Statistica 10.0 software was used for all statistical analyses. Further details related to the 2^3 factorial planning used are provided in the Supporting Information.

After the extraction step, the IL aqueous solutions were separated from the biomass by centrifugation (at 5000 rpm for 10 min using an Eppendorf centrifuge 5804), and the supernatant was filtered using a 0.20 μm syringe filter. A 200 μL aliquot was taken, mixed with 800 μL of mobile phase (ultrapure H_2O + 0.2% acetic acid) used in the high-performance liquid chromatography—diode-array detector (HPLC-DAD) analysis, and filtered over a 0.2 μm syringe filter. The quantification of syringic acid in each solution was carried out using an HPLC-DAD apparatus (Shimadzu, model PROMINENCE). HPLC analyses were performed with an analytical C18 reversed-phase column (250 × 4.60 mm), Kinetex 5 μm C18 100 Å, from Phenomenex. The mobile phase consisted of 77.5% of ultrapure H_2O + 0.2% acetic acid and 22.5% of acetonitrile. The separation was conducted in isocratic mode at a flow rate of 1.0 mL·min^{-1} and using an injection volume of 10 μL. DAD was set at 271 nm. Each sample was analyzed at least in duplicate. The column oven and the autosampler operated at 30 °C. Calibration curves were prepared using pure and commercial syringic acid aqueous solutions. For comparison purposes, methanol and dichloromethane were also used as solvents to carry out the extraction of syringic acid from pear peels under the optimized conditions. The reported syringic acid extraction yield corresponds to the percentage ratio between the weight of syringic acid extracted and the total weight of dried biomass.

Reusability of Biomass and Solvent and Syringic Acid Recovery. To develop a sustainable extraction and recovery process as well as to infer the solvent saturation effects and the maximum amount of the target compound present in the biomass, two strategies were investigated: (i) reuse of the biomass employing five new aqueous solutions of ILs to the same biomass sample and (ii) reuse of the solvent by applying five successive cycles of extraction using the same IL aqueous solution. Both approaches were applied under the optimum operational conditions. These assays also allowed us to propose the use of IL aqueous solutions in a continuous countercurrent mode extraction process.

After five extraction cycles with the reuse of the IL aqueous solution, which allowed the solvent saturation, water was finally added as an antisolvent, inducing the precipitation and the recovery of syringic acid. Tests were carried out by the addition of 1, 5, 10, 15, and 25 mL of distilled water to 0.5 mL of the IL aqueous solutions containing syringic acid after the extraction step. Next, the solution was centrifuged at 5000 rpm for 15 min and vacuum-filtered with a 0.45 μm microporous membrane. HPLC-DAD analysis of the aqueous solutions was carried out to determine the recovery yield of syringic acid by precipitation. The recovery yield corresponds to
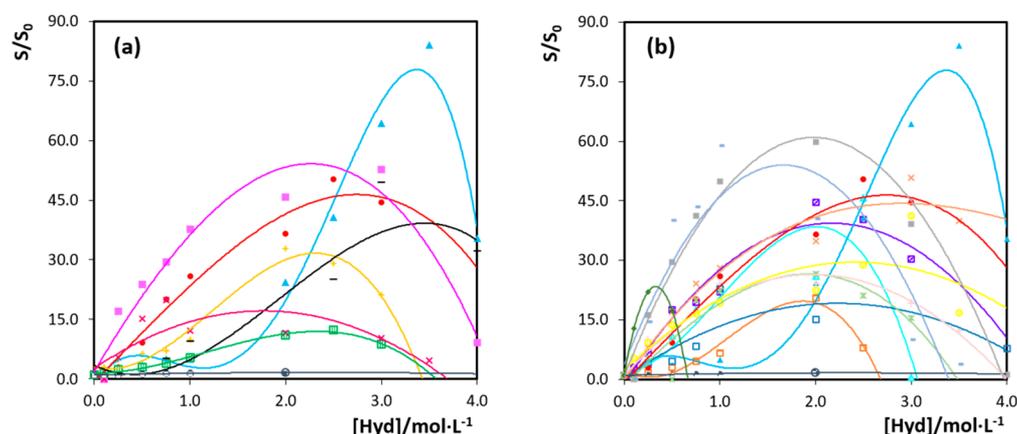
Figure 2. Solubility enhancement of syringic acid in aqueous solutions of ILs. (a) (blue ▲) $[C_4C_1im]Cl$, (red ✗) $[C_8C_1im]Cl$, (red ●) $[P_{4444}]Cl$, (yellow +) $[N_{4444}]Cl$, (green □) $[C_4C_1pyrr]Cl$, (—) $[C_4C_1pip]Cl$, (pink ■) $[C_4C_1py]Cl$, (gray ○) $[Ch]Cl$. (b) (blue ▲) $[C_4C_1im]Cl$, (turquoise △) $[C_4C_1im][TOS]$, (orange □) $[C_4C_1im][HSO_4]$, (purple □) $[C_4C_1im][N(CN)_2]$, (dark blue □) $[C_4C_1im][SCN]$, (orange ✗) $[C_4C_1im][Ac]$, (green *) $[P_{i(444)1}][TOS]$, (red ●) $[P_{4444}]Cl$, (gray ○) $[Ch][Cl]$, (light pink +) $[Ch][Ac]$, (yellow ○) $[Ch][But]$, (gray ■) $[Ch][Hex]$, (light blue —) $[Ch][Oct]$, and (green ◆) $[Ch][Dec]$. Lines have no physical meaning and are only guides for the eye.

the percentage ratio between the total weight of precipitated syringic acid and the weight of syringic acid initially present in the IL aqueous solution. The obtained precipitate/solid residue was dried in an air oven at room temperature for 2 days and further analyzed by HPLC-DAD to guarantee its stability and purity.

■ RESULTS AND DISCUSSION

Solubility of Syringic Acid in Ionic Liquid Aqueous Solutions. In a first set of experiments, we determined the solubility of syringic acid in aqueous solutions of ILs at concentrations ranging from 0.1 to 4.0 mol·L^{-1} at 30 °C, aiming at better understanding the role of ILs to improve the solubility of natural phenolic acids in aqueous media and to identify the most promising IL aqueous solutions to proceed with the syringic acid extraction from food industry waste, namely, pear peels. The solubility results are given in Table S2. The solubility of syringic acid at 30 °C in pure water determined by us is 1.43 ± 0.08 g·L^{-1} (0.0072 mol·L^{-1}). The effect of the IL chemical structure and the IL concentration on the solubility of syringic acid at 30 °C is depicted in Figure 2. These results are shown as solubility enhancement, namely, S/S_0, where S and S_0 represent the solubility of the syringic acid in each IL aqueous solution and in pure water, respectively.

The results obtained reveal a synergetic effect of the two solvents (water and IL) on the solubility of syringic acid, where a maximum in solubility occurs along the IL concentration. The IL concentration where this maximum occurs depends, however, on the IL chemical structure and hydrotrope or surfactant behavior, with surfactants usually performing better at lower concentrations. A similar behavior was reported by Cláudio et al.[14] on the solubility of vanillin and gallic acid in aqueous solutions of ILs. Among all ILs studied, $[C_4C_1im]Cl$ is the best IL identified with an increase in the solubility of syringic acid in aqueous media up to 84-fold (120.3 ± 0.3 g·L^{-1} in the IL aqueous solution versus 1.43 ± 0.08 g·L^{-1} in pure water).

Figure 2a shows results for the following ILs: $[C_4C_1im]Cl$, $[C_8C_1im]Cl$, $[P_{4444}]Cl$, $[N_{4444}]Cl$, $[C_4C_1pyrr]Cl$, $[C_4C_1pip]Cl$, and $[C_4C_1py]Cl$, which share a common anion (chloride), thus allowing us to evaluate the IL cation effect on enhancing the syringic acid solubility. Among these, only $[C_8C_1im]Cl$ presents a surfactant behavior, with a previously reported

CMC of 238 mM,[34] whereas the remaining ILs of this series are expected to act as hydrotropes. The overall capacity of these ILs to improve the solubility of syringic acid (appraised at the maximum solubility of syringic acid) follows the order: $[C_4C_1im]Cl$ > $[C_4C_1py]Cl$ > $[P_{4444}]Cl$ > $[C_4C_1pip]Cl$ > $[N_{4444}]Cl$ > $[C_8C_1im]Cl$ > $[C_4C_1pyrr]Cl$ > $[Ch]Cl$. The obtained trend reflects the ability of the IL cation to act as a hydrotrope in the solubility of syringic acid. With the exception of cholinium- and pyrrolidinium-based ILs that perform worse than the surfactant $[C_8C_1im]Cl$, all remaining ILs display a significant ability to increase the solubility of syringic acid while behaving as hydrotropes. In particular, with $[Ch]Cl$, the solubility of syringic acid only slightly increases, reaching a maximum solubility enhancement of 1.64, suggesting that neither $[Ch]^+$ nor Cl$^-$ has a significant effect on improving the solubility of the target phenolic compound. When comparing the solubility of syringic acid in aqueous solutions containing $[C_4C_1im]Cl$ and $[C_8C_1im]Cl$, it is clear that ILs with shorter alkyl chains and with hydrotrope characteristics perform better at enhancing the solubility.

When using ILs with surfactant characteristics, the solubility enhancement occurs due to the IL self-aggregation and the possibility of incorporating hydrophobic solutes in the micelle core. With this type of ILs, the enhancement in solubility is more pronounced at low concentrations of IL, close to the CMC, but seems to quickly saturate at low concentrations, above which a much weaker effect on the solubility of the syringic acid is observed. This behavior was observed by Cláudio et al.[14] while evaluating the variation of the solubility of vanillin in aqueous solutions of $[C_nC_1im]Cl$ ILs, with $2 \leq n \leq 14$, concluding that ILs with shorter alkyl chain lengths ($[C_nC_1mim]Cl$, $n = 2-6$) behave as hydrotropes, whereas ILs with longer alkyl side chains ($[C_nC_1im]Cl$, $n = 8-14$)[34,35] behave as surfactants. However, the data corresponding to $[C_8C_1im]Cl$ and $[Ch][Oct]$ (cf. Figure 2a and the discussion below on the IL anion effect) seem to indicate the presence of combined effects and mechanisms, particularly when dealing with moderately hydrophobic species such as syringic acid. These combined effects seem to appear with ILs with alkyl side chains that are in the length threshold to form micelles, being this the case of $[C_8C_1im]Cl$ and $[Ch][Oct]$. Hydrotropes cannot form micelles, and no competitive or combined effects

occur with these. However, for ILs with surfactant behavior and depending on the solute hydrophobicity, the solubility may be enhanced by the formation of micelles and by the formation of solute–IL aggregates. For instance, with $[Ch][Dec]$ that has a lower CMC, the maximum solubility value of syringic acid occurs at a concentration of IL < 0.5 M, whereas for ILs acting as hydrotropes, the maximum solubility values occur for concentrations of IL > 2 M. With $[C_8C_1im]Cl$ and $[Ch][Oct]$, the maximum in the solubility of syringic acid occurs in between, thus indicating that combined effects of both phenomena may exist.

Although the formation of solute–hydrotrope complexes based on $\pi \cdots \pi$ interactions (between the aromatic moieties of the substrate and aromatic hydrotropes) has been used to explain the hydrotropy concept,[36,37] the results obtained with nonaromatic ILs, such as $[N_{4444}]Cl$, $[P_{4444}]Cl$, $[C_4C_1pip]Cl$, and $[C_4C_1pyrr]Cl$, reveal that the hydrotropic effect cannot be explained as resulting only from this type of interactions. This observation is in agreement with the findings of Cláudio et al.[14] as well as with other works in which conventional hydrotropes have been studied.[38−41] Overall, hydrotropes enhance the solubility of the target solute by the formation of solute–hydrotrope aggregates, which are formed due to favorable interactions between the two species, including dispersion forces between less polar moieties and other specific interactions such as hydrogen bonding and $\pi−\pi$ interactions.

Figure 2b shows the results of solubility enhancement for the two following series of ILs: (i) $[C_4C_1im]Cl$, $[C_4C_1im][TOS]$, $[C_4C_1im][HSO_4]$, $[C_4C_1im][N(CN)_2]$, $[C_4C_1im][SCN]$, and $[C_4C_1im][Ac]$ and (ii) $[P_{i(444)1}][TOS]$ and $[P_{4444}]Cl$. These two sets of ILs share a common or similar cation, allowing to address the IL anion effect on the syringic acid solubility. In the same figure, additional results for the ILs $[Ch][Ac]$, $[Ch][But]$, $[Ch][Hex]$, $[Ch][Oct]$, and $[Ch][Dec]$ are given to address the effect of carboxylate-based anions combined with the cholinium cation to improve the syringic acid solubility in water. Among these, $[Ch][Oct]$ and $[Ch][Dec]$ display surface-active properties.[42,43]

All ILs investigated with the $[C_4C_1im]^+$ cation display an important hydrotropic effect, thus improving the solubility of syringic acid in aqueous media according to the following anion trend (taken at the maximum solubility enhancement): $Cl^- > [Ac]^- > [TOS]^- > [N(CN)_2]^- > [SCN]^- > [HSO_4]^-$. With the phosphonium-based ILs, the same trend was observed for the ILs comprising the Cl^- and $[TOS]^-$ anions. If compared with previous trends obtained for ILs used to improve the solubility of vanillin and gallic acid,[14] then these results again confirm that the hydrotropy dissolution is solute-dependent. According to the literature, most of the industrially used hydrotropes are anionic and often contain a phenyl group, such as tosylate.[44] However, according to the results shown in Figure 2b, $[C_4C_1im]Cl$ and $[C_4C_1im][Ac]$ perform better than $[C_4C_1im][TOS]$, and $[P_{4444}]Cl$ performs better than $[P_{i(444)1}][TOS]$, demonstrating that tosylate does not act as an hydrotrope able to improve the solubility of syringic acid in aqueous solutions. As observed with the cationic hydrotropes previously discussed, this result further supports the idea that $\pi \cdots \pi$ interactions do not contribute to the hydrotropic effect.[38−40,45] Although chloride is not a hydrotrope, and has a marginal effect on the solubility of syringic acid, as shown by the results of $[Ch]Cl$, aqueous solutions of $[C_4C_1im]Cl$ are the best solvents identified. All of these results therefore indicate that for syringic acid there is not a synergetic effect of both IL

ions to improve its solubility, as would be expected by using ILs where both ions have hydrotrope characteristics, for example, $[C_4C_1im][TOS]$ and $[C_4C_1im][N(CN)_2]$.

It has been previously reported that the solubility enhancement by hydrotropes is more effective for more hydrophobic solutes,[14] as ascertained when comparing the solubility of vanillin and gallic acid (with values of the logarithm of the octanol–water partition coefficient, $\log(K_{ow})$, as follows: 1.23 and 0.72, respectively[46]). Syringic acid has an intermediate $\log(K_{ow})$ value of 1.04,[46] but more significant improvements in solubility have been observed applying ILs as hydrotropes if compared with vanillin and gallic acid. Furthermore, in the current work, the IL cation plays a major role in the design of effective hydrotropes. These results suggest that the strengths of interactions between ILs and phenolic compounds are different, being solute-specific, which could, however, be useful to design selective solvents and effective recovery strategies.

In addition to $[C_4C_1im]$-based ILs, cholinium-based ILs have been investigated. Both short alkyl side-chain cholinium carboxylates (acetate, butanoate, and hexanoate), which could act as hydrotropes, and long alkyl side-chain cholinium carboxylate (octanoate and decanoate), able to form micelles in aqueous solutions and with reported CMCs,[42,43] were studied. Contrary to the $[C_8C_1im]Cl$ previously discussed that is a cationic surfactant, $[Ch][Oct]$ and $[Ch][Dec]$ are anionic surfactants. The results obtained show that the maximum in the syringic acid solubility occurs at lower IL concentrations as the alkyl side chain at the carboxylate anion is increased. Furthermore, the maximum in solubility enhancement occurs with $[Ch][Hex]$ and $[Ch][Oct]$ but strongly decreases with the better surfactant, $[Ch][Dec]$. The surfactant-based cholinium carboxylate ILs perform better than $[C_8C_1im]Cl$, meaning that anionic surfactants are more appropriate to increase the solubility of syringic acid in aqueous media. However, favorable and specific interactions occurring between the carboxylate anions and syringic acid cannot be discarded because $[C_4C_1im][Ac]$ is one of the best ILs (after $[C_4C_1im]Cl$) identified in the imidazolium-based series of ILs. Still, $[C_4C_1im][Ac]$ is a better hydrotrope to enhance the solubility of syringic acid than $[Ch][Ac]$, reinforcing the relevance of cationic IL hydrotropes. These results disclose that the IL cation and anion may have different roles, as the hydrotropy effect toward syringic acid was dominated by the IL cation. Overall, according to the results discussed above and considering that aqueous solutions of $[C_4C_1im]Cl$ at 3.5 mol·L^{-1} were identified as the best solvents, able to increase the solubility of syringic acid 84-fold when compared with pure water, aqueous solutions of this IL were used to optimize the operational conditions of the extraction of syringic acid from Rocha pear peels by a response surface methodology, as described below.

Extraction of Syringic Acid from Rocha Pear Peels Using an Aqueous Solution of Ionic Liquids. Although pure ILs have been described as solvents for the extraction of value-added compounds from biomass, for example, ellagic acid,[47] artemisinin,[48] limonene,[49] betulin,[50] among others, aqueous solutions of ILs display a high potential and additional advantages due to the use of lower amounts of IL, with intrinsic environmental and economic benefits. Aqueous solutions of ILs are solvents of lower toxicity and cost when compared with the respective pure ILs while decreasing the overall viscosity of the solvent and enhancing the mass transfer. Furthermore, aqueous solutions of ILs are more selective, not
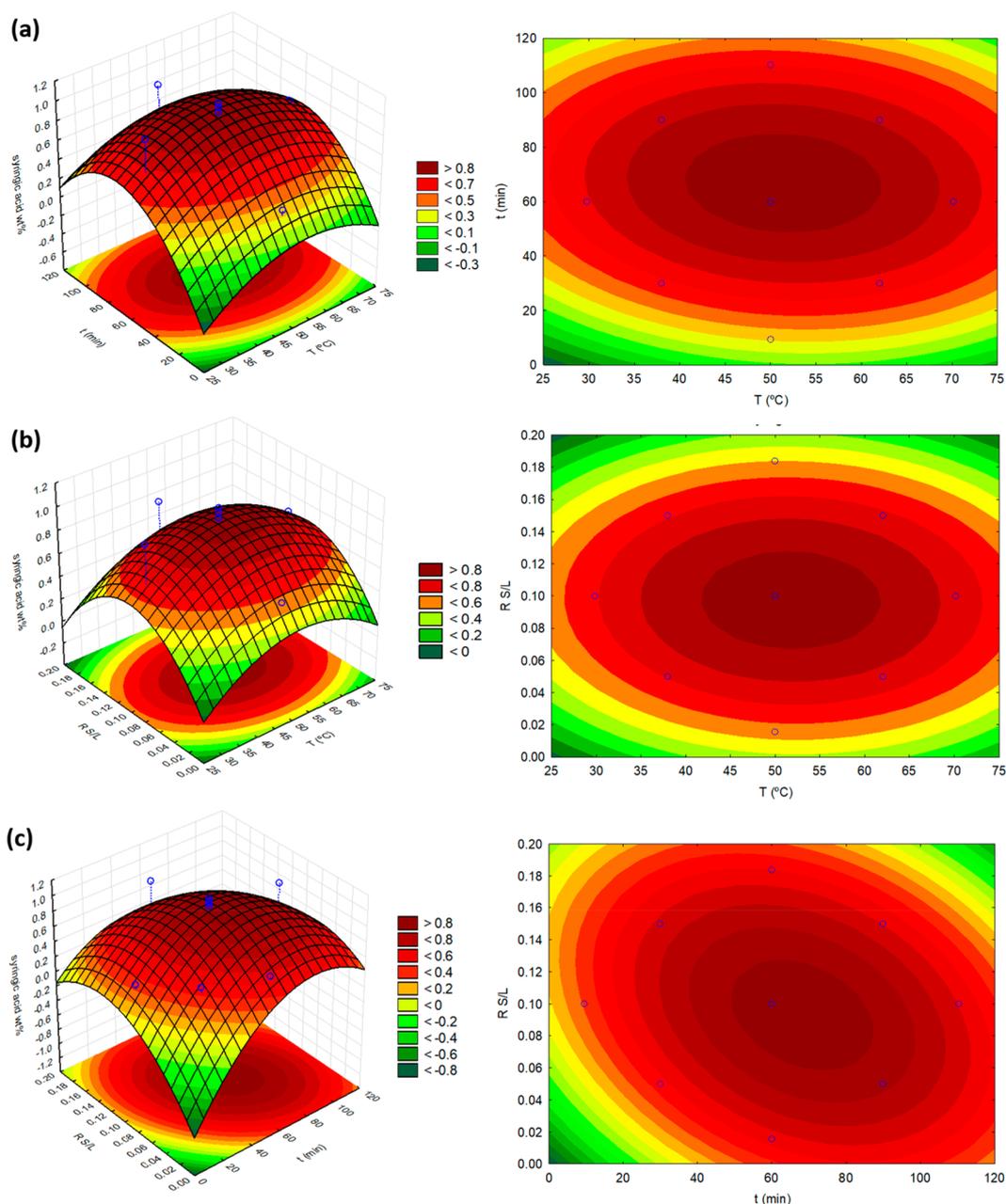
Figure 3. Response surface plots (left) and contour plots (right) on the extraction yield of syringic acid with the combined effects of (a) T (°C) and t (min), (b) T (°C) and S/L ratio, and (c) S/L ratio and t (min), using aqueous solutions of $[C_4C_1im]Cl$ at 3.5 M.

allowing the dissolution of all biomass. Accordingly, whenever possible, IL aqueous solutions should be used instead of pure ILs.

After evaluating the best IL aqueous solutions as solvents for syringic acid, a factorial planning of 2^3 (three factors and two levels) was used to optimize the operational conditions for the syringic acid extraction from Rocha pear peels. The results obtained were analyzed statistically with a confidence level of 95% (data shown in Table S5 and Figure S1). This methodology allows the study of the relationship between the response (extraction yield of syringic acid) and the independent variables/operational conditions that influence the extraction yield, namely, the extraction time (t, min), the biomass–solvent weight ratio (S/L ratio, weight of dried biomass per weight of solvent), and the temperature (T, °C). The extraction yield corresponds to the percentage ratio

between the weight of extracted syringic acid and the weight of dried biomass (pear peels). On the basis of the solubility results shown in Figure 2 and the maximum solubility enhancement of syringic acid of 84-fold, aqueous solutions of $[C_4C_1im]Cl$ at 3.5 mol·L^{-1} were used. Additional studies by increasing the IL concentration were not carried out because the maximum in solubility occurs at 3.5 M and because an increase in the IL concentration increases the solution viscosity, thus not favorably contributing to the mass-transfer phenomenon. Moreover, an increase in the IL concentration increases the solvent cost and toxicity.[46]

Variance analysis (ANOVA) was used to estimate the statistical significance of the variables and their interactions. The experimental points used in the second factorial planning, the model equation, the extraction yield of syringic acid obtained experimentally, and the respective calculated values

using the correlation coefficients obtained in the statistical treatment as well as all of the statistical analyses are shown in the Supporting Information. On the basis of the statistical model and results (Tables S4 and S5) given in detail in the Supporting Information, the average relative deviation between the experimental and the predicted values is 0.45%, supporting the good description of the experimental results by the statistical model.

The influence of the three variables on the extraction yield of syringic acid is illustrated in Figure 3, with the respective detailed data given in Table S4. It is evident that extraction time is a significant parameter, leading to a region of maximum yield of extraction at 60 min. The solid−liquid ratio also has a relevant impact on the syringic acid extraction yields, increasing by increasing the solvent volume. Additionally, higher temperatures are more efficient for the extraction of syringic acid from pear peels, although this is the variable with the weakest influence on the extraction yield of syringic acid (between 45 and 60 °C). Overall, the parameters that have a higher impact on the extraction yield of syringic acid (as can be seen in the pareto chart, Figure S1), are the extraction time and the solid−liquid ratio. The optimized operational conditions found for the extraction of syringic acid occur at a temperature of 50 °C, an extraction time of 60 min, and a solid−liquid ratio of 0.10, providing a syringic acid extraction yield of 1.05 wt %.

Some organic solvents were also evaluated under the optimized conditions for comparison purposes, with dichloromethane and methanol leading to extraction yields of 1.51 and 1.68 wt %, respectively. Although a lower extraction yield is obtained with IL aqueous solutions, these are still competitive solvents because the use of volatile organic solvents is avoided. Furthermore, by reusing the IL aqueous solutions, similar yields are obtained, as shown below, supporting their high potential as alternative solvents to extract syringic acid from biomass.

The two last sets of results on the solubility and extraction of syringic acid from biomass suggest that the high performance demonstrated by IL aqueous solutions may be a major outcome of the enhanced solubility afforded by ILs with hydrotrope characteristics and not only from the biomass disruption, as usually reported.

Reusability of Biomass and Solvent and Syringic Acid Recovery. Aiming to infer the maximum amount of syringic acid present in biomass, the same sample of Rocha pear peels was sequentially extracted with "fresh" IL aqueous solutions using the optimum conditions previously identified in five successive extraction cycles. The results obtained are shown in Figure 4a and given in detail in Table S6. It is shown that the syringic acid present in the biomass sample is not fully extracted in the first cycle (1.05 wt %) of extraction, and it is possible to achieve a maximum yield of 2.22 wt % after five extraction cycles with "fresh" IL aqueous solutions. Thus, in a single extraction approach, half of the syringic acid still remains in biomass; however, if several extraction cycles are implemented, then the total extraction yield can surpass the ones obtained with conventional organic solvents.

The reusability of the extraction solvent using new Rocha pear peels was also investigated for five cycles to maximize the cost efficiency and sustainability character of the developed process (Figure 4b; detailed results given in the Table S7). After each extraction, the solid−liquid mixture was filtered, and the IL aqueous solution was reused with new pear peel samples. As summarized in Figure 4b, the extraction yield
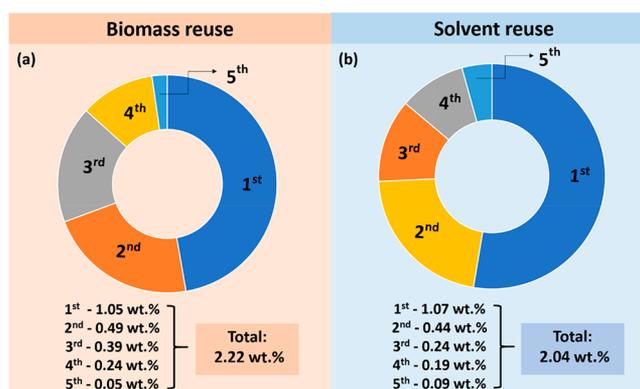

Figure 4. Syringic acid extraction yields from Rocha pear peels with the (a) biomass and (b) solvent reuse under the optimized operational conditions.

obtained in the first extraction cycle (1.07 wt %) could be improved by reusing the solvent and applying it to new biomass samples, achieving a yield of 2.04 wt % after the fifth cycle of reuse of the IL aqueous solution.

These improvements in the extraction yield were not identified before in the factorial planning due to constraints of the solid−liquid ratio and mass-transfer phenomenon, but if both the solvent and biomass are reused, then a significant increase in the extraction yields is obtained. Accordingly, an extraction continuous process operating in countercurrent, in which the solvent and biomass are reused in a continuous mode, seems to be the most adequate option to be applied in large-scale applications. A schematic representation of the envisioned process is given in Figure 5.
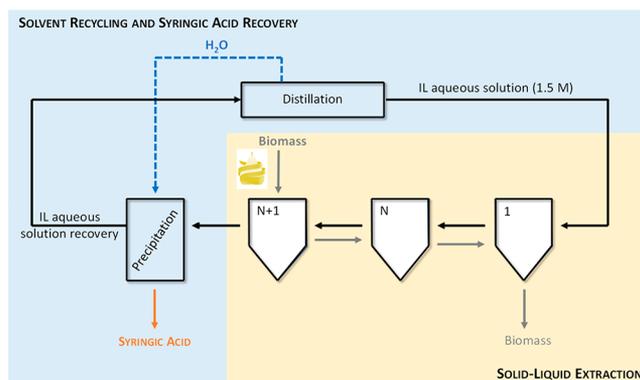

Figure 5. Scheme of the continuous extraction process operating in countercurrent.

Although the use of aqueous solutions of aprotic ILs has been shown to be an alternative to pure ILs to extract added-value compounds from biomass, the nonvolatile nature of aprotic ILs represents a major drawback when envisaging the target compound recovery because a simple evaporation step cannot be applied. On the basis of this limitation and knowing that the solubility of the target compound largely depends on the IL (hydrotrope) concentration, as shown in Figure 2, the recovery of syringic acid from the IL aqueous solution was carried out by dilution with water, which acts as an antisolvent. At the end of the fifth extraction cycle of the previous experiments (reuse/saturation of the solvent), the saturated IL aqueous solution (0.5 mL) was diluted with increased volumes

of water (1, 5, 10, 15, and 25 mL) (cf. Table S8 and Figure S2). By applying this process, 77% of the extracted syringic acid can be recovered by precipitation by the addition of the largest volume of water and with high purity (~94%), as shown in the chromatogram given in the Figure S3. The impurities addressed mainly comprise other phenolic acids and aromatic compounds absorbing in the same wavelength and present in pear peels, such as arbutin, gallic acid, (+)-catechin, chlorogenic acid, caffeic acid, (−)-epicatechin, coumaric acid, and ferulic acid.[30] Finally, the recovery of syringic acid by this process allows the elimination of the IL from syringic acid, thus overcoming the toxicity concerns that could be associated with ILs, and the IL recycling after an evaporation step to decrease the water content, as shown in the process given in Figure 5. Although the addition of a large amount of water to recover syringic acid may not be the most sustainable approach, syringic acid can be recovered by other approaches, such as solid-phase extraction, as carried out by Quental et al.[51] to recover phenolic acids from IL aqueous solutions.

Even though syringic acid obtained by synthetic routes is not an expensive compound, the same is not true for syringic acid obtained from natural sources. Nowadays, there is a high demand for natural products with relevant bioactive properties by the food and cosmetic industries,[52] justifying the interest behind the developed and proposed process. Furthermore, it is usually claimed that ILs are expensive compounds, thus compromising their application on a large scale. It should be remarked that if obtained on a large scale, a low-cost IL was applied; a cost analysis for the application of several ILs on a large scale can be found in the literature.[9]

Overall, the results obtained demonstrate that aqueous solutions of ILs with hydrotropic characteristics are improved solvents to extract syringic acid from biomass. Furthermore, it is possibility to recover syringic acid by the addition of water, inducing its precipitation while allowing the IL recycling.

CONCLUSIONS

It was shown that aqueous solutions of ILs that behave as cationic hydrotropes are remarkable solvents for syringic acid, leading to enhancements up to 84-fold in solubility when compared with pure water. Because of these solubility enhancements, the same IL aqueous solutions lead to good extraction yields of syringic acid from pear peels. The operational extraction conditions were optimized by factorial planning, resulting in a maximum extraction yield of 1.05 wt %. With the goal of developing sustainable extraction strategies, both the biomass and the IL aqueous solutions were reused, allowing to reach extraction yields of syringic acid of 2.04 and 2.22 wt %, respectively. These values are higher than those obtained with dichloromethane and methanol under the same operational conditions (1.51 and 1.68 wt %, respectively). On the basis of these results, and with the possibility of reusing both the solvent and biomass, a continuous process was conceptualized and proposed for large-scale applications, acting in a continuous and countercurrent mode, in which the solvent is recycled after the recovery of syringic acid by precipitation with water as an antisolvent. This strategy allows to recover 77% of the extracted phenolic acid. The results reported here have a significant impact on the understanding of the role of IL aqueous solutions in the extraction of value-added compounds from biomass and on the design of processes for their recovery based on the hydrotropy concept.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssusche-meng.9b02808.

Additional information on the factorial planning, the solubility of syringic acid in IL aqueous solutions, experimental points used in the factorial planning, model equations, yields of syringic acid experimentally obtained, the statistical analysis connected to the response surface methodology, the yield of syringic acid by the reuse of biomass and IL aqueous solution, the percentage recovery of syringic acid with the addition of water, and the HPLC-DAD chromatogram of the recovered syringic acid (PDF)

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Notes
The authors declare no competing financial interest.

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