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Evaluation of bio-based solvents for phenolic acids extraction from aqueous matrices

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ABSTRACT

In the current context of a growing demand for environmentally friendly technologies, this study aims to evaluate and develop an efficient liquid-liquid extraction procedure of phenolic acid antioxidants from aqueous environments using bio-based solvents. Due to their abundance in industrial effluents and their importance for human health, a better understanding of how the molecular structures of phenolic antioxidants impact their recovery for pharmaceutical and fine chemical applications is required. Following the principles established by Green Chemistry, the use of eco-friendly solvents including 2methyltetrahydrofuran (2-MeTHF), cyclopentyl methyl ether (CPME) and D-limonene (LIM) was evaluated in comparison with the conventional organic solvent, ethyl acetate (EA), for liquid-liquid extraction of nine representative phenolic acids: five hydroxybenzoic acids and four hydroxycinnamic acids. The distribution of the target compounds in each phase after the extraction process was obtained by UV-Visible spectrophotometry. The highest extraction yields, up to 100%, were obtained with 2-MeTHF, followed by the conventional solvent EA and CPME. On the contrary, LIM showed the lowest extraction efficiencies. The effect of the molecular structures of the compounds involved in the extraction process was analysed. In addition, the recyclability of 2-MeTHF in consecutive extraction cycles was demonstrated. Overall, a simple and more environmentally friendly liquid-liquid extraction process was developed for the recovery of hydroxybenzoic and hydroxycinnamic acids, while providing insights into the behaviour of the extraction process of phenolic acids using more sustainable solvents.

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1. Introduction

Phenolic acids are one of the most pervasive groups of plant phenolic compounds. They are bioactive substances widely found as secondary metabolites with a general C_6 - C_1 structure [1,2]. They are distinguishable from other phenolics by their structure, which typically contains a carboxyl group (-COOH) and one or more hydroxyl groups (-OH) or methoxy groups (-OCH₃) bonded to the aromatic ring. Hydroxyl groups and other functional groups attached to the aromatic ring establish the variety and determine the bioactive properties of phenolic acids [1,2]. Phenolic acids represent one-third of the phenolic compounds consumed in the human diet [1,3]. These substances are found in all foods of plant origin and they are abundant in cereals, legumes, oilseeds, fruits, vegetables, fruit juices and herbs [1,4]. As a consequence, they are also widely present in the effluents derived from the industrial production of these food of plant origin [5-7]. The phenolic acids and their esters have the potential to bring about beneficial human

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https://doi.org/10.1016/j.molliq.2021.116930 0167-7322/© 2021 Elsevier B.V. All rights reserved. health effects due to their antioxidant and anti-inflammatory actions, help in the prevention of cardiovascular diseases and various cancers, protect against oxidative damage diseases, and exhibit antimicrobial, antimutagenic, hypoglycaemic and antiplatelet aggregating activities. Phenolic acids can also serve as reducing agents, quenchers of singlet oxygen formation, and scavengers of free radicals, among others [1,3,4]. They also impart color, flavor, astringency, and harshness, which contribute to the typical organoleptic characteristics of the foods [3]. Phenolic acids are industrially relevant compounds, which find use and application in the food, pharmaceutical, cosmetic, and chemical industries [2]. The global phenolic antioxidant market was valued at US\$ 1.69 million in 2019 and is expected to register an estimated compound annual growth rate (CAGR) of 5.10% from 2020 to 2027, reaching US\$ 2.40 million by 2027, due to the favourable food and safety regulations and the growing consumer awareness of health benefits related to phenolic antioxidant consumption [8,9].

Two natural types of phenolic acids are mainly distinguished: the hydroxybenzoic acids and the hydroxycinnamic acids; these are derived from non-phenolic molecules of benzoic and cinnamic acid, respectively [4,7,10]. The chemical structures of the different

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phenolic acids employed in this study are shown in Fig. 1. Compounds derived from hydroxybenzoic acid are characterized by a C₆-C₁ backbone obtained from benzoic acid and its most common derivatives include *p*-hydroxybenzoic acid (HA), protocatechuic acid (PA), gallic acid (GA), vanillic acid (VA), and syringic acid (SA), among others [4,10]; they are usually present in bound form and structural changes occur because of aromatic ring hydroxylation and methylation [1,3]. Meanwhile, the compounds derived from hydroxycinnamic acid are characterized by a nine carbon (C_6-C_3) skeleton with a side chain double bond (with cis or a trans configuration); they are mainly represented by cinnamic acid (CiA), *p*-coumaric acid (*p*CA), caffeic acid (CA), and ferulic acid (FA) [4,10]. They are encountered most frequently in plants and food than hydroxybenzoic acids [3,11]. These acids are rarely found in free form, but they commonly occur in foods and beverages conjugated with sugars or organic acids [1,11].

Apart from fruits and vegetables for human consumption, liquid agri-food waste effluents, whether solid or liquid, has great potential as a cheap source of antioxidants, many of which belong to phenolic acids. The valorisation of agri-food by-products, nonedible food, and waste is a valuable opportunity and has aroused great interest [6,12]. Extraction techniques seem a suitable option for the recovery and isolation of these high added-value compounds [6,13]. In this context, and in order to comply with the principles of the green economy, the recovery of phenolic compounds from agri-food wastes should be achieved using environmentally friendly, sustainable and possibly low-cost procedures [5]. The recovery of phenolic compounds from waste effluents is influenced by the extraction technique, the extraction time, the stirring rate, the temperature, the pH, the other compounds present in the sample matrix, the solvents used and the solvent to feed ratio, among others [1,13]. Currently, certain techniques are available to extract, isolate, and quantify these components from natural sources [1]. Besides conventional extraction techniques such as liquid-liquid extraction, pressurized liquid extraction or dispersive liquid-liquid microextraction have been recently applied [13,14]. Despite its disadvantages, conventional methods remain as widely used techniques, mainly because of their ease of use, efficiency, and wide-ranging applicability [1,15]. Solvent extraction is a separation process that involves contacting of two immiscible phases, allowing a solute (a compound of interest) to distribute from one phase to another [16]. Commonly used hydrophobic extraction solvents are ethyl acetate, toluene, diethyl ether, hexane or mixtures of hydrocarbon solvents [15,17]. However, these solvents classified as volatile organic compounds (VOCs) are usually derived from petrochemical sources and present different drawbacks including high volatility, flammability and toxicity, being hazardous toward the environment and human health [18,19]. Its use is being extensively limited by different international regulations, including

PHENOLIC ACID			
Hydroxybenzoic acids	R1 R2		0
<i>p</i> -Hydroxybenzoic acid (HA)	Н	Н	R1.
Protocatechuic acid (PA)	н	OH	ОН
Gallic acid (GA)	ОН	ОН	но
Vanillic acid (VA)	Н	OCH_3	
Syringic acid (SA)	OCH ₃	OCH_3	κz
Hydroxycinnamic acids	R1	R2	0
Cinnamic acid (CiA)	Н	Н	С
<i>p</i> -Coumaric acid (<i>p</i> CA)	ОН	н	
Caffeic acid (CA)	ОН	ОН	R1
Ferulic acid (FA)	OH	OCH ₃	RŻ

Fig. 1. Chemical structures and functional groups of the phenolic acids, hydroxybenzoic acids and hydroxycinnamic acids, used in this study.

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REACH (EC 1907/2006; i.e. registration, evaluation, authorization and restriction of chemicals) [20]. Several extraction studies of phenolic compounds (phenols, phenolic acids or flavonoids) from liquid matrices have already been efficiently carried out with conventional solvents [21–24] or more environmentally-friendly neoteric solvents such as ionic liquids or eutectic solvents [25–29].

Taking into consideration the goal of good environmental practices and the principles of Green Chemistry, flammable and toxic petroleum solvents should ideally be completely replaced in the future [17,30]. Recently, bio-based solvents (BioSs) have arisen as a promising alternative to be solidly considered. They are defined as solvents produced from renewable biomass sources such as energy crops, forest products, aquatic biomass, and waste materials [12,17]. These solvents can be classified according to different criteria such as the agricultural origin of the biomass used for their production, the petroleum-based solvent they were intended to replace or their functional groups. They can also be classified as hydrophilic (such as glycerol, biodiesel, γ -valerolactone or ethyl lactate) or hydrophobic (such as 2-methyltetrahydrofuran, cyclopentylmethyl ether, α -pinene, *p*-cymene or *D*-limonene) solvents, according to their affinity for water; in this case, since the objective is to extract these compounds from aqueous media, hydrophobic solvents will be used to guarantee the formation of the two phases during the extraction [12,16,31].

These solvent must come from renewable feedstocks, be recyclable using eco-efficient treatments, show similar properties to conventional solvents, high boiling point, low vapour pressure and enhanced biodegradability under normal environmental conditions, to be qualify as green solvents [31]. They have similar physicochemical properties than their petrochemical counterparts, so they could provide a direct replacement to established solvents in chemical processes and product formulations [32]. Despite the early stage of the bio-based chemicals area, the annual bio-based solvent use in the European Union was projected to grow to over one million tonnes by 2020 [33]. Recently, some relevant biobased solvents such as 2-methyltetrahydrofuran (2-MeTHF), cyclopentyl methyl ether (CPME) or *D*-limonene (LIM) have been evaluated in solvent extraction process to obtain compounds of interest from different matrices.

2-methyltetrahydrofuran (C₅H₁₀O) is an excellent bio-based solvent proven for the extraction of bioactive components due to its wide range of solvation and physical properties. It is an aprotic Lewis base with low miscibility with water and higher boiling point and enhanced stability compared to other cyclic-based solvents such as THF [17,34,35]. It can be produced from renewable resources (cellulose, hemicelluloses or lignin) that are transformed into levulinic acid or furfural, and both are converted into 2-MeTHF by hydrogenation or by hydration [17,33]. It is biodegradable, easy to recycle, has a promising environmental footprint and good preliminary toxicology assessments [35,36]. It can potentially replace many common solvents such as tetrahydrofuran, toluene, dichloromethane and diethyl ether in certain applications. Furthermore, preliminary toxicological investigations suggest that exposure to 2-MeTHF is not linked to mutagenicity or genotoxicity [33]. Cyclopentyl methyl ether (C₆H₁₂O) is an aprotic solvent used in organic chemistry as a multipurpose solvent. CPME can be manufactured by the methylation of cyclopentanol or the addition of methanol to readily available cyclopentene, which can be derived from furfural or from (bio-based) adipic acid, respectively [17,37]. These routes are those taken into account in this work to consider it as a bio-based solvent. This solvent has become a greener alternative to extensively used solvents such as tetrahydrofuran, tert-butyl methyl ether or 1,4-dioxane [17]. The advantageous features of CPME are: high hydrophobicity and therefore very easy to dry, low rate of by-products peroxide formation, stability under acidic and basic conditions, relatively high boiling point, low vaporization

energy, and narrow explosion range [37,38]. From the toxicity point of view, CPME takes advantage of a lack of mutagenic and genotoxic activities in vitro test in accordance with regulatory guidelines [38–40]. As regards D-limonene ($C_{10}H_{16}$), it is a biodegradable high-boiling monocyclic monoterpene hydrocarbon with a distinctive odour and low polarity. It is the main component of citrus oils and is mainly extracted from citrus peels by distillation using cold pressing or Clevenger apparatus [33,41], or by solvent extraction [42]. D-limonene presents very low toxicity to humans and is currently registered in the U.S. Code of Federal Regulations as substances that are generally recognized as safe (GRAS) for use as flavouring agents and supplements in food for human consumption [41,43]. Solvents that are commonly replaced with D-limonene solvent include methyl ethyl ketone, acetone, hexane, toluene, glycol ethers and numerous fluorinated and chlorinated solvents [17,41]. Various approaches have been carried out in the substitution of petroleum solvents to extract compounds of interest from liquid matrices with these alternative bio-based solvents described and mentioned above. More specifically, 2-MeTHF has been successfully evaluated to extract levulinic acid and other low molecular weight acids from dilute aqueous solution [44], fat and oils from food (edible oil) by-products [45] and, as CPME, to extract high added-value vanilla-derived compounds from aqueous environments [46], fatty acids from fish oil [38] or bioorganic acids from fermentation broths [47]. Regarding Dlimonene, its potential as an alternative green solvent in the extraction of drugs from human plasma has been reported [48].

It is noteworthy, despite the current interest, that there are no studies in the literature on the application of the aforementioned bio-based solvents in the extraction of phenolic acid compounds from aqueous matrices, to the best of our knowledge. In this framework, the feasibility of using sustainable bio-based solvents as an alternative to conventional volatile organic solvents in the extraction of natural antioxidants from aqueous environments was experimentally evaluated herein. In particular, this work evaluates and optimizes a liquid-liquid extraction method developed for the extraction of five representative hydroxybenzoic acids (gallic acid, p-hydroxybenzoic acid, protocatechuic acid, syringic acid and vanillic acid) and four representative hydroxycinnamic acids (cinnamic acid, p-coumaric acid, caffeic acid and ferulic acid) from aqueous solutions using three different bio-based solvents (2methyltetrahydrofuran, cyclopentyl methyl ether and limonene) with low water miscibility. In addition, the reuse and recyclability of the best extractive hydrophobic BioS was studied in consecutive extraction procedures.

2. Materials and methods

2.1. Materials and chemicals

Experimental assays were performed using ethyl acetate (EA) (purity 98 wt%), 2-methyltetrahydrofuran (2-MeTHF) (purity 98 wt%), cyclopentyl methyl ether (CPME) (purity 98 wt%) and *D*-limonene (LIM) (purity 98 wt%) as extraction solvents. They were saturated with water to ensure a stable volume of both phases after the extraction process. The chemical structures and relevant properties of the extraction solvents are specified in Table 1. The phenolic acids employed in this study were: *p*-hydroxybenzoic acid (HA) (purity 98 wt%), protocatechuic acid (PA) (purity 98 wt%), gallic acid (GA) (purity 98 wt%), vanillic acid (VA) (purity 98 wt%), syringic acid (SA) (purity 98 wt%), cinnamic acid (CiA) (purity 97 wt%), *p*-coumaric acid (*p*CA) (purity 98 wt%), caffeic acid (CA) (purity 98 wt%), and ferulic acid (FA) (purity 99 wt%). Stock solutions of the phenolic acids were prepared in filtered and deionized water (18 MΩ/cm). All chemicals and reagents were used

without any further purification step. Sigma-Aldrich (MERCK, Spain) supplied all solvents and phenolic acids. Sodium hydroxide (NaOH pellets) and orthophosphoric acid (H₃PO₄ 85 wt% in H₂O) used for the solvent recycling and reuse were also provided by Sigma Aldrich (MERCK, Spain).

Aqueous stock solutions of each phenolic acid were prepared daily at 50, 100 and 500 mg/L to carry out the studies. The solutions were protected against sunlight and stored at 276–278 K.

2.2. Phenolic acids extraction

The extraction of two families of phenolic acids (hydroxybenzoic and hydroxycinnamic acids) was evaluated using three hydrophobic bio-based solvents (2-MeTHF, CPME and LIM), and compared against a conventional organic solvent (EA). Extraction assays were carried out to ensure the effectiveness of the phenolic acid extraction process from an aqueous matrix, and as a quantitative comparison of extraction based on the distinctive chemical structure of compounds within the same family. The liquid-liquid extraction method to be used was developed starting from base case operating conditions (15 min of stirring time at 750 rpm, 100 mg/L of each compound, S:F = 1:1 and 24 h at rest after extraction, all at 298 K); afterwards, the effect of the operating parameters in the extraction process was evaluated through single factor experiments, varying the stirring time, solvent to feed (S:F) volume ratio and sample concentration. The aforementioned parameters have been shown to have significant impact on the extraction efficiency of compounds [50,51]. The extraction parameters selected as the base case to carry out the optimization of the process and the optimal values are related to those obtained in previous works of our research group [25,26,46]. Once the optimization studies were performed, the optimal operating conditions for the liquidliquid extraction process were stablished as follows: 2 mL of each phenolic acid solution at a known concentration was mixed with 2 mL of each extracting solvent (1:1, solvent to feed volume relation ratio) in a vial glass tube and placed in a MS-M-S10 Magnetic Stirrer (Scilogex, The United States) at 750 rpm for 30 min. Then, the tubes were kept at rest for 24 h at 298 K to allow complete phase separation driven by the different densities and immiscibility and to ensure that thermodynamic equilibrium had been reached. This resting time was selected according to previous liquid-liquid extraction studies with similar compounds in the literature [52–54], although in future studies it could be optimised by including techniques such as centrifugation or considering other aspects such as the influence of the geometry of the vessel in which the extraction is performed. After this time, the water-rich phase (at the bottom) was collected and separated from the extractantrich phase (on top, less dense), and subjected to further analysis by UV-Vis spectrophotometry. Based on the results obtained, the interactions between the phenolic acids and the solvents involved in the extraction process were analysed. All extraction experiments were always conducted in triplicate. In addition, the pH of the aqueous solutions was measured before and after the extraction process to confirm that the acids were in their molecular form, giving the solution an acid pH value (pH = 3.5-4.5) lower than the pKa of each compound evaluated (Table 2).

2.3. UV- visible spectrophotometric determination method

The phenolic acid content after and before the extraction procedure in the water-rich phase was determined using a JASCO V-730 UV–Vis spectrophotometer (JASCO, Spain). Each phenolic acid was analysed at 298 K and monitored at its corresponding experimental wavelength of maximum absorbance, shown in Table 2. Using the previously experimentally obtained calibration lines (from six points between 0 and 100 mg/L concentration, in the range where

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Table 1

Chemical structures and relevant physicochemical properties of water (H₂O), ethyl acetate (EA), 2-methyltetrahydrofuran (2-MeTHF), cyclopentyl methyl ether (CPME) and D-limonene (LIM) [16,32,37,49].

Properties	H ₂ O	EA	2-MeTHF	CPME	LIM
Molecular structure	н∕⁰∕н		CH3	H ₃ C ₀	H ₂ C CH ₃
Empirical formula Molecular weight (g/mol) Density at 298 K (g/mL) Viscosity at 298 K (cP) Boiling point ($^{\circ}$ C) Flash Point ($^{\circ}$ F) Heat of vaporization (kJ/mol) Dielectric constant at 298 K	H ₂ O 18.02 0.997 0.89 99.9 - 40.80 78.40	C ₄ H ₈ O ₂ 88.11 0.902 0.42 77.1 24.0 35.60 6.02	$C_{5}H_{10}O$ 86.13 0.854 0.60 78.0 14.0 30.70 6.97	$\begin{array}{c} C_{6}H_{12}O\\ 100.16\\ 0.863\\ 0.55\\ 106.0\\ 30.0\\ 33.00\\ 4.76\end{array}$	C ₁₀ H ₁₆ 136.23 0.841 0.83 175.5 123.8 39.50 2.36
Water solubility at 298 K (M)	-	0.9100	1.8100	0.1098	0.0001

Table 2

Calibration line parameters (UV-visible absorbance vs concentration, obtained from six points at the range of concentrations between 10 and 100 mg/L for each compound), maximum absorption wavelength, pK_a and n-octanol/water partition coefficient (Log Kow) values [55–57] for each phenolic acid.

F	Phenolic acid name	Calibration line	R ²	λ max (nm)	pKa	Log Kow
Hydroxybenzoic acids p	p-Hydroxybenzoic acid (HA)	y = 0.075x + 0.215	0.9985	257	4.38	1.58
F	Protocatechuic acid (PA)	y = 0.062x - 0.052	0.9994	258	4.26	0.80
(Gallic acid (GA)	y = 0.045x - 0.015	0.9953	270	4.40	0.70
١	Vanillic acid (VA)	y = 0.029x - 0.003	0.9994	291	4.51	1.43
S	Syringic acid (SA)	y = 0.046x - 0.006	0.9995	269	3.93	1.11
Hydroxycinnamic acids C	Cinnamic acid (CiA)	y = 6.537x-0.258	0.9987	274	4.44	2.13
p	p-Coumaric acid (pCA)	y = 8.490x-0.318	0.9991	308	4.65	1.79
(Caffeic acid (CA)	y = 11.576x + 0.514	0.9922	325	4.62	1.15
F	Ferulic acid (FA)	y = 10.500x + 0.640	0.9967	320	4.61	1.51

a linear behaviour is ensured) shown in Table 2 and in the Supplementary material (Fig. S1-Fig. S9), the concentration of each acid in the aqueous phase before and after the extraction procedure was determined, and the solvent extraction efficiency (EE) was calculated according to Eq. (1):

$$EE(\%) = \frac{C_{ACID,i}^{qq} - C_{ACIDf}^{qq}}{C_{ACID,i}^{qq}} \times 100$$
(1)

where $C_{ACID,i}^{aq}$ and $C_{ACID,f}^{aq}$ are the concentrations of phenolic acids in the water phase before and after extraction, respectively. Hence, the percentage extracted and contained in the corresponding extraction solvent studied in each case was obtained through mass balance. Spectrophotometric analyses were carried out in triplicate and distilled water was used as blank sample. The results were always expressed as extraction efficiency (%) ± relative standard deviation (RSD, %). The deviations were calculated with the Eq. (2), dividing the standard deviation of the group of triple values (N = 3; $\sum_{i=1}^{3} x_i$) by the average of the values (\bar{x}).

$$RSD(\%) = \frac{\sqrt{\frac{1}{N-1} \cdot \sum_{i=1}^{N} (x_i - \bar{x})^2}}{\bar{x}} \times 100$$
(2)

2.4. Bio-based solvent recyclability and reuse

From an economic and sustainable point of view, it is critical to have a solvent that can be regenerated and recycled after the solute extraction process without losing its extraction capacity. The main challenge is to achieve a cost-efficient process and the implementation of a circular process, where the bio-based solvents can be cleaned and subjected several consecutive times to the same extraction process. Previously, several authors have already carried out the recovery of phenolic compounds from the solvent after the extraction process using a 0.1 M NaOH solution, since phenolic compounds easily react with NaOH to form the corresponding sodium phenolates [58,59]. The procedure carried out to test the recyclability of the best bio-based solvent was the one described below: first, the solvent was used to extract the corresponding phenolic acid from an aqueous solution; then, the same extraction solvent after the first extraction was mixed with 0.1 M NaOH to remove the target compound extracted; afterwards, such solvent can be used again to extract phenolic acids from a new "fresh" sample. The NaOH solvent regeneration and "fresh" sample extraction were consecutively replicated. The phenolic acid removal efficiencies in each extraction cycle were calculated using Eq. (1), described beforehand. It must also be mentioned that after the 2 mL of solvent was in contact with the 0.1 M NaOH basic solution and before using it again, it was mixed with 20 µL of phosphoric acid solution (85% w/w) to restore the pH of the solvent.

2.5. Statistical analysis

All studies were carried out in triplicate, and the means and standard deviation of the three samples were calculated accordingly. Statistical analyses were complemented by ANOVA with post-hoc Tukey's test using Graphpad Prism (version 9) in cases where it was more difficult to choose the best result based on the values obtained. The significance of the results obtained in the different assays was compared between them; the level of significance was defined as $p \leq 0.05$ (95% confidence interval).

3. Results and discussion

3.1. Evaluation of extraction process parameters by single factor experiments

The extraction of phenolic acids from their aqueous matrix was carried out by means of a liquid–liquid extraction process evaluat-

ing the use of a conventional solvent (EA) and three bio-based solvents (2-MeTHF, CPME and LIM). The optimization of the extraction procedure was performed by analysing the impact of the stirring time (15, 30, 60 and 90 min), the solvent to feed volume ratio (1:1, 0.5:1 and 0.25:1) and the solute concentration (50, 100 and 500 mg/L). The values of the parameters under study were chosen based on preliminary experiments and operational limits. The effect of the extraction parameters was studied on the hydroxybenzoic acids: p-hydroxybenzoic acid, protocatechuic acid, gallic acid, vanillic acid and syringic acid; and on the hydroxycinnamic acids: cinnamic acid, *p*-coumaric acid, caffeic acid and ferulic acid. The quantification of the phenolic acid content in each phase after extraction was carried out using the UV-visible spectrophotometry method described above. Although temperature can have a significant effect on the extraction process, it is a more influential parameter in the extraction from solid matrices. In the case of liguid matrices, the miscibility between both solvent phases may increase and the extraction efficiency may decrease or only increase slightly, and therefore not compensate the heating costs [29,58]. Moreover, for the specific case of phenolic antioxidants, high temperatures lead to degradation and oxidation of the target compounds [60-62]. In addition, the solvents evaluated have rather low viscosity values (Table 1), which facilitates the extraction process without the need to apply temperature.

3.1.1. Effect of stirring time

The effect of the stirring time on the extraction of phenolic acids from aqueous solutions was evaluated. Mixing time is a crucial parameter for solvent extraction experiments, as it affects the mass transfer equilibrium of the target compounds to the extraction solvent phase. For this study, the p-hydroxybenzoic acid (HA) and cinnamic acid (CiA) were taken as the representative phenolic compounds of each of the two families (on the one hand, for hydroxybenzoic acids and on the other, for hydroxycinnamic acids, respectively) since they present the simplest structures within the compounds under study. Three hydrophobic bio-based solvents (2-MeTHF. CPME and LIM) were evaluated as extractants along with the ethyl acetate as benchmark conventional organic solvent for comparative purposes. The impact of using 15, 30, 60 or 90 min of magnetic stirring time was evaluated taking as a base case the rest of the operating conditions involved in the liquid-liquid extraction process (100 mg /L of the corresponding phenolic acid, ratio 1:1 solvent to phenolic acid solution, 24 h of rest for phase separation and the whole process at 298 K).

As can be seen in Fig. 2, the experimental values obtained in the present study indicated that 30 min is the optimal stirring time for the representative solutes, reaching extraction efficiencies (EE) between 96.94 and 100% for the p-hydroxybenzoic acid and 96.06-100% for the cinnamic acid when EA, 2-MeTHF and CPME were used. The 2-MeTHF turned out to be the best extraction bio-based solvent, obtaining yields of 100% for HA and 96.06 \pm 0. 08% for CiA; meanwhile, D-Limonene provided the lower extraction values of 15.29 \pm 1.32% for HA and 72.96 \pm 0.36% for CiA. In general, increasing extraction time from 15 min to 30 min enhanced solute recovery; however, extraction times longer than 30 min slightly decreased extraction yields, which could be due to degradation or oxidation of the phenolic compounds in the presence of air and light [61,63,64]. When the data were analysed with one way ANOVA Tukey's test, if there was a significant difference at a 95% confidence interval in the mean value obtained with respect to the mean value achieved in the previous time evaluated within each compound and solvent, a new letter (a, b, c or d) was assigned to the assay (Fig. 2). The results indicated that for the cases where the extraction efficiency increased (target of interest) between one time value and another, mainly between 15 and 30 min, there was a significant difference (p < 0.05) in most cases (represented by the

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Fig. 2. Extraction efficiencies (%) of the phenolic acids, *p*-hydroxybenzoic acid and cinnamic acid, with the evaluated solvents (EA, 2-MeTHF, CPME and LIM) as a function of the stirring time (15, 30, 60 and 90 min) at 750 rpm at base case of other LLE process parameters (100 mg/L of each compound, S:F = 1:1, 24 h at rest and at 298 K).

change of letter $a \rightarrow b$). Therefore, 30 min was chosen as the optimal stirring time, providing the best extraction results, while being also interesting from a sustainable and industrial viability point of view.

3.1.2. Effect of solvent:feed volume ratio

In order to evaluate the performance of the solvents proposed in the extraction of each one of the phenolic acids (the five hydroxybenzoic acids and the four hydroxycinnamic acids studied) from aqueous matrices, different solvent to feed volume ratios (1:1, 0.5:1 and 0.25:1) were examined. An initial concentration of 100 mg/L of each acid was used. As can be seen in Table 3, the highest extraction yields for all the acids studied were obtained when the S:F volume ratio used was 1:1. However, it must also be mentioned that with 0.5:1 good extraction values were generally accomplished. The highest extraction efficiency values were achieved when 2-MeTHF, CPME and EA were used as extraction solvents (green cells in the heat map). In the case of hydroxybenzoic acids, especially for p-hydroxybenzoic acid (HA) with 2-MeTHF, very high extraction values ranging between 80.26 and 100.00% with RSD < 0.17% were obtained using the volumetric S: F ratios under study. Extraction values higher than 68.69 ± 0.94% were also reached for vanillic acid (VA) with the aforementioned solvents. Considering the extraction efficiencies, syringic acid (SA), protocatechuic acid (PA) and gallic acid (GA) would follow as good extraction values. Regarding hydroxycinnamic acids, pcoumaric acid was the one showing the highest recovery values with most extraction solvents, reaching an efficiency of 100% when using 2-MeTHF with 1:1 vol ratio. Extraction values between 39.66 and 100.00 % with RSD < 1.07% were also obtained for cinnamic acid, followed by ferulic acid and caffeic acid. It should be noted that when 2-MeTFH was used, values greater than $58.21 \pm 0.61\%$ were reached for all acids. In the specific case of D-limonene used as extraction solvent, practically null extraction efficiencies were obtained for HA, VA and SA. The rest of the phenolic acids could be extracted under the selected conditions but within the range of 1.60-72.97% with RSD < 2.06%. In this case, the one-way ANOVA Tukey's test denoted that the extraction efficiencies were significantly different (p < 0.05) from each other in all cases evaluated at 95% confidence interval. On the whole, extraction solvents can be ordered in terms of the extraction yield achieved as follows: 2-MeTHF > EA > CPME > LIM. Taking into account all the results obtained, an equal solvent: feed volume ratio (1:1) was considered optimal due to the 100.00% extraction yields achieved, especially for HA, VA and pCA; this means that total transfer of the compounds from the aqueous solution to the extractant solvent, 2-MeTHF, occurred.

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Table 3

Heat map of the extraction efficiencies (%) of hydroxybenzoic acids (HA, PA, GA, VA and SA) and hydroxycinnamic acids (CiA, pCA, CA and FA) in aqueous solutions of 100 mg/L using EA and the bio-based solvents (2-MeTHF, CPME and LIM) as extractants as a function of the solvent: feed volume ratio (1:1, 0.5:1 and 0.25:1) with a stirring time of 30 min at 750 rpm and 24 h at rest, at 298 K.

	S:F	Extraction efficiencies ± RSD (%)								
	Ratio		Hyd	roxybenzoid	: acids		Hydroxycinnamic acids			
		HA	PA	GA	VA	SA	CiA	pCA	CA	FA
	1	96.94 ± 0.14	87.05 ± 0.29	66.05 ± 0.39	97.71 ± 0.66	92.65 ± 0.38	100.00	98.20 ± 0.33	95.93 ± 0.16	98.22 ± 0.06
EA	0.5	93.25 ± 0.15	78.36 ± 0.32	55.22 ± 0.47	88.99 ± 0.73	80.28 ± 0.44	93.42 ± 0.14	94.02 ± 0.31	90.14 ± 0.67	94.87 ± 0.17
	0.25	76.72 ± 0.18	58.37 ± 0.43	40.97 ± 0.64	72.23 ± 0.89	62.13 ± 0.57	91.56 ±0.17	87.19 ± 0.33	81.33 ± 1.27	90.31 ± 0.28
	1	100.00	88.76 ± 0.28	95.52 ± 0.27	100.00	95.71 ± 0.22	96.06 ± 0.12	99.65 ± 0.25	93.54 ± 0.17	91.97 ± 0.46
2-MeTHF	0.5	98.81 ± 0.14	82.03 ± 0.31	85.77 ± 0.31	92.94 ± 0.69	87.63 ± 0.41	82.80 ± 0.98	95.89 ± 0.23	92.77 ± 0.36	90.01 ± 0.43
	0.25	80.26 ± 0.17	62.79 ± 0.40	64.56 ± 0.41	68.69 ± 0.94	58.21 ± 0.61	91.83 ± 0.41	87.30 ± 0.72	78.11 ± 0.64	85.64 ± 0.45
	1	97.48 ± 0.14	69.92 ± 0.36	49.15 ± 0.53	96.73 ± 0.67	88.08 ± 0.23	96.61 ± 0.15	97.71 ± 0.14	89.57 ± 0.17	87.23 ± 0.26
СРМЕ	0.5	90.76 ± 0.15	63.25 ± 0.39	40.88 ± 0.64	86.34 ± 0.75	74.10 ± 0.48	93.11 ± 0.51	92.67 ± 0.14	82.6 ± 0.36	86.24 ± 0.95
	0.25	78.18 ± 0.18	59.29 ± 0.42	10.48 ± 2.50	76.72 ± 0.84	30.01 ± 1.18	90.74 ± 0.38	86.03 ± 0.21	73.97 ± 0.76	83.13 ± 0.87
	1	1.20 ± 0.11	19.35 ± 1.29	17.67 ± 1.48	0.00	5.66 ± 1.54	72.97 ± 0.87	37.56 ± 0.94	53.19 ± 0.89	56.52 ± 0.69
LIM	0.5	0.91 ± 0.13	12.13 ± 2.06	18.33 ± 1.43	0.00	1.19 ± 0.09	62.78 ± 0.75	1.60 ± 1.22	11.25 ± 1.14	9.67 ± 1.44
	0.25	0.00	18.78 ± 1.33	3.36 ± 0.87	0.00	1.17 ± 0.34	39.66 ± 1.07	6.45 ± 1.19	3.10 ± 1.13	2.38 ± 1.23
	Low extraction							High ex	traction	

3.1.3. Effect of phenolic acid concentration

Then, after selecting the optimal stirring time (30 min) and the best extraction S:F volume ratio (1:1), the effect of the initial concentration of the phenolic acid aqueous solutions in the extraction efficiency with the solvents tested was investigated. Solutions of each acid were evaluated at 50 mg/L, 100 mg/L and 500 mg/L. These values were selected according to the concentration range (20–735 mg GAE/L), reported in the literature, present in the wastewater generated in the production of wine or fruit juices rich in phenolic compounds [65–67]. It should be also mentioned that in all assays where the concentration is out of range with respect to the linear range of the calibration curves, the aqueous phase samples after the extraction process were diluted with filtered and deionized water before being measured in the spectrophotometer in order to be able to use the calibration lines obtained.

The results, reported in Table 4, indicated that there was no relevant variation in the extraction efficiencies within the concentration range studied (50-500 mg/L), and high values between 45. 23 ± 0.27% and 100.00% were obtained in all cases with EA and two of the bio-based solvents (2-MeTHF and CPME). 2-MeTHF was the bio-based solvent providing the highest extraction yields for the different solute concentrations studied, achieving extraction efficiencies of up to 100% for HA, VA, CiA and pCA at 500 and 100 mg/L. The HA, VA, CiA and pCA were the best extracted compounds followed by caffeic acid, ferulic acid, protocatechuic acid and then by gallic acid. For compounds that were extracted to a lesser extent, it was noticed that, in general, increasing the concentration of the initial solution slightly enhanced the extraction yield. Except in the case of some systems with the CPME with which this tendency is not so pronounced and when D-limonene is used. LIM, as in previous studies, provided the lowest phenolic acid extraction values ranging from zero to <74.34 ± 0.39% for all tests. With a view to industrial application, it would be interesting to evaluate the selectivity of the extraction efficiency in multicomponent samples in future studies.

3.2. Selection of the extraction solvent

The choice of a suitable and environmentally friendly extraction solvent that ensures good extraction efficiencies is essential. The yield is not just related to the solubility of target compounds in the extraction solvents, it also depends on the physicochemical properties of the solvents and solutes involved in the extraction process. In this sense, to achieve the purpose of this work, the optimal extraction solvents should predictably have low viscosity, be poorly soluble in water, be easily dispersible and have a good affinity for phenolic compounds that would facilitate the extraction. Three different bio-based solvents were selected and evaluated based on the extraction recovery rates of the analytes in contrast to a conventional organic solvent classified as VOC (i.e., ethyl acetate). Due to the good extraction recoveries provided for all phenolic acids, 2-MeTHF was selected as the most suitable extraction solvent. The affinity between this solvent and the target compounds is extremely high. Potentially, it could be considered as a good solvent alternative to recover phenolic acids from liquid matrices in a more environmentally friendly way, replacing, for instance, EA with which very high extraction values were also achieved in all cases. CPME could also be considered as a good extraction solvent for the compounds of interest, especially for phydroxybenzoic acid and vanillic acid within the family of hydroxybenzoic acids, and for cinnamic acid and p-coumaric acid within the family of hydroxycinnamic acids. On the contrary, Dlimonene would not be, in this case, a suitable extraction solvent for phenolic acids based on the results obtained since it has a lower affinity for them.

For large-scale and industrial applications, costs must also be considered for solvent selection. Currently, the price of BioSs in general is higher than VOCs, but it should be commented that taking into account the costs associated with environmental externalities as compliance with regulations or insurance, extraction processes based on BioSs are quite attractive [6,68,69]. In addition,

Table 4

Heat map of the extraction efficiencies (%) of hydroxybenzoic acids (HA, PA, GA, VA and SA) and hydroxycinnamic acids (CiA, *p*CA, CA and FA) in aqueous solutions using EA and the bio-based solvents (2-MeTHF, CPME and LIM) as extractants as a function of the phenolic acid concentration (50, 100 and 500 mg/L) with a stirring time of 30 min at 750 rpm, S:F = 1:1 and 24 h at rest, at 298 K.

	Acid	Extraction efficiencies ± RSD (%)								
	Acia	Hydroxybenzoic acids				Hydroxycinnamic acids				
	[116/1]	HA	PA	GA	VA	SA	CiA	<i>p</i> CA	CA	FA
	500	100.00	84.64 ± 0.21	74.21± 0.23	100.00	94.60 ± 0.18	100.00	97.35 ± 0.43	98.49 ± 0.16	97.82 ± 0.16
EA	100	96.94 ± 0.14	87.05 ± 0.29	66.05 ± 0.39	97.71 ± 0.66	92.65 ± 0.38	100.00	98.20 ± 0.33	95.93 ± 0.16	98.22 ± 0.06
	50	93.65 ± 1.25	77.16 ± 0.47	64.42 ± 0.53	93.78 ± 0.67	89.75 ± 0.27	100.00	99.20 ± 0.06	95.34 ± 0.64	99.39 ± 0.22
	500	100.00	93.48 ± 0.38	98.55 ± 0.06	100.00	85.42 ± 0.50	100.00	100.00	81.00 ± 0.21	80.00 ± 0.46
2-MeTHF	100	100.00	88.76 ± 0.28	95.52 ± 0.27	100.00	95.71 ± 0.22	96.42 ± 0.19	100.00	93.54 ± 0.17	91.81 ± 0.26
	50	95.82 ± 1.26	88.62 ± 0.41	94.51 ± 0.36	95.71 ± 0.65	91.47 ± 0.27	98.52 ± 0.32	98.02 ± 0.57	96.17 ± 0.26	93.15 ± 0.25
	500	99.23 ± 0.14	63.87 ± 0.55	45.23 ± 0.27	85.93 ± 0.65	83.07 ± 1.72	89.45 ± 0.46	84.14 ± 0.45	65.90 ± 0.75	71.01 ± 0.42
CPME	100	97.48 ± 0.14	69.92 ± 0.36	49.15 ± 0.53	96.73 ± 0.67	88.08 ± 0.23	96.61 ± 0.15	97.71 ± 0.14	89.57 ± 0.17	87.23 ± 0.26
	50	88.12 ± 1.94	69.23 ± 0.15	46.42 ± 0.74	90.96 ± 0.69	84.22 ± 0.28	95.30 ± 0.37	93.12 ± 0.69	90.23 ± 0.16	84.88 ± 0.39
	500	0.76 ± 0.68	0.00	4.85 ± 0.75	0.00	5.25 ± 1.54	39.33 ± 1.56	26.68 ± 1.29	1.34 ± 1.06	24.16 ± 1.17
LIM	100	1.20 ± 0.11	19.35 ± 1.29	17.67 ± 1.48	0.00	5.66 ± 1.54	72.97 ± 0.87	37.56 ± 0.94	53.19 ± 0.89	56.52 ± 0.69
	50	7.23 ± 0.86	23.55 ± 1.23	21.35 ± 0.57	0.00	9.23 ± 1.69	71.29 ± 0.87	58.26 ± 0.96	74.34 ± 0.39	71.85 ± 0.77
	Low extraction								traction	

it is estimated that the price of the bio-based solvents will decrease as demand increases and they are produced on a larger scale [70]. Compared to VOCs, the BioSs used in this study have a host of advantages such as bio-renewability, less toxicity, versatility, and offer a promising way to reduce waste disposal costs. They comply with the requirements of Green Chemistry, avoid the use and disposal of organic reagents harmful to the environment, and with them a sustainable process could be achieved [6,68,71]. However, rigorous evaluation of the overall impact of BioSs on the environment or human health still needs further investigation.

3.3. Effect of molecular structure

The impact of the molecular structure of the phenolic acids and solvents was studied in order to obtain a fundamental insight into their behaviour during the extraction process. The characteristics of the compounds were studied separately, as well as the relationship established between them. The interactions between the solvents participating in the extraction process and those of the solutes with each of the two solvents (water or extraction solvent) were analysed. These molecular interactions are based on the functional groups present (which determine the establishment and strength of intermolecular forces), polarity, size of the molecules and possible steric effects (which influences the conformation and reactivity of ions and molecules) [72].

As already specified, the effect of the molecular structure of nine phenolic acids belonging to two different families (hydrox-ycinnamic and hydroxybenzoic acids) was evaluated using a conventional solvent and three BioSs as extractants. For this purpose, the selected phenolic acids display representative molecular structural changes (one or two different functionalities) which allow evaluating the impact of functional groups on the extraction process. In general, as shown in Table 3 and Table 4, it can be observed that the extraction efficiencies followed the order of HA \approx VA > SA > PA > GA for hydroxybenzoic acids, and the order of CiA \approx pCA > FA \approx CA for hydroxycinnamic acids. It was noticed that the more hydrophobic and simpler the compounds were, the better

they were extracted with the solvents that have a greater extracting power, as it will be explained below. It is worth noting that within each family, compounds with higher n-Octanol/Water Partition Coefficients (log Kow) values (Table 2) are better extracted as they are less hydrophilic, i.e. they present less affinity for water. Comparing the extraction between the two families, hydroxycinnamic acids were better extracted than hydroxybenzoic acids with all the solvents tested, which is probably due to the fact that they are molecules with fewer hydroxyl groups in the base structure and less water solubility according to the log Kow values. Regarding the effect of the structure of the phenolic acid, the different numbers of hydroxyl (-OH) and methoxy (-OCH₃) groups located in different positions of the aromatic ring were evaluated. The functional groups of the benzene ring affect the distribution of the electron cloud and the interactions with the solvent of the aqueous phase and of the organic phase, which has a great influence on the extraction process. The higher recovery efficiencies achieved with some and not with other phenolic acids, can be due to the lower presence of hydroxyl groups in their structure, which are hydrophilic groups that establish strong hydrogen bonds with the water molecules, making their extraction more difficult [21,73]. Moreover, the phenolic solutes displaying more hydroxyl groups have larger polarity and acidity, so they present a greater solubility in polar solvents as water [21,74,75]. This fact was observed with PA, GA and CA, the phenolic acids showing lower extraction vields. By contrast, the other phenolic acids evaluated presented higher recoveries, probably due to the lower number of -OH groups in the molecule and the presence of $-OCH_3$ groups, which increase the electrophilic substitution reactivity of benzene in the structure. In addition, HA, CiA and pCA could be considered as the simplest compounds and present the lowest steric impediment towards its extraction. Additional molecular simulation studies could be useful to further underpin the specific intermolecular interactions between phenolic compounds and the BioSs.

The chemical structure of the bio-solvents was also evaluated. 2-MeTHF was proven as the best BioS for the extraction. Although it has a partial miscibility in water, is defined as a strong Lewis

base and provides a clean separation of the organic-aqueous phase (without excess of emulsions) [76,77]. The compounds studied are strong Lewis acids and therefore strong interactions can be established between them and such extraction solvent. Furthermore, due to the combination of the delocalization of the electron pair of the oxygen atom by the furan ring and the presence of the methyl group, 2-MeTHF solvent present higher affinity to the target compounds than CPME constituted by a benzene ring and a methoxy group [78,79]. However, when compared to EA, there is not a big difference in the extraction efficiencies, suggesting that the main driving force for extraction are the lone electron pairs of the oxygen atoms. On the other hand, the lower extraction efficiency of the non-polar terpene LIM can be due to steric hindrance and hydrophobic functional groups that did not promote attractive interactions with the phenolic acids to favour extraction. Even though, it is worth noting the better extraction of the hydroxycinnamic acids compared to the minimal extraction of the hydroxybenzoic acids when using this solvent. In fact, an opposite trend is observed than with the rest of solvents in terms of extraction efficiencies, despite having lower values. In terms of polarity, the solvents used in this work can be classified according to their dielectric constant as follows: H₂O > 2-MeTHF > EA > CPME > LIM (as shown previously in Table 1). This order may support the results obtained, as the more polar extraction solvents presented a better performance for the recovery of phenolic acids from water, which in turn shows an extremely high polarity. The present study focuses on evaluating the efficiency of the solvents to specifically extract the compounds of interest, and to analyse the effect of the molecular structure of the solvents and solutes in the extraction process. However, it is worth mentioning that these biobased solvents have also recently been successfully applied to evaluate the extraction capacity of phenolic compounds from complex aqueous matrices, such as vanilla effluents [80], as well as their efficient recycling and reuse in consecutive extractions cycles.

3.4. Bio-based solvent recyclability and reuse

The recyclability and reuse of 2-MeTHF (the best BioS) was evaluated to recover the most efficiently extracted compound from each family (p-hydroxybenzoic acid and p-coumaric acid) with this solvent. The procedure carried out was that described in Section 2.4, consisting of three extraction cycles, each one made up of a normal extraction of the acid from an aqueous solution by the solvent, and by the back-extraction of the extracted compounds with a 0.1 M NaOH solution to clean up the solvent and be able to use it again in the next cycle. As can be seen in Fig. 3, the high extraction yields achieved by his solvent remained practically constant throughout the three cycles, with values between 97.43 and 98.56% for HA and between 96.97 and 100.00% for pCA (with RSD < 0.31% in all cases). In view of the promising results, it is appropriate to conclude that 2-MeTHF can be recycled and reused in the phenolic acid extraction process without losing its extraction efficiency. All assays were carried out in triplicate and under the optimal extraction conditions (initial concentration of 100 mg/L of each compound, stirring time 30 min at 750 rpm, 1:1 S:F volume ratio and 24 h at rest, at 298 K). The NaOH solution was used as an effective back extraction agent for solvent recycling and reuse. Nevertheless, from the point of view of recovering the solid solutes itself, it would be interesting to perform future studies using other techniques such as distillation or ion exchange. In addition, toxicological studies and complementary analytical techniques are required to ensure the stability of the extracted compounds over long periods of time and that they can be used in subsequent applications in food, pharmaceutical and chemical industry. Finally, it would be necessary to carry out in-depth techno-economic studies taking into account the energy require-

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Fig. 3. The extraction efficiencies of *p*-hydroxybenzoic acid and *p*-coumaric acid from aqueous solutions at 100 mg/L using 2-MeTHF as extractant in consecutive extraction cycles. 0.1 M NAOH was used to back-extract the acid and regenerate the solvent between each extraction cycle at the optimal LLE conditions: stirring time 30 min at 7500 rpm, S:F = 1:1, and 24 h at rest, at room temperature.

ments for recovery and regeneration methods, as well to quantify the greenness of the process for each solvent using life cycle assessments and methods such as National Environmental Methods Index (NEMI) or Analytical Eco-Scale and Analytical GREEnness metric approach (AGREE).

4. Conclusions

The aim of this study was to evaluate three hydrophobic biobased solvents (2-methyltetrahidrofuran, cyclopentyl methyl ether and D-limonene) as extractants of phenolic acids from aqueous solutions. An environmentally friendly liquid-liquid extraction process was developed and applied to recover five hydroxybenzoic acids and four hydroxycinnamic acids. The effect of the stirring time, the solvent to feed volume ratio, the initial concentration of the feed phase and the structure of the chemical compounds involved in the liquid-liquid extraction process were investigated. The values of the operating parameters in the extraction process were optimized through single-factor experiments, seeking the maximum recovery efficiency by the solvents. The optimal conditions stablished were 30 min of stirring time at 750 rpm, S: F = 1:1, and 24 h at rest for a correct phase separation, at 298 K. After evaluating the effect of three different concentrations at values expected to be found in agri-food industrial effluents, it was observed that a higher concentration slightly favoured, in general terms, the recovery.

The experimental results suggest that the bio-based solvent 2-MeTHF has great potential for the extraction of phenolic acids from aqueous solutions, providing very high recoveries in some cases up to 100.00% (for p-hydroxybenzoic acid, vanillic acid, cinnamic acid and *p*-coumaric acid) under optimal operating conditions. The high values achieved are similar to the extraction results with EA and even slightly higher for most of the compounds. Moreover, good extraction yields were also obtained with CPME (between 45.23% and 99.23% with RSD < 1.94%) but lower than with 2-MeTFH. On the contrary, the extraction efficiency obtained with D-limonene was inferior than with the other solvents, below 72.97 \pm 0.87% for all cases. The optimized extraction method has been applied to the recovery of two representative families of phenolic acids (i.e., hydroxybenzoic acids and hydroxycinnamic acids) with distinct chemical structures; specifically, the functional groups present in the compounds, the electrophilic aromatic substitution and the complexity of the molecular structure of solutes and solvents were analysed to explain the experimental extraction trends. Overall, lower number of hydroxyl groups, simpler structures that minimize steric hindrance, and a higher polarity of the solvents favour the extraction. Finally, the recycling and reuse of the best

bio-solvent extractant, 2-MeTHF, was effectively tested in consecutive extraction cycles of representative compounds from each of the two families of phenolic acids considered.

Therefore, the results obtained herein supports the potential of bio-based solvents such as 2-MeTHF to replace organic solvents (i.e., ethyl acetate) for the recovery of phenolic acids from aqueous environments.

CRediT authorship contribution statement

Raquel Cañadas: Investigation, Writing - original draft. María González-Miquel: Conceptualization, Writing - review & editing, Visualization, Supervision. Emilio J. González: Conceptualization, Writing - review & editing, Visualization, Supervision. Ismael Díaz: Writing - review & editing, Visualization. Manuel Rodríguez: Writing - review & editing, Visualization, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.molliq.2021.116930.

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