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REVIEW

The Use of Ionic Liquids and Deep Eutectic Solvents in the Extraction of Phytochemicals with Bioactive Properties: A Review

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Abstract

Innovative solvents like Ionic Liquids (ILs), Deep Eutectic Solvents (DES), and more recently, Natural Deep Eutectic Solvents (NaDES) have emerged as promising alternatives to conventional organic solvents for the extraction of bioactive compounds from plants. These solvents have gained attention due to their efficiency, lower environmental impact, and potential to enhance the selectivity of target compound extraction. Despite significant advancements in this field, a literature review revealed a lack of systematic reviews on the application of these solvents in plant bioactive extraction, over the past five years. Therefore, this study aims to compare ILs, DES, and NaDES in terms of efficiency, applicability, usability, and environmental impact, providing a comprehensive overview of the trends and challenges in this emerging field. The PRISMA methodology was used for article selection, resulting in a total of 77 studies analyzed. The findings indicate a growing number of studies on the use of DES and NaDES, whereas research on ILs for this purpose remains relatively scarce within the investigated period. Furthermore, an increasing trend in combined extraction methods was observed, with a particular emphasis on ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE), which have shown promising effects when used alongside these solvents to enhance bioactive compound extraction. This review contributes to a deeper understanding of the emerging role of DES and NaDES in plant bioactive extraction and highlights the need for further investigations on ILs, particularly within the context of sustainable and cost-effective extraction methodologies.

Highlights

- NaDES are innovative green solvents that enhance the sustainable extraction of bioactive compounds.
- Choline chloride is the most used HBA, appearing in 74,2% of NaDES formulations for phytochemical extraction.
- DES and NaDES outperformed conventional solvents by 1.17 to 9.82 times in the extraction of phytochemicals with bioactive properties.
- The combination of ILs or DES with ultrasound was used in 51.9% of studies to maximize extraction yield.
- Over 30% of studies focused on agro-industrial waste, demonstrating the sustainability of NaDES.

Keywords Green solvents · Sustainable extraction · Plant bioactive compounds · Ultrasound-assisted extraction · Microwave-assisted extraction

Introduction

Bioactive compounds are predominantly secondary metabolites produced by various plant species. These metabolites play a crucial role in plant defense mechanisms against ultraviolet radiation and pathogen attacks while also contributing to sensory attributes such as color, flavor, aroma, and astringency in fruits [1–4]. In addition to their biological functions in plants, these phytochemicals are widely

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recognized for their beneficial effects on human health and have been extensively studied for their bioactive properties. The extraction of these compounds is traditionally performed using organic solvents such as methanol, ethanol, and acetone or through steam distillation. However, these methods often require high temperatures, which can compromise the chemical stability of thermosensitive compounds, leading to degradation and a reduction in extract quality. Additionally, exposure to elevated temperatures and the use of organic solvents pose environmental and safety concerns [5].

In this context, ionic liquids (ILs) have emerged as a promising alternative to conventional solvents. These compounds were first described in 1914 when Paul Walden reported the synthesis of ethyl ammonium nitrate. Since then, ILs have been regarded as potential replacements for organic solvents due to their chemical and thermal stability, non-flammability, high conductivity, excellent solubility, negligible vapor pressure at room temperature, and tunable polarity and selectivity for various applications [6]. ILs are organic salts that remain in a liquid state at temperatures below 100 °C, typically composed of organic cations and either organic or inorganic anions. Their structure can be modified and tailored to specific needs, making them suitable for a wide range of applications, including the extraction and purification of natural compounds [7, 8]. Despite these advantages, some IL constituents have been reported to exhibit toxicity and irritant properties, raising concerns about their environmental persistence and potential contamination of aquatic ecosystems. These limitations have driven the search for more sustainable and biodegradable solvents, such as choline- and amino acid-based ILs [6, 7].

The need for safer and more environmentally friendly solvents led to the development of Deep Eutectic Solvents (DES). This term was introduced by Abbott et al. [9], who observed that mixtures of quaternary ammonium salts, such as choline chloride (ChCl) and urea, in a 1:2 ratio, formed eutectic systems that were liquid at room temperature and exhibited unique solvent properties. One of the key characteristics of DES is the significant depression of the melting point of the mixture compared to its components, attributed to intermolecular interactions between urea molecules and chloride ions. These solvents are composed of Lewis or Brønsted-Lowry acids and bases and can contain a variety of anionic and cationic species [10]. Their structure allows for the formation of eutectic mixtures with low glass transition temperatures, resulting from the combination of high-melting-point materials through hydrogen bonding interactions.

The versatility of DES has been widely highlighted in the literature. Francisco, Bruinhorst, and Kroon [11] emphasized the ability of these solvents to dissolve a wide range of solutes, while Durand, Lecomte, and Villeneuve [12] noted that DES retains the advantages of ILs, offering lower toxicity, greater biodegradability, and simpler preparation. These solvents have shown promising applications across various industries, including food, cosmetics, and pharmaceuticals, where they are used for oil purification and the extraction of active ingredients from natural products [6, 13].

Approximately a decade after the emergence of DES, Natural Deep Eutectic Solvents (NaDES) were developed as a new generation of truly green solvents, obtained exclusively from natural substances. This characteristic distinguishes them from DES, which may be synthesized from artificial compounds. According to Yang [14], NaDES offers numerous advantages, including low cost, sustainability, biocompatibility, high solubilization capacity, and remarkable selectivity. These solvents were first introduced by Choi et al. [15] in studies investigating the role of secondary metabolites found in large quantities in living cells, such as sugars, amino acids, choline, and organic acids. The researchers identified that these substances could form a third type of cellular liquid, characterized by its high viscosity, which could potentially function as a solvent for dissolving and transporting metabolites and macromolecules with poor water solubility. This phenomenon could partially explain the biosynthesis, storage, and transport of these compounds within cells and their role in the survival of organisms under extreme conditions. NaDES consists of mixtures of natural compounds, including organic acids and bases, amino acids, sugars, alcohols, and polyols, which interact through hydrogen bonding and liquefy when combined in specific molar ratios [16].

Given the growing relevance of ILs, DES, and NaDES, numerous studies have addressed their synthesis, properties, and applications. A review of the current literature revealed comprehensive investigations on ILs and their applications [8], as well as research focused on DES [10], including polysaccharide extraction [17], anthocyanin extraction [18, 19], extraction optimization strategies [20], and studies on NaDES [16]. However, few studies have conducted a comparative analysis of these solvents for the extraction of phytochemicals with bioactive properties, considering solvent characteristics, extraction conditions, efficiency, and environmental impact. To address this gap, the present study conducts a systematic literature review aimed at elucidating the specific roles of ILs, DES, and NaDES in the extraction of plant-derived bioactive compounds, with a focus on scientific articles published in high-impact journals over the past five years.

Methodology

This Systematic Literature Review (SLR) was conducted following the guidelines established by the PRISMA protocol. The Mendeley software was used as an auxiliary tool for organizing and selecting the articles. Publications were retrieved from the PubMed, Science Direct, Scopus, and Web of Science databases using the search terms ("ionic liquids" OR "deep eutectic solvents") AND "bioactive extraction", considering only articles published in English. Initially, studies from the past 10 years were included; however, in the final selection stage, the period was narrowed to five years (2020–2025).

After importing the articles, duplicate entries were automatically removed using Mendeley, and the remaining data were organized in an Excel spreadsheet for further analysis. Next, the Qualis CAPES classification of each journal was verified. Qualis CAPES is a system that ranks scientific publications in Brazil, with A1 being the highest level of relevance.

The inclusion criteria considered studies that used ILs, DES, or NaDES for the extraction of phytochemicals with bioactive properties, published between 2020 and 2025, published in A1-ranked journals. Conversely, studies were excluded if they: employed different extraction methodologies, which addressed the extraction of other types of compounds, were published in journals ranked below A1, were reviewed articles, monographs, dissertations, or theses, or were published before 2020. After the initial screening, the titles and abstracts of the selected articles were independently evaluated, applying the eligibility criteria and excluding non-relevant studies, such as systematic reviews and book chapters.

In the final selection, 77 articles remained for analysis and discussion. The comparative investigation of ILs, DES, and NaDES aimed to assess key aspects such as extraction efficiency, applicability, ease of use, and environmental impact in the extraction of plant-derived bioactives. Additionally, current research trends in this field were analyzed, and future perspectives were discussed to provide an updated overview of the potential of these emerging technologies for bioactive compound extraction.

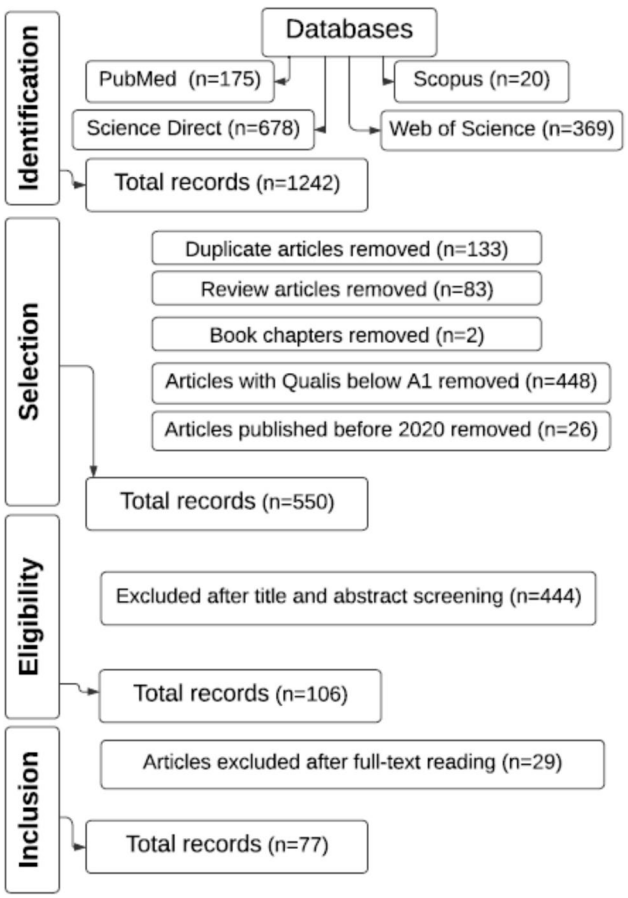

Fig. 1 Flowchart of the systematic review process, following the PRISMA protocol

Results and Discussion

Study Selection

The results of the PRISMA protocol applied in the study selection process are presented in Fig. 1.

After applying the search terms to the selected databases, a total of 1242 studies were identified, distributed as follows: 175 in PubMed, 678 in Science Direct, 20 in Scopus, and 369 in Web of Science. The initial selection process involved the exclusion of duplicates, review articles, book chapters, studies with a Qualis rating lower than A1, and publications before 2020.

In the next stage, 550 articles underwent title and abstract screening. Of these, 444 were excluded for employing extraction methodologies different from those considered in this review or for not applying ILs or DES in the extraction of phytochemicals with bioactive properties.

Subsequently, the articles were fully analyzed, and thirty were excluded for not fully meeting the established inclusion criteria. As a result, 77 articles were selected for this review. The included studies were published between 2020 and 2025, as shown in Fig. 2, which illustrates the cumulative sum of annual distribution of the selected articles on the use of ILs, DES and NaDES as solvents for extracting bioactive compounds from plant sources.

Based on the characteristics of the selected studies, there has been a significant increase in research utilizing DES and NaDES for the extraction of bioactive compounds. On the other hand, there is a noticeable scarcity of studies addressing the use of ILs for this purpose over the period analyzed.

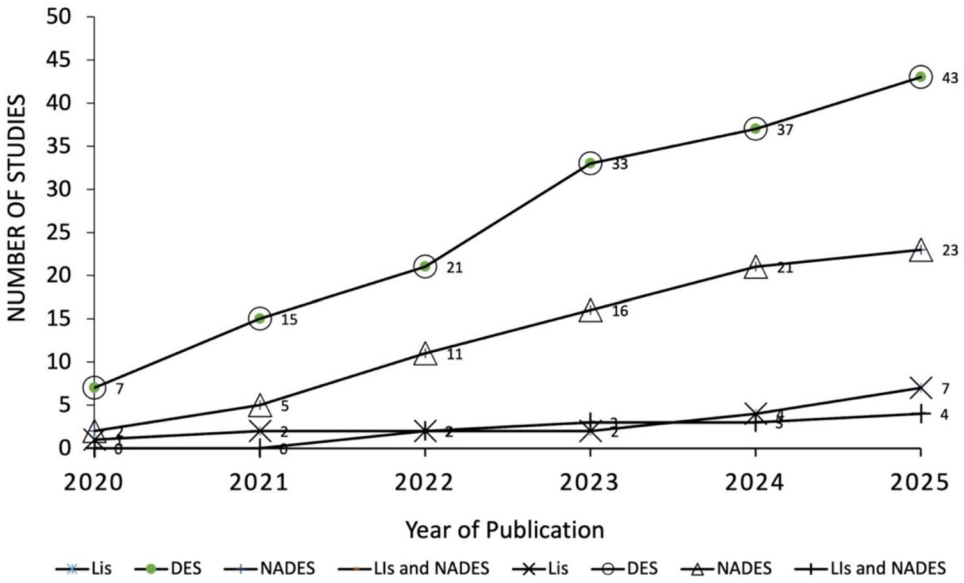

Fig. 2 Number of studies included in the review accumulated by year and solvent used

In the past five years, several authors, as presented in Tables 1 and 2, have focused on investigating alternative solvents such as ILs, DES, and NaDES. Additionally, a portion of these studies explored the combination of these solvents with other methodologies, with ultrasound and/or microwave-assisted extraction standing out as prominent approaches (Fig. 3).

In Fig. 3, it can be observed that most of the articles published in recent years on the extraction of bioactive compounds using DES and NaDES aimed to integrate these methodologies with other techniques. Notably, ultrasound application stood out, being employed in 54.5% of the studies on ILs and in 51.5% of the studies on DES or NaDES selected for this review.

Ionic Liquids in the Extraction of Bioactive Compound

Table 1 presents a list of articles on ionic liquids included in this review, detailing the key extraction parameters of bioactive compounds. The information covers the type of extracted compound, the plant source, the reagents used in the solvent composition, their concentration, the percentage of added water, the solid-to-liquid ratio, the extraction conditions, the final yield obtained, and the quantification method.

The analyzed studies on the extraction of bioactive phytochemicals using ionic liquids (ILs) demonstrated the effectiveness of these solvents in extracting polyphenols, flavonoids, carotenoids and saponins from leaves, bark, and fruits of various plant sources. It is possible to observe a trend toward the use of ultrasound in the extraction process [22, 25–29] and studies employing small volumes of solvent, referred to as microextraction [25, 27, 31]. Some authors, such as Toledo Hijo et al. [21], Sillero et al. [22], Feng et al. [24], and Ueda et al. [30], provided a general description of the IL synthesis process, whereas others reported the commercial acquisition of the solvent [23, 25–29, 31]. Given the extensive availability of publications on the synthesis of ionic liquids and their presence in the market, this study will not address synthesis but rather focus on the application of these compounds as solvents.

Olivier-Bourbigou, Magna, and Morvan [97] highlight the diversity of IL preparation and purification methods, describing different synthetic routes, such as anion metathesis, base neutralization with Brønsted acids, alkylation of alkylimidazole, and the use of dimethyl carbonate (DMC) as a methylating agent to replace alkyl halides. Wasserscheid and Welton [98] also discussed IL synthesis and purification in both editions of the book Ionic Liquids in Synthesis.

Characteristics of ILs

Recent studies emphasize the influence of pH on the extraction of phenolic compounds. Wu et al. [31], Ashraf et al. [32], and Zannou & Koca [33] highlight this relationship, which is further supported by Sillero et al. [22], who observed that ILs with lower pH values yielded higher flavonoid extraction rates. However, when the pH exceeded 4, the extraction efficiency decreased.

To better understand molecular interactions between solvents, Toledo Hijo et al. [21] calculated the excess molar volume based on solvent densities. The high negative deviations indicate that ILs, DES, and ethanol exhibit significant molecular interactions with water, likely due to hydrogen bonding, with ILs showing the strongest interactions.

Solute-solvent polarity plays a crucial role in the extraction process, a property widely considered in the selection

Table 1 List of Studies on ILs Included in the Review

Reference	Extracted Compound	Plant Source	Best Performing IL	Concentration	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Toledo Hijo et al. [21]	Polyphenols	Yerba mate leaves	Monoethanolammonium acetate [MEA][Ace]	25%	75%	1:10 g/ml	50 °C under stirring at 170 rpm for 5 hours	66 mg/g	UV/Vis Spectrophotometer
Sillero et al. [22]	Flavonoids	*Larix decidua* bark	1-Butyl-3-methylimidazolium bromide [C_4mim]Br	25%	75%	1:10 g/ml	UAE amplitude 100%, 58 °C for 120 sec/94 min	779±32 mg CE/g DBE	UV/Vis Spectrophotometer
Mesquita et al. [23]	Carotenoids	*Bactris gasipaes* fruits	1-Decyl-trimethylammonium bromide	140 mM in aqueous solution	–	S/L = 0.15 (0.75 g/5 ml)	8.2 min (5000 rpm, 15 °C for 15 min)	88.7±0.9 µg carotenoids/g dry biomass	HPLC-DAD
Feng et al. [24]	Flavonoids	Tartary buckwheat	[C_4mim]Br	1.4 mol/L in aqueous solution	–	1:40 g/ml	25 °C for 60 min with agitation (150 rpm)	41.17 mg/g	UV/Vis Spectrophotometer
Ferreira et al. [25]	β-carotene	Buriti fruit (*Mauritia flexuosa)*	1-butyl-3methylimidazolium tetrafluoroborate [C_4mim][BF4]	Diluted in ethanol 1:1 (p/p)	–	1:1 g/ml	Homogenized by UAE for 12 min	19.21 and 13.13 mg/100 g	HPLC-DAD
Hou et al. [26]	Phenolics	*Chaenomeles speciosa* leaves	[C_4mim]Br	1.33 mol/L in aqueous solution	–	1:22 g/ml	Ultrasonic power of 380 W for 10 min	78.14±0,35 mg/g	UPLC–QqQ–MS/MS
Karpitskiy et al. [27]	Naringenin Viscidulin II Wogonin Scullcapflavone I Scullcapflavone II	*Scutellaria baicalensis G.*	1-hexyl-3-methylimidazolium bis(trifluoromethylsulfonyl) imide (C6MImNTF2)	Dissolved in methanol	–	500 µl/25 mg (1:20 g/ml)	Sonication at 35 kHz for 40–60 min, followed by the addition of IL dissolved in methanol	–	HPLC-ESI-MS
	Iristectorigenin A Iristectorigenin B Resveratrol Irisolidone	*Iris sibirica L.*							
Li et al. [28]	Quercetin	*Pinus koraiensis* seed	chitosan-Cu-Fe/1-Butyl-3-methylimidazolium bromide [C_4mim]Br	1:1.5 (Cu:Fe) 0.016 mol de [C4mim]Br/L	–	1:12 g/mL	Ultrasound at 100 W and 53 °C for 14 min	2.92±0.02 mg/g	UV/Vis Spectrophotometer
Shang et al. [29]	Saponins	*Platycodon grandiflorum*	1-butyl-3-methylimidazolium bromide [C_4mim]Br	0.8 mol/L	–	1:40 g/mL	Ultrasound at 500 W and 40 °C for 40 min	1.53 mg/g	UV/Vis Spectrophotometer
Ueda et al. [30]	Carotenoid	*Eugenia uniflora L* pulp	choline bicarbonate and octanoate (1:1); choline bicarbonate and decanoate (1:1)	Dissolved in 50% (*w*/*v*) ethanol	–	1:40 g/mL	Glass cell and thermostatic bath under agitation (1500 rpm) for 1 h at 25 and 45 °C	–	UV/Vis Spectrophotometer
Wu et al. [31]	Protocatechuic aldehyde	*Perillae folium*	1-Hexyl-3-methylimidazolium Bromide [C_6MIM]Br, surfactant (sodium dodecyl sulfate) and monosodium phosphate (NaH_2PO_4)	146.529 mM [C_6MIM]Br, 70 mg de sulfactante e 0.626 g de NaH_2PO_4	–	85 mg/2.15 ml (1:25 g/ml)	134.013 s of vortexing	9.43 mg/g	HPLC
	Caffeic acid							1.92 mg/g	
	Cynaroside							38.82 mg/g	
	Rosmarinic acid							30.63 mg/g	
	luteolin							0.78 mg/g	

of ILs for this process [27, 28]. Sillero et al. [22] used the solvatochromic polarity scale to confirm structural differences between ILs and their respective intermolecular interactions. Toledo Hijo et al. [21] reinforced this concept by applying the COSMO-SAC model to assess the interaction of chlorogenic acid, caffeic acid, and quercetin, observing that these compounds have extensive nonpolar regions and smaller areas capable of forming hydrogen bonds with polar solvents. The polarity ranking of the solvents was established as follows: water >choline chloride >acetic acid >monoethanolamine >ethanol.

Overall, the studies reviewed show that the physicochemical characteristics of ionic liquids—such as pH, polarity, and capacity for molecular interactions—play a central role in the efficiency of phytochemical extraction. Lower pH values favor flavonoid extraction, whereas higher pH reduces efficiency. Thermodynamic models and polarity analyses confirm that ILs exhibit strong intermolecular interactions, especially hydrogen bonding, which explains their high affinity for phenolic compounds. In addition, proper tuning of solvent polarity aligns IL properties with the polar and nonpolar regions of the target phytochemicals, maximizing solubilization. Thus, an integrated understanding of pH, polarity, and solute–solvent interactions is essential not only for selecting more suitable ILs but also for designing extraction processes that are more selective, efficient, and sustainable.

Addition of Water to ILs

The controlled addition of water to ionic liquid (IL) solutions is a common strategy for phytochemical extraction, mainly because it (i) reduces solvent viscosity and thus improves mass transfer, (ii) tunes solvent polarity/ionicity, aligning with the "like dissolves like" principle, and (iii) alters the hydrogen-bond network and the microstructure of the system, directly affecting solubilization and partition mechanisms of the analytes. In two studies, solutions with 75% water were viewed positively by Toledo Hijo et al. [21], who reported lower viscosity and solvent cost with gains in extraction efficiency. In turn, Mesquita et al. [23] used water as an antisolvent to isolate carotenoids after IL-mediated extraction, demonstrating the feasibility of water-driven precipitation/separation.

At the molecular level, water breaks and/or reorganizes the network of interactions (hydrogen bonds, ionic forces, and van der Waals forces) typical of ILs and analogous DES, leading to higher local mobility, lower viscosity, and higher conductivity—effects that improve extraction performance up to an optimal threshold. Above certain mass fractions, the system can shift to an "IL-in-water" (or "DES-in-water") regime, losing the designed solvent character and reducing the ability to solvate hydrophobic compounds [99, 100].

Chemically, water can promote new interactions relevant to polar phytochemicals (e.g., phenolics and flavonoids): (a) strengthening/competing hydrogen bonding with IL sites (cation/anion) and with analyte functional groups (–OH, –COOH); (b) protonic/protolytic solvation that adjusts protonation states (affecting the effective pKa and partition coefficient); and (c) disruption of intermolecular interactions among phytochemicals (e.g., π–π stacking), aiding disaggregation and, in turn, extraction [8, 101]. For carotenoids and other hydrophobic compounds, however, excessive dilution with water reduces the IL's solvato-hydrophobic activity and hinders solubilization; in such cases, low-to-moderate water fractions are recommended, and water can be reserved for the recovery step as an antisolvent [23].

Summary of predominant mechanisms upon adding water to ILs/DES:

- Viscosity ↓ → diffusion/mass transfer ↑ → faster, more efficient extraction.
- Polarity/ionicity tuned → solubilization ↑ for polar compounds; may ↓ for hydrophobics if water is excessive.
- Reconfigured H-bond network → new solvent–solute interactions and possible breakup of phytochemical aggregates.
- Optimal composition window → beyond it, IL/DES-in-water regime with loss of solvating power for apolar compounds.

Extraction Conditions

Extraction conditions reported in the literature vary widely, with temperatures between 15 °C and 58 °C and times from a few minutes to several hours, depending on the solvent, matrix, and method used. Studies such as Sillero et al. [22], Ferreira et al. [25], Hou et al. [26], Karpitskiy et al. [27], Li et al. [28], and Shang et al. [29] showed that combining ILs with intensification techniques, such as ultrasonication, enhances the extraction of flavonoids, phenolics, carotenoids, and saponins, increasing overall process efficiency.

From a critical standpoint, temperature plays a dual role in extraction efficiency: on the one hand, higher values reduce the viscosity of ILs/DES, increase diffusivity, and accelerate mass transfer [8]; on the other hand, they can cause thermal degradation of thermosensitive phytochemicals, such as carotenoids and anthocyanins [102]. Thus, there is an optimal operating window in which extraction is favored by greater solubilization without compromising compound stability.

With respect to extraction time, short periods can lead to insufficient yields due to incomplete diffusion, whereas

Table 2 List of studies on DES and NaDES included in the review

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Toledo Hijo et al. [21]	Polyphenols	Yerba mate leaves	Choline chloride + Acetic acid (1:2)	75%	1:10 g/mL	50 °C under stirring at 170 rpm for 5 hours	55 mg/g	UV/Vis Spectrophotometer
Feng et al. [24]	Flavonoids	Tartary buckwheat	magnetic nanofluid N888-Cl/lauric acid (1:2)	–	1:40 g/mL	25 °C for 60 min with agitation (150 rpm)	35.29 mg/g	UV/Vis Spectrophotometer
Karpitskiy et al. [27]	8-Methoxyquercetin-3- O-[6″−3-hydroxy3-methylglutaroyl)]-glycoside	*Citrus reticulata B*	Choline chloride + urea (1:2)	–	500 µl/25 mg (1/20 g/mL)	Vortex mixing, ultrasound at 35 kHz for 40–60 min, pH adjustment	–	HPLC-ESI-MS
	Chlorogenic acid Quercetin-3-glucoronide	*Hypericum perforatum L.*						
	Flavone Methylated wogonoside	*Scutellaria baicalensis G.*						
	Flavonoid-O dihexoside 4′O-methylapigenin-8-Chexoside	*Iris sibirica L.*						
Ueda et al. [30]	Carotenoid	*Eugenia uniflora L* pulp	DLMenthol and octanoic acid (1:1) e DLMenthol and decanoic acid (1:1)	Dissolved in 50% (w/v) ethanol	1:40 g/mL	Glass cell and thermostatic bath under agitation (1500 rpm) for 1 h at 25 and 45 °C	–	UV/Vis Spectrophotometer
Ashraf et al. [32]	Polyphenols	Fenugreek seeds	Choline chloride + Malic acid (1:2)	20%	1:20 g/mL	40 °C for 30 min (ultrasound 400 W)	69.16 ± 3.12 mg/g	UV/Vis Spectrophotometer
	Flavonoids						35.17 ± 1.58 mg/g	
	Kaempferol						10.65 ± 0.49 mg/g	HPLC - DAD
	Rutin						18.33 ± 0.84 mg/g	
	Quercetin						10.82 ± 0.59 mg/g	
Zannou & Koca [33]	Total Phenolics	Black mulberry (*Rubus* spp)	Choline chloride + Glucose (1:2)	20%	0.5:10 g/mL	25 °C for 20 min with ultrasound	9.35 ± 0.39 mg GAE/g	UV-VIS spectrophotometer
	Flavonoids	Black mulberry (*Rubus* spp)	Choline chloride + Ethylene glycol (1:2)	20%	0.5:10 g/mL	25 °C for 20 min with ultrasound	104.72 ± 5.17 mg ECE/100 g	UV-VIS spectrophotometer
	Anthocyanins	Black mulberry (*Rubus* spp)	Choline chloride + Acetic acid (1:2)	20%	0.5:10 g/mL	25 °C for 20 min with ultrasound	115.37 ± 0.43 mg CGE/100 g	UV-VIS spectrophotometer

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Jiménez-Ortega et al. [34]	Flavonoids	Pepper Biomass Residues *(Capsicum annuum L.)*	ChCl/1,6-hexanediol (1:1)	30%	0,05:1 g/mL	40 °C for 15 min with ultrasound (20 kHz, 300 W) and 35 s in pulse mode	10.31 ± 0.16 mg quercetin equivalent/g dry	Microplate Spectrophotometer
Xia, Li & Jiang [35]	Flavonoids	*Polygonatum odoratum* rhizomes	Choline chloride + Lactic acid (1:2)	27%	1:22 g/mL	51 °C for 21 min, UAE 180 W	11.47 mg/g	UV/Vis Spectrophotometer
Grudniewska & Popłoński [36]	Xanthohumol	Hop residues	Choline chloride + Propylene glycol (1:2)	5%	1:50 (*w*/w)	60 °C for 1 h	2.30 mg/g	HPLC
Bottu et al. [37]	Polyphenols (Procyanidin B2, chlorogenic acid, epicatechin hydrate, vanillin and phloridzin)	Apple pomace	Choline chloride + Ethylene glycol (1:4)	–	1/10 (w/w)	60 °C for 30 min	–	HPLC
Wei et al. [38]	Flavonoids	*Moringa oleifera* leaves	Choline chloride + glycerol (1:15)	–	1:66 g/mL	90 °C for 81 min	70.4 ± 0.47 mg/g	UV/Vis Spectrophotometer
Pontes et al. [39]	Phenolic compounds	Olive pomace	Choline chloride + malonic acid (1:1)	50%	3:100 g/mL	66.8 °C for 3 h	19.76 mg GAE/g	UV/Vis Spectrophotometer
Alañón et al. [40]	Oleuropein Gallic acid Luteolin	Olive leaves (*Olea europaea*)	Choline chloride + Ethylene glycol (1:2)	43.3%	0,2:1.5 g/mL	79.6 °C for 16.7 min, microwave irradiation	1.82 ± 0.21 mg/g 25.00 ± 2.34 mg/g 1.54 ± 0.13 mg/g	HPLC
Alibade et al. [41]	Polyphenols Anthocyanins	Grape pomace	Glycerol + Sodium benzoate (9:1)	70%	1:20 g/mL	50 °C at 500 rpm for 150 min (ultrasound for 15 min)	8630.94 µg/g 3887.50 µg/g	UV/Vis Spectrophotometer
Cui et al. [42]	Proanthocyanidins	Cottonseed hulls	Choline chloride + levulinic acid (1:2)	33.21%	1:36.25 g/mL	7.4 min, UAE 1200 W, ice-water bath	75.26 ± 2.08 mg/g	HPLC–MS/MS

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
González-Rivera et al. [43]	Phenolic compounds	Chestnut shell	Choline chloride + oxalic acid (1:1)	25%	1:10 g/mL	65 °C for 30 min	108.6±3.1 mg GAE/g	UV-VIS spectrophotometer
	Gallic acid					65 °C for 5–60 min	751.2±42.5 a 2235.9±67.1 µg/g	HPLC-DAD
	Ellagic acid						582.8±17.5 e 735.8±22.1 µg/g	
	Catechin hydrate						458.1±21.45 a 882.2±22.1 µg/g	
	Procyanidin B2						38.6±7.4 a 48.4±8.7 µg/g	
Koraqi et al. [44]	Phenolic compounds	*Urtica dioica L.* (nettle)	Citric acid + maltose (1:2)	20%	1/10–30 g/mL	70 °C for 30 min + ultrasound	2.423mgGAE/100 g	UV-VIS spectrophotometer
	Flavonoids						134.71mgCE/100 g	
	Quercetin-3-Orutinoside						134.71 mg/100 g	HPLC-DAD-ESI-MS/MS
	5-ocaffeoylquinic acid						426.55 mg/100 g	
	Caffeoyl malic acid						1557.55 mg100/g	
Li et al. [45]	Anthocyanins	Rose flower petals	Choline chloride + lactic acid (1:1)	30%	1/30 g/mL	50 °C for 10 min, ultrasound (40 KHz, 400 W)	8.265 mg/g	UV spectrophotometer
Liu et al. [46]	Antioxidants	*Hibiscus manihot* L. flowers	Choline chloride +1,4-butanediol (1:2)	20%	1:26 g/mL	73 °C for 20 min, microwave-assisted	16.704 mg/g	HPLC
Liu et al. [47]	Scutellarin	*Erigerontis Herba*	Choline chloride + acetamide (1:4)	30%	1/20 g/mL	25 °C, ultrasound 500 W and 40 KHz for 30 min	34.39±0.55 mg/g	HPLC-DAD
Meng et al. [48]	Chlorogenic acid	*Eucommia ulmoides* leaves	Choline chloride + malic acid (1:1)	20%	1:15 g/mL	30 min at 25 °C, 25 min ultrasound 600 W at 50 °C	42.6±0.9 mg/g	UPLC
Pavlović et al. [49]	Theobromine Caffeine	Cocoa Bean Shell	Choline chloride + oxalic acid (1:1)	30%	0,5:10 g/mL	60 °C for 10 min, microwave-assisted	5.004 mg/g 1.599 mg/g	HPLC-DAD

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Vargas-Serna, Ochoa-Martínez & Vélez-Pasos [50]	Phenolic compounds	Pineapple peel	Choline chloride + glycerol (1:2)	–	1:60.5 g/mL	67 °C, microwave 2.55 MHz at 60% max power (420 W) for 87 s	35.95 mg gallic acid eq/g	spectrophotometer
Xing et al. [51]	Glabridin Isoliquiritigenin	*Glycyrrhiza glabra* (licorice)	Choline chloride + lactic acid (1:1)	20%	1:24 g/mL	62.5 °C for 18 min, pretreated with ultrasound 480 W	7034.5 ± 7.29 µg/g 859.29 ± 2.79 µg/g	HPLC
Liu et al. [52]	Biflavonoids	*Selaginella chaetoloma*	Tetrapropylammonium bromide +1,4-butanediol (3.7:1)	22%	1:20 g/mL	57 °C, UAE power 280 W for 30 min	21.68 ± 0.78 mg/g	HPLC-DAD
Ali et al. [53]	carnosic acid carnosol	*Rosmarinus officinalis L.*	Geraniol + dodecanol (1:1)	–	1:20 g/mL	UAE at 37 kHz and 40 °C for 30 min	5.61 mg/g 3.61 mg/g	HPLC
Alsaud, Shahbaz & Farid [54]	β-caryophyllene	Manuka leaves (*Leptospermum scoparium*)	Menthol + lactic acid (1:2)	–	14.99:100 g/mL	Under agitation for 1.09 h at 25.07 °C	10.25 mg/g	HPLC-DAD
Alsaud et al. [55]	Polyphenols	Manuka leaves (*Leptospermum scoparium*)	Choline chloride + ethylene glycol (1:2)	–	5/100 g/mL	50 °C for 1.07 h, centrifugation at 10,000 rpm for 10 min	59.82 mg GAE/g	UV-VIS spectrophotometer
Barbieri et al. [56]	Polyphenols	Rosemary (*Rosmarinus officinalis L.*)	1,2-propanediol +choline chloride (1:2)	10%	0.150: 2.85 g/mL	Ultrasound at 50–60 Hz and 40 °C for 30 min, vortex for 1 min, centrifugation at 9500 rpm for 3 min	62.21 ± 3,85 mgAG/g	UV-VIS spectrophotometer
Benvenutti et al. [57]	Anthocyanin	jabuticaba pomace *(Myrciaria cauliflora)*	Choline chloride + propylene glycol (1:2)	50%	1:30 g/mL	After 60 min of maceration, the extract was centrifuged at 412×g for 15 min	279.45 ± 25.44 mg/100 g	UV-VIS spectrophotometer

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Bi et al. [58]	Anthocyanins	mulberry	Choline chloride + lactic acid (1:2)	3.19%	1:10.76 g/mL	57.24 °C for 31.54 min	6.84±0.21 mg/g	pH differential method
Cañadas et al. [59]	Polyphenols	winery wastewater	trimethyloctylammonium chloride ($N_{8881}Cl$)+Octanoic acid (1:1)	–	1:1 g/mL	Extraction for 15 min at 500 rpm followed by centrifugation for 15 min at 3500 rpm.	Extraction yield of 84.83%	UV-VIS spectrophotometer
Carbonell-Rozas, Romero-González & Francech [60]	gallocatechin, epigallocatechin gallate, epicatechin, catechin, caffeic acid, epicatechin gallate, ferulic acid, narirutin, miquelianin, rutin, isoquercetin,kaempferol, eriodyctiol, quercetin,naringenin, luteolin	Tea (*Camellia sinensis*)	Lactic acid, glycerol and water (1:1:3)	–	0.5:10 g/mL	Vortex for 10 s, ultrasonic bath at 35 °C for 30 min, centrifugation at 9500×g for 5 min	0.3 a 29.125 mg/kg	UHPLC-QqQ-MS
Chisha et al. [61]	Rosmarinic acid	*Rosmarinus officinalis*	Choline chloride + lactic acid (1:2)	13.5%	ratio of 34	69 °C for 5.6 h	Extraction yield of 6.10%	HPLC
Cui et al. [62]	Polyphenols	green tea	Choline chloride + Ethylene glycol(1:2)	29%	ratio of 44	84 °C for 39 min	Extraction yield of 20.12%	UV-VIS spectrophotometer
Domínguez-Rodríguez et al. [63]	Polyphenols hesperidin	tangerine leaves *Citrus reticulata*	Choline chloride + glycerol (1:2)	57%	0.2:10 g/mL	Ultrasound at 25 °C for 50 min, centrifugation at 5000 rpm for 15 min	40±1 mg GAE/g 18.4±0.3 µg/mg of extract	UV-VIS spectrophotometer HPLC-DAD
Fernández-Prior et al. [64]	Phenolic compounds hydroxytyrosol	olive oil extraction waste (alperujo)	Choline chloride, glycolic and oxalic acid (1:1,7:0,3)	–	1:1 (p/v)	150 °C for 5 min	189.8 mg/g 85.81 mg/g	UV-VIS spectrophotometer HPLC
Hikmawanti et al. [65]	Phenolic compounds flavonoids	*Pluchea indica (L.)*	Choline chloride +urea (1:3)	26%	0.5:10 g/mL	Ultrasound at 40 kHz and 52 °C for 15 min	71.380±1907 mgGAE/g 9.713±0.243 mg QE/g	Microplate Spectrophotometer

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Khalid et al. [66]	Polyphenols	chickpea *(Cicer arietinum L.)*	Citric acid + glycerol (33:33) v/v	33%	50 mg/ml	Sonication (40 kHz) for 30 min, centrifugation at 3000 rpm for 10 min	128.0 ± 0.2 mg GAE/100 g	UV-VIS spectrophotometer
	flavonoids	chickpea *(Cicer arietinum L.)*	Citric acid + glycerol (66:16) (*v*/v).	16%	50 mg/ml	Sonication (40 kHz) for 30 min, centrifugation at 3000 rpm for 10 min	38.61 ± 0.03 mg CE/100	
	catechin coumaric acid Epicatechin rutin gallic acid kaempferol 3-glucoside ferulic acid chlorogenic acid syringic acid	chickpea *(Cicer arietinum L.)*	Citric acid + glycerol (33:33) v/v	33%	50 mg/ml	Sonication (40 kHz) for 30 min, centrifugation at 3000 rpm for 10 min	8.25 mg/g 0.02 mg/g 3.15 mg/g 0.90 mg/g 0.76 mg/g 0.06 mg/g 0.03 mg/g 7.25 mg/g 1.20 mg/g	HPLC-DAD
Lai et al. [67]	Flavonol glycosides	*Ginkgo biloba*	Choline chloride + acetic acid and 1,2-propanediol (1:2:3)	20%	0.42:10 g/mL	Ultrasound at 320 W and 32.5 °C for 63.6 min	5.60 mg/g	HPLC
Liu et al. [46]	flavonoids Neochlorogenic acid, chlorogenic acid, caffeic acid, rutin, hyperin, isoquercetin, hibifolin, myricetin, quercetin-3′ -O-glucoside e quercetin	*Hibiscus manihot L.* Flower	Choline chloride +1,4-butanediol (1:2)	20%	1:26 g/mL	Microwave-assisted extraction at 500 W and 73 °C for 20 min	15.641 mg/g 0.879, 0.287, 0.276, 0.202, 5.036, 3.647, 4.961, 0.137, 0.505 e 0.231 mg/g	– HPLC
Marinaccio et al. [68]	Lycopene	Tomato skin waste	Menthol:thymol (1:1)	–	1:2 g/mL	Ultrasound (20 kHz, 400 W) at 36 °C for 20 min, centrifugation at 4400 rpm for 25 min	484.2 mg/g	HPLC-DAD
Meng et al. [69]	Flavonoids	*Cercis glabra* leaves	Choline chloride + levulinic acid (1:2)	20%	1:25 g/mL	40 °C for 39 min	8.01 mg/g	HPLC-PDA

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Ni et al. [70]	quercetin rutin	*Sophora japonica* buds waste	Choline chloride + Citric acid (1: 1)	10%	0,1 g/mL	60 °C for 30 min, centrifugation at 8000×g for 20 min at 25 °C	38.7 ± 1.6 mg/g 10.1 ± 0.5 mg/g	HPLC
Peng et al. [71]	Polyphenols	*Moringa oleifera* Lam. leaves	Betaine+maleic acid (2:1)	30%	1:38,4 g/mL	Ultrasound at 560 W and 40 °C for 33 min	44.19 ± 0.23 mg GAE/g	UV-VIS spectrophotometer
Pusty et al. [72]	Phenolic anthocyanins flavonoids	red cabbage (*Brassica oleracea L.*)	Choline chloride + Citric acid (2:1)	26%	1:25 g/ml	Ultrasound at 252 W and 52 °C for 20 min	7.527 mg GAE/g 0.736 mg/g 0.489 mg QE/g	UV-VIS spectrophotometer
Rico et al. [73]	Polyphenols	Melon peels	Sodium acetate+urea (1:3)	10%	2:100 g/mL	90 °C for10min	4.35 mg GAE/g	UV-VIS spectrophotometer
Saar-Reismaa et al. [74]	chlorogenic acid derivatives flavone glycosides iridoid glycosides	*Dipsacus fullonum*	Choline chloride + lactic acid (1:2,4)	35%	1:27 g/mL	Maceration for 1 h, ultrasound (640 W, 350 kHz) at 40 °C for 30 min	0.38–1.65 mg/g 0.47–2.28 mg/g 0.17–0.92 mg/g	HPLC-DAD
Silva et al. [75]	caffeine	coffee pulp	guanidinium chloride, lactic acid and water (10:17:15)	–	1:10 g/mL	Maceration at 1000 rpm and 60 °C for 30 min	8.88 ± 0.55 mg/g	UHPLC-PAD/UV
	chlorogenic acid	coffee beans	Choline chloride + Sorbitol (4:1)	–	1:10 g/mL	Maceration at 1000 rpm and 60 °C for 30 min	64.39 ± 2.06 mg/g	UHPLC-PAD/UV
Suresh et al. [76]	Rebaudioside A Stevioside	*Stevia rebaudiana*	Lactic acid, glycerol, malic acid and glucose (1:1:1:1)	–	1:10 g/mL	Ultrasound (200 W, 40 kHz) for 30 min at 50 °C	38.24 ± 2.22 mg/g 114.58 ± 5.89 mg/g	UHPLC-PDA
Tang et al. [77]	Saponins	seed pomace of *Camellia oleifera*	L-proline, glycerol and sucrose (4:10:1)	30%	1:15 g/mL	Ultrasound (100 W) for 20 min at 60 °C	Yield (23.22 ± 0.28%)	UV-VIS spectrophotometer

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Vázquez-González et al. [78]	phenolics	Strawberry extrudate	Choline chloride, Glycolic acid and Oxalic acid (1:1,7:0,3)	–	1:1 g/mL	15 min of agitation, 10 min of centrifugation at 1765×g	5791.94±214.34 µg GAE/g FW	UV-VIS spectrophotometer
	phenolics	raspberry extrudate					3355.71±7.94 µg GAE/g FW	
	anthocyanins	strawberry extrudate					1.38±0.11 mg CGE/100 g	
	anthocyanins	raspberry extrudate					0.38±0.03 mg CGE/100 g FW	
	uronic acid	strawberry extrudate					1.88 mg/g	
Vinas-Ospino et al. [79]	Carotenoids	orange peel	Octanoic acid and L-proline (4:1)	–	1:20 g/mL	Ultrasound at 120 W and 45 °C for 20 min	46.01 µg/g	UV-VIS spectrophotometer
Wawoczny et al. [80]	Phenolics Flavonoids	*Calendula officinalis* petals	Choline chloride and levulinic acid (1:2)	–	4:30 g/mL	80 °C with agitation (400 rpm) for 2 h	16.1 mg/g 12.2 mg/g	UV-VIS spectrophotometer
Wen et al. [81]	gallic acid	*Paeoniae Radix Rubra*	Betaine and malonic acid (1:1)	50%	1:3 g/mL	Vortex for 4 min, centrifugation at 14,000 rpm for 10 min	0.24 a 1.33 mg/g	UPLC - PDA
	catechin						0.35 a 0.94 mg/g	
	albiflorin						0.71 a 28.93 mg/g	
	paeoniflorin						15.6 a 25.79 mg/g	
	paeonol						0 a 0.19 mg/g	
Wen, Fan & Cao [82]	crocetin	*Gardenia jasminoides* Ellis fruit	Benzyltriethylammonium chloride and oxalic acid dihydrate (1:1,5)	–	1:20 g/mL	80 °C for 30 min	8.485 mg/g	UPLC - PDA
Zannou et al. [83]	Anthocyanins	Blackberry fruits (*Rubus* spp.)	Choline chloride + glycerol (1:4,22)	20%	1:15 g/mL	Ultrasound for 15 min	193.03 mg CGE/100 g de TAC	–
	cyanidin-3-glucoside	Blackberry fruits (*Rubus* spp.)	Choline chloride + glycerol (1:4,22)	20%	1:15 g/mL	Ultrasound for 15 min	596.29 mg/kg	UPLC - PDA
	cyanidin-3-rutinoside						104.57 mg/kg	
	pelargonidin-3-glucoside						16.57 mg/kg	
	cyanidin chloride						37.35 mg/kg	
Zhang et al. [84]	Phenolics	*Polygonatum cyrtonema* Hua	Choline chloride + lactic acid (1:2)	30%	1:20 g/mL	Ultrasound at 50 °C and 500 W	–	UV-VIS spectrophotometer

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
	Phenolics	*Polygonatum cyrtonema* Hua	Choline chloride + lactic acid (1:2)	30%	1:40 g/mL	Microwave extraction for 30 s and 60 s, cooled for 2 min (3 times)	–	UV-VIS spectrophotometer
	Ferulic acid	*Polygonatum cyrtonema* Hua	Choline chloride+ glycerol (1:2)	30%	1:20 g/mL	Ultrasound at 50 °C and 500 W	129.2 µg/g	HPLC-MS-MS
	Rutin	*Polygonatum cyrtonema Hua*	Choline chloride + lactic acid (1:2)	30%	1:20 g/mL	Ultrasound at 50 °C and 500 W	281.1 µg/g	HPLC-MS-MS
Zhang et al. [85]	Luteolin	Peanut shells	Choline chloride + Ethylene glycol (1:5)	20%	1:32 g/mL	Microwave at 601 W for 92 s	2.90 ± 0.02 mg/g	HPLC
Zannou & Koca [86]	Total Phenolics and Flavonoids	Alkanet root (*Alkanna tinctoria*)	Sodium acetate + Formic acid (1:4)	45%	0.25:10 g/mL	25 °C for 20 min with ultrasound	Total phenolics: 390.16 mg GAE/g, Total flavonoids: 10.69 mg ECE/g	UV-VIS spectrophotometer
Carmona et al. [87]	Total Phenolics	Olive oil residues	Citric acid + Fructose (1:1)	19%	10:10 (*w*/w)	25 °C for 60 min	3988.74 mg/kg	HPLC
Gomez-Urios et al. [88]	Total Phenolics	*Citrus sinensis* Peel	Choline chloride + Malic acid (1:1)	75%	1/10 g/mL	40 ± 5 °C for 20 min	1053 mg GAE/100 g	UV-VIS spectrophotometer
	Flavonoids						94.7 mg catechin equivalent (CE)/100 g	UV-VIS spectrophotometer
	Ascorbic Acid						430 mg/100 g	HPLC-UV/VIS
García-Roldán, Piriou & Jauregi [89]	Gallic acid	spent coffee grounds	Choline chloride +1,2-Propanediol (1:2)	50%	1/15 g/mL	65 °C for 150 min	138.5 ± 1.09 mg/kg	HPLC-UV/Vis
	3-O-caffeoylquinic acid						131.34 ± 0.75 mg/kg	
	Caffeic acid						63.17 ± 0.53 mg/kg	
Airouyuwa et al. [90]	Phenolic Compounds	Date seeds (*Phoenix dactylifera* L.)	Choline chloride + Lactic acid (1:2)	–	1:30 g/mL	35 and 40 °C for 15 min with ultrasound at 80% amplitude	145.54 ± 1.54 mg GAE/g of date seed powder	UV-VIS spectrophotometer
Cao et al. [91]	Phenolic Compounds	Broccoli leaf residues	Choline chloride +1,2-Propylene glycol (1:2)	30%	1:36.35 g/mL	49.5 °C for 31.4 min; ultrasonic power 383 W	4.91 mg/g of dried leaves	UV-VIS spectrophotometer
	Neochlorogenic acid						647 ± 6,49 mg/kg	liquid chromatography-mass spectrometry (LC-MS)
	Chlorogenic acid						19.2 ± 1,05 mg/kg	
	Caffeic acid						16.2 ± 0,97 mg/kg	
	Sinapinic acid						94.2 ± 2,09 mg/kg	
	Ferulic acid						310 ± 3,98 mg/kg	

Table 2 (continued)

Reference	Extracted Compound	Plant Source	Best Performing DES	Water	Solid-Liquid Ratio	Extraction Conditions	Bioactive Compound Yield	Detection/Quantification Method
Lin et al. [92]	Anthocyanins (cyanidin-3-O-galactoside, cyanidin-3-O-glucoside, cyanidin-3-O-arabinoside, cyanidin-3-O-xyloside, cyanidin-3,5-O-dihexoside, and the dimer of cyanidin-hexoside)	*Aronia melanocarpa*	Choline chloride + Glycerol (1:2)	30%	1:15 g/mL	50 °C for 300 s with ultrasonic power of 200 W	448.873 mg/g of *A. melanocarpa* pulp	HPLC-MS
Plaza et al. [93]	Polyphenols	Mangosteen (*Garcinia mangostana L.*) Peel	Choline chloride + Lactic acid (1:2)	18.8%	0.5:10 g/mL	60% ultrasound amplitude for 15 min	2447 mg Epicatechin/100 g	UV-VIS spectrophotometer
Santos-Martín et al. [94]	Phenolic Compounds	Blueberry leaves	Lactate, Sodium acetate, and Water (3:1:2)	–	1:15 *w/v*	Sonication for 45 min at 65 °C	135 ± 1 mg GAE/g	spectrophotometer
Stupar et al. [95]	β-Carotene	Pumpkin (*Cucurbita maxima*)	Caprylic acid: Capric acid (C8:C10) (3:1)	–	1:7 g/mL	50 °C, ultrasonic power 60% (52.5 W/cm^3) for 10 min	151.41 µg/mL	spectrophotometer
Zhang et al. [96]	Saponins	*Polygonatum sibiricum*	Butyric acid + Urea (4:1)	60% + 15 mg $FeCl_3$	1:15 g/mL	Ultrasonic bath (30 °C, 40 Hz) for 30 min	~75 mg/g	UV–Vis spectrophotometer

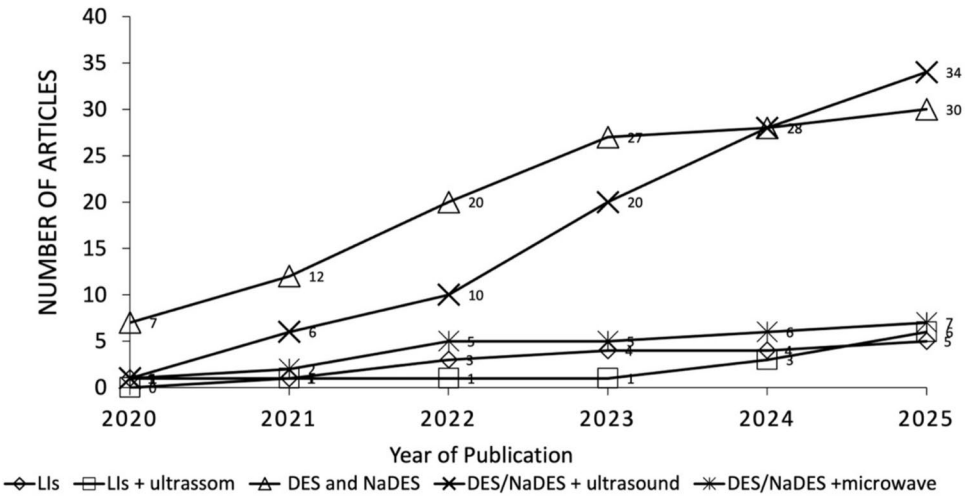

Fig. 3 Number of articles combining ultrasound and/or microwave included in the review

overly long times often provide no proportional gains because of solvent saturation and, in some cases, may even promote phytochemical oxidation [103]. Strategies such as ultrasound and microwaves markedly reduce the time needed to reach extraction equilibria, improving selectivity and energy efficiency [25, 28].

The solid–liquid ratio also has a strong impact. Higher solvent volumes favor extraction by reducing competition among solutes, but they increase solvent use and reduce process sustainability. Recent studies suggest that moderate ratios, optimized with statistical methods (e.g., factorial design or response surface methodology, RSM), can balance yield, selectivity, and cost [102].

Another relevant aspect is the choice of the hydrogen bond donor (HBD) in DES/NaDES. The different performance of some HBDs is directly linked to their chemical features: functional groups able to form multiple hydrogen bonds (e.g., lactic acid, glycerol) and polarity/π–π interaction profiles determine greater affinity for specific classes of phytochemicals [102]. The recent work by Jiménez-Ortega et al. [34] shows that HBDs rich in hydroxyl groups promote additional interactions with phenolics, improving selectivity and yield, while less polar HBDs are more suitable for hydrophobic compounds.

Therefore, a critical analysis of extraction conditions indicates that performance should not be judged by overall yield alone, but by the interplay between operating variables and the chemical features of both the solvent and the phytochemicals. An integrated approach—considering time, temperature, solid–liquid ratio, and HBD selection—is essential to design more selective, efficient, and sustainable processes.

Extraction Efficiency

Studies show that ILs can enhance the extraction of bioactive compounds. Sillero et al. [22] reported higher flavonoid yields with 1-butyl-3-methylimidazolium bromide and 1-butyl-3-methylimidazolium tetrafluoroborate, with the bromide providing the highest antioxidant activity. Toledo Hijo et al. [21] demonstrated that extraction time directly influences the yield of polyphenolic compounds. Mesquita et al. [23] found that aqueous IL solutions were more efficient for carotenoid extraction than conventional solvents. Ferreira et al. [25] demonstrated that the use of IL improved the extraction efficiency of β-carotene compared to acetone (19.21 and 13.13 mg/100 g, respectively) and provided greater pigment stability during light, thermal, and color stability tests. Hou et al. [26] obtained higher total phenolic yields using ionic liquid combined with ultrasound than those achieved through thermal reflux extraction with 70% ethanol for 2 h, as well as those obtained using ethanol combined with ultrasound.

Environmental Impact

The studies assessed environmental impact using carbon footprint analysis, E-factor, toxicity assessment, and energy consumption. Sillero et al. [22] highlighted the limited biodegradability of ILs, particularly those containing halides. Mesquita et al. [23] demonstrated that IL-based extraction resulted in lower carbon footprints and waste generation compared to conventional solvents. The simultaneous extraction with ultrasound and microwaves was the most energy-efficient method (<0.03 kW/h).

DES and NaDES in the Extraction of Bioactive Compounds

Table 2 presents the studies selected in this review that used DES or NaDES as solvents for bioactive compound extraction, including parameters such as the extracted substance, plant source, solvent composition, molar ratio, and extraction conditions.

According to Table 2, various bioactive compounds were extracted using DES. Among these, 32.3% did not target specific components but rather extracted total phenolic compounds and/or flavonoids. Additionally, 36,4% of the studies focused on extracting bioactive compounds from residues generated during vegetable processing, contributing to the promotion of sustainability within agricultural supply chains.

Regarding the constituents of DES, choline chloride was the most used reagent among the selected studies, appearing in 74,2% of them. Abbott et al. [9] and Francisco, Bruinhorst, and Kroon [11] highlighted that choline chloride acts as a hydrogen bond acceptor (HBA) that binds to a hydrogen bond donor (HBD). The HBDs used in these studies varied considerably, with lactic acid, malic acid, and oxalic acid being the most frequently employed in the best-performing DES formulations for bioactive extraction.

The optimal molar ratios for DES or NaDES formulations ranged between 1:1 [30, 43, 45, 48, 49, 51, 53, 59, 68, 70, 81] and 1:15 [38]. The water content varied from 3,19% [58] to 75% [21, 88] while the solid-liquid ratio ranged from 25/500 mg/µL [27] to 3/100 g/mL [39]. The extraction temperature spanned from 25 °C [47, 54, 63] to 150 °C [64], and the extraction time ranged from 87 seconds [50] to 5.6 hours [61].

A total of 60% of the studies employed complementary techniques, with 50.77% using ultrasound and 10.77% employing microwave-assisted extraction. The extracted compound yields ranged from 38.6 ± 7.4 µg/g of procyanidin B2 from chestnut shell [43] to 448.873 mg/g of phenolic compounds *A. melanocarpa* pulp [92].

Synthesis of DES and NaDES

DES and NaDES are mixtures formed by the interaction between a HBA and a HBD in specific ratios. This interaction creates a hydrogen-bond network that yields a stable supramolecular structure with a lower melting point than the pure components [34, 64]. In general, synthesis consists of mixing the reagents at predefined molar ratios, followed by heating and stirring until a homogeneous, clear liquid is obtained.

In the literature, the synthesis temperature for DES/NaDES varies widely between 40 and 100 °C [58, 60]. This range is directly linked to the physicochemical nature of the HBDs used. HBDs with lower molar mass and low melting points (e.g., glycerol or ethylene glycol) can form homogeneous liquids at milder temperatures, near 40 °C. In contrast, solid HBDs with higher melting points, such as sugars (sucrose, xylose) or polycarboxylic organic acids, often require temperatures close to 100 °C to ensure solubilization and efficient formation of the hydrogen-bond network [64, 78].

For example, Fernández-Prior et al. [64] observed that mixtures of choline chloride with sucrose, xylitol, or 1,2-propanediol did not form clear liquids when heated at 60 °C, requiring the addition of water to solubilize the components and promote interaction. Similarly, Vázquez-González et al. [78] reported prior dissolution in water for DES containing sucrose, indicating that the amount of added water can be decisive to overcome fusion and crystallization energy barriers.

Ultrasound-assisted synthesis emerges as a sustainable strategy. Jiménez-Ortega et al. [34] showed that applying ultrasound at 80 °C for 30–45 min accelerates the formation of homogeneous liquids and reduces energy use compared with conventional heating. However, the final stability also depends on the HBD chosen: for instance, the NaDES prepared with 1,6-hexanediol showed recrystallization after 24 h at room temperature, indicating that HBD selection influences not only the required synthesis temperature but also the stability of the resulting solvente.

From a chemical standpoint, the effectiveness of HBDs in phytochemical extraction is tied to their structural features: short chains and a high density of hydroxyl groups in alcohols favor multiple hydrogen bonds; amide groups with higher methylation may show better compatibility with aromatic compounds; and for organic acids, the degree of carboxylation and the nature of the target (aglycone vs. glycoside) strongly affect efficiency [104]. Thus, selecting the synthesis temperature should not be arbitrary, but considered together with HBD properties to ensure complete solubilization, efficient hydrogen-bond network formation, and solvent stability.

Therefore, the broad 40–100 °C range reported in the literature should be viewed not only as methodological variation, but as a direct reflection of differences in melting points, physical states, polarity, and degrees of hydroxylation/carboxylation of the HBDs employed. Careful temperature selection, controlled water addition, and the use of alternative techniques such as ultrasound can improve efficiency,sustainability, and reproducibility in DES and NaDES synthesis.

Characteristics and Properties of DES and NaDES

Pontes et al. [39] emphasize that understanding the properties of solvents is crucial for optimizing the extraction of phenolic compounds from raw materials. Meng et al. [69] highlight that these properties act synergistically to enhance solvent penetration, solute interaction, and mass transfer. Dai et al. [6] warn that the different components of DES significantly influence their physicochemical properties, such as polarity, viscosity, and solubilization capacity, which affect the efficiency of target compound extraction. Given the relevance of these parameters, this study addresses density, viscosity, polarity, pH, and electrical conductivity.

Boateng [105] reported that the density of DES is influenced by molecular packing and interactions among its constituents, explaining that an increase in density indicates additional hydrogen bond formation, which reduces system volume. Pontes et al. [39] found that the density of choline chloride:malonic acid (1:1) ranged from 1.2331 to 0.9778 g/cm^3, decreasing linearly with increasing temperature and water addition, approaching the density of water. Similarly, Ashraf et al. [32] reported that all DES had densities above 1.0, with the citric acid-choline chloride eutectic solvent showing the highest density (1.257 ± 0.05) among the tested solvents. Ali et al. [53] observed that hydrophobic DES exhibited lower densities than water (0.866 to 0.91 g/cm^3), that the density of these solvents was influenced by the HBAs, and that denser starting components resulted in denser DES. Conversely, Bi et al. [58] reported densities for DES (1.0411 ± 0.01–1.2577 ± 0.03 g/cm^3) higher than those of water and conventional organic solvents, which are like conventional ILs. They further observed that densities gradually increased with the density of the HBDs, indicating that not only HBAs but also HBDs strongly influenced the density of DES.

Viscosity, a material property that measures a fluid's resistance to flow when an external force is applied [106], influences mass transfer and, consequently, extraction efficiency, as discussed by authors such as Wei et al. [38], González-Rivera et al. [43], and Boateng [105], who noted that DES and NaDES exhibit higher viscosity compared to conventional solvents, which hinders their use in extraction due to mass transport limitations. Zannou & Koca [33] observed that NaDES viscosity varies with composition. Using the same molar ratio (1:2), tartaric acid-sorbitol exhibited the highest viscosity, followed by choline chloride-glucose, tartaric acid-xylitol, malic acid-sorbitol, choline chloride-xylitol, malic acid-xylitol, acetic acid-sorbitol, and lactic acid-sorbitol. They emphasized that high viscosity can be attributed to the formation of hydrogen bonds that limit molecular mobility, a phenomenon confirmed by Crespo et al. [107] and Meng et al. [69], who stated that high viscosity correlates with strong hydrogen bonding interactions, van der Waals forces and electrostatic interactions between the components. Bi et al. [58] further stated that the greater the number of acidic or hydroxyl groups, the more hydrogen bonds can be formed, making the eutectic mixture more viscous.

Water addition and temperature influence viscosity, which decreases with increasing temperature and water content. Pontes et al. [39] observed that as water content increases, the effect of temperature on viscosity decreases. The relationship between viscosity and temperature is described by Bi et al. [58], who demonstrated a decreasing trend in viscosity values with increasing temperature from 30 °C to 70 °C. The implications of water addition in DES and NaDES are described in section Extraction efficiency.

Cui et al. [62] and Gomez-Urios et al. [88] highlighted the importance of solvent polarity in the extraction process, emphasizing its effect and the necessity of tuning solvent-solute polarity. This property arises from the uneven distribution of electric charge in bonds or molecules [69]. Alibade et al. [41] clarified that DES polarity can be adjusted by selecting an HBA with appropriate polarity and that extractability can be fine-tuned by combining DES with water. Meng et al. [48] emphasized that highly polar DES are suitable for extracting polar compounds, whereas lower-polarity DES are better suited for extracting nonpolar compounds. González-Rivera et al. [43] assessed DES polarity (ChCl-oxalic acid) using the solvatochromic parameter (π^*), finding that oxalic acid-ChCl ($\pi^* = 1.16$) exhibited lower polarity than oxalic acid dihydrate-ChCl ($\pi^* = 1.21$). Alañón et al. [40] highlighted that ethylene glycol has significant polar interactions (dipole interactions and hydrogen bonding) with phenolic compounds and that its linear structure facilitates interactions between target compounds and choline chloride more effectively than branched structures like 1,2-propanediol or xylitol. Meng et al. [69] highlight that DES with choline chloride as the hydrogen bond acceptor exhibit slightly higher polarity than those with L-proline. Consequently, ChCl-based DES form stronger hydrogen bonding and electrostatic interactions with flavonoids, thereby improving extraction efficiency. This corroborates the findings of Silva et al. [75], who reported a greater influence of the HBA component (choline chloride, guanidinium chloride, and menthol) on polarity, with a secondary effect from the HBD. Ali et al. [53] reported few differences in the polarities of hydrophobic DES, given that the HBAs have similar functional groups.

Regarding pH, Meng et al. [69] highlighted that pH affects the interaction between solvents and plant materials, thereby influencing extraction efficiency, while Ashraf et al. [32] emphasized its importance in the preparation of DES, noting that alcohol-based DES were predominantly neutral

or nearly neutral and exhibited lower extraction yields compared to DES containing carboxyl groups with varying degrees of acidity, ranging from strong to weak acids. Zannou and Koca [33] investigated the pH behavior of sixteen NaDES, demonstrating that the components used in their formation directly influenced the final solvent pH. The highest pH was observed in choline chloride-urea (9.99 ± 0.01). In NaDES where organic acids were combined with sorbitol or xylitol, the pH values ranged between 1.03 ± 0.01 and 2.20 ± 0.03, confirming that acid-based DES had the lowest pH, followed by sugar-based and alcohol-based NaDES.

Electrical conductivity reflects the ease with which electric charge flows through a substance and indicates the ability of ions to migrate; consequently, it affects extraction performance [69]. Zannou and Koca [33] also analyzed electrical conductivity, observing that NaDES composed of polyalcohol and choline chloride exhibited higher electrical conductivity values (695.00 ± 3.46 to 1141.67 ± 53.41 µS/cm). Conversely, NaDES in which organic acids were used as HBA had the lowest electrical conductivity, ranging from 0.88 ± 0.00 to 15.90 ± 0.06 µS/cm. They highlighted that conductivity values appeared to correlate with viscosity, as more viscous NaDES displayed lower conductivity.

It is important to emphasize that the ideal parameters for solvent physical properties depend on the compound to be extracted. For example, Liu et al. [47] observed that the polarity and solubility of DES were positively correlated with the extraction efficiency of scutellarin, whereas the conductivity and pH of DES were negatively correlated with the extraction rate.

Water Addition to DES and NaDES

The amount of water added to NADES in the selected studies ranged from 3.2% to 75% (Table 2). This procedure is generally justified by the high viscosity of eutectic solvents, which can impair extraction efficiency, as mentioned in section Characteristics and Properties of DES and NaDES. This is confirmed by Cañadas et al. [59], who highlight that water content can adjust some physical and chemical properties of solvents. Alañón et al. [40] and Zhang et al. [84] reiterated the need to adjust the viscosity of the extraction solvent, as the high viscosity of NaDES hinders handling and is not conducive to the efficient dissolution of target compounds. Cui et al. [42] and Liu et al. [46] pointed out that the addition of water can decrease viscosity and modulate polarity, thereby accelerating compound dissolution and increasing extraction efficiency. García-Roldán, Piriou, and Jauregi [89] observed that a more polar environment enhances the extraction of phenolic compounds. However, excessive dilution may disrupt the supramolecular structure of these solvents, as water molecules compete with components for hydrogen bonding. Dai et al. [108] studied the effect of dilution on the structure and properties of NaDES, observing strong hydrogen bond interactions between NaDES components. Their findings indicated that dilution with water weakened these interactions, and when water content reached approximately 50% (*v*/v), interactions between NaDES components disappeared. Cañadas et al. [59] emphasize that, in general, the addition of 10–30% (*w*/w) water has a beneficial influence on the extraction yield of both polar and nonpolar compounds, while warning of the need to seek a balance between reducing viscosity and avoiding the unfavorable decrease in hydrogen-bonding interactions.

Extraction Conditions

The extraction conditions for bioactive phytochemicals using DES and NaDES were detailed in the studies, mainly involving relatively low temperatures over variable periods, sometimes in combination with additional extraction methods. The studies employed temperatures ranging from 25 °C to 70 °C, with some exceptions. For instance, Liu et al. [46] used 73 °C for 20 minutes to extract antioxidants from *Hibiscus manihot* L. flowers; Alañón et al. [40] used 79.6 °C for 16.7 minutes to extract phenolic compounds from *Olea europaea* (olive) leaves; Cui et al. [62] extracted polyphenols from green tea at 84 °C for 39 minutes; and Wawoczny et al. [80] and Wen, Fan, and Cao [82] applied 80 °C for 2 hours and 30 minutes, respectively, for the extraction of bioactives. The highest temperatures were reported by Wei et al. [38] and Rico et al. [73], who conducted extractions of flavonoids and polyphenols at 90 °C for 81 and 10 minutes, respectively, and by Fernández-Prior et al. [64], who used 150 °C for 5 minutes to extract phenolic compounds and hydroxytyrosol from olive oil extraction by-products (*alperujo*). Alañón et al. [40] highlighted that higher temperatures improve extraction yield, whereas Zhang et al. [84] reported instability and rapid loss of phenolic compounds under high-temperature conditions.

Some studies used centrifugation to aid in the extraction process [41, 55–57, 59, 60, 63, 66, 68, 70, 78, 81, 90], while others employed resins for solute-solvent separation, which is discussed in section Separation of Solute and Solvent. It is worth noting that many of these parameters resulted from process optimization studies, as detailed in section Optimization of Experiments.

Regarding the use of combined methods, 60% of the selected studies employed additional techniques alongside eutectic solvents to improve extraction efficiency, as outlined in Table 2.

Extraction Efficiency

The efficiency of the extraction process was primarily evaluated based on extraction yield and comparisons with extractions that also employed conventional solvents, as shown in Table 3.

It can be observed in Table 3 that most studies (88.2%) achieved higher extraction yields using DES or NaDES compared to conventional solvents. For example, Toledo Hijo et al. [21], using systems composed of choline chloride and acetic acid, obtained polyphenol extraction yields from yerba mate leaves (~47–55 mg/g dw) higher than those achieved with aqueous ethanolic mixtures (~16–29 mg/g); however, their performance was lower than that of ionic liquids (~41–66 mg/g dw).

Similarly, Wei et al. [38] found that the extraction rates of flavonoids from *Moringa oleifera* leaves using DES (70.4 ± 0.47 mg/g dw) were higher than those obtained with ethanol (24.3 ± 0.11 mg/g dw) and water (9.1 ± 0.14 mg/g dw). Alsaud, Shahbaz, and Farid [54] obtained β-caryophyllene extraction yields from manuka leaves using a DES composed of menthol and lactic acid (3.32 mg/g dw), steam distillation (1.13 mg/g dw), and Soxhlet extraction with n-hexane (2.38 mg/g), noting that the β-caryophyllene concentration with DES was 1.39 and 2.93 times higher than with Soxhlet and steam distillation, respectively. In addition to the greater quantity extracted, the authors emphasized that Soxhlet extraction resulted in higher levels of impurities and greater energy consumption, as it required more

Table 3 Comparison between the use of DES/NaDES and conventional solvents in the extraction of phytochemicals based on the studies selected for this review

Reference	Extracted compound	DES/NaDES	Conventional solvent	Increase with DES/NaDES
Toledo Hijo et al. [21]	Polyphenols	~47–55 mg/g (NaDES)	EtOH/water (~16–29 mg/g)	1.62 a 3.44x
Xia, Li & Jiang [35]	Flavonoids	11.47 mg/g (DES e UAE)	EtOH 70% (12.12 mg/g)	–
Grudniewska & Popłoński [36]	Xantohumol	2.30 mg/g (DES)	Acetone (3.31 mg/g)	–
			MeOH (4.45 mg/g)	
Wei et al. [38]	Flavonoids	70.4 mg/g (DES)	EtOH (24.3 mg/g)	2.9x
Alsaud, Shahbaz and Farid [54]	β-caryophyllen	3.32 mg/g (DES)	2.38 mg/g (n-hexano)	1.39x
			1.13 mg/g (steam)	2.93x
Barbieri et al. [56]	Phenolic compounds	57.60–62.21 mgAG/g (DES e UAE)	49.14 mgAG/g (Ethanol)	1.17 a 1.26x
Benvenutti et al. [57]	Anthocyanins	279.45 mg/100 g (NaDES)	EtOH 50%	1.6 a 3.5x
			50% acidic EtOH	
Chisha et al. [61]	Rosmarinic acid	3.85% (NaDES)	1.82% (EtOH)	2.1x
Hikmawanti et al. [65]	Polyphenols	71.38mgGAE/g	EtOH50% (61.190mgGAE/g)	1.17x
			MeOH (22.964 mgGAE/g)	3.11x
	Flavonoids	9.713 mg QE/g	EtOH50% (7.486mgQE/g)	1.3x
			MeOH (6.343mgQE/g)	1.53x
Meng et al. [69]	Flavonoids	DES	EtOH 80%	1.31x
Peng et al. [71]	Polyphenols	NaDES e UAE	EtOH and UAE	1.56x
Saar-Reismaa et al. [74]	Chlorogenic acid and derivatives	DES e UAE	EtOH 70%	1,8 a 2,9
Suresh et al. [76]	Rebaudioside A and Stevioside	38.24/114.58 mg/g (NaDES e UAE)	EtOH 50%	~1.2x
Vinas-Ospino et al. [79]	Carotenoids	46.01 µg/g (DES)	Hexano (39.28 µg/g)	1.17x
Wawoczny et al. [80]	Phenolics	16.1 mg/g (DES)	EtOH (8.1 mg/g)	1.99x
	Flavonoids	12.2 mg/g (DES)	EtOH (7.9 mg/g)	1.54x
Zhang et al. [84]	Polyphenols	NaDES + MAE	EtOH	7.88x
	Rutin	281.1 µg/g (NaDES e UAE)	EtOH (Hot reflux)	9.82x
Carmona et al. [87]	Polyphenols	3.988,74 mg/kg (NaDES)	MeOH 50%	~1.5x

time (3 hours) and a higher temperature. In contrast, DES extraction was performed at room temperature (Table 2).

Benvenutti et al. [57] reported that all NaDES tested in their study yielded higher anthocyanin levels than water, and only two showed lower extraction performance than 50% ethanol and 50% acidified ethanol solutions. They further highlighted that the best-performing NaDES provided yields 1.6 to 3.5 times higher than the tested ethanolic solutions. The highest recovery was achieved using NaDES composed of chloride and propylene glycol, 279.45 mg/100 g (Tables 2 and 3). Chisha et al. [61] obtained 3.85 ± 0.04% rosmarinic acid from *Rosmarinus officinalis* using choline chloride and lactic acid, a higher value than that obtained with ethanol (1.82 ± 0.05%). Meng et al. [69] reported a 1.31-fold increase in flavonoid extraction efficiency from *Cercis glabra* leaves compared to 80% ethanol.

Suresh et al. [76] reported rebaudioside A and stevioside yields from *Stevia rebaudiana* of 38.24 ± 2.22 and 114.58 ± 5.89 mg/g, respectively, using NaDES (lactic acid:glycerol:malic acid:glucose, 1:1:1:1), values higher than those obtained with water (32.52 ± 3.13 and 90.95 ± 9.7 mg/g) and 50% ethanol (32.38 ± 4.61 and 90.6 ± 8.18 mg/g).

Vinas-Ospino et al. [79] extracted carotenoids from orange peel using DES (octanoic acid and proline) and found that DES showed higher efficiency (46.01 µg/g) compared to hexane (39.28 µg/g). Wawoczny et al. [80], in extracting phenolics and flavonoids from *Calendula officinalis* with ethanol in Soxhlet, obtained 8.1 mg/g and 7.9 mg/g, respectively, whereas DES (choline chloride and levulinic acid) yielded 16.1 mg/g phenolics and 12.2 mg/g flavonoids. Carmona et al. [87] reported that the studied NaDES achieved higher polyphenol yields than methanol extraction, with the citric acid–fructose solvent extracting 33.31% more phenolics than methanol. On the other hand, Alañón et al. [40] found no significant differences in oleuropein yield between eutectic solvent (choline chloride and ethylene glycol) and conventional solvent (methanol/water – 80:20). However, they noted that DES facilitated the recovery of glycosylated derivatives of some secoiridoids and flavonoids.

Some studies have shown that combining DES or NaDES with ultrasound improves extraction efficiency. For example, Barbieri et al. [56] observed that three of the four DES used for extracting phenolic compounds from *Rosmarinus officinalis* L., when combined with UAE, yielded higher values (57.60–62.21 mg GAE/g) than ethanol (49.14 mg GAE/g). In this study, the ethanol extract showed antioxidant capacity (49.13 mM Trolox equivalent/g) approximately three times lower than that of DES extracts (126.23–183.82 mM Trolox equivalent/g), and kinetic degradation assays demonstrated that the ethanolic extract had the lowest capacity to stabilize phenolic compounds.

Similarly, Hikmawanti et al. [65] found that extracts obtained with choline chloride and urea combined with ultrasound contained significantly more phenolic compounds (71.380 ± 1.907 mg GAE/g dw), flavonoids (9.713 ± 0.243 mg QE/g dw), and exhibited higher antioxidant activity (DPPH 124.942 ± 4.510 µmol QE/g dw, FRAP 225.595 ± 3.865 µmol TE/g dw, and ABTS 203.418 ± 0.078 µmol TE/g dw) than those obtained with 50% ethanol and methanol, which yielded 61.190 ± 4.084 and 22.964 ± 3.184 mg GAE/g dw of polyphenols, 7.486 ± 0.187 and 6.343 ± 1.030 mg QE/g dw of flavonoids, 122.941 ± 0.619 and 52.129 ± 2.255 µmol QE/g dw of DPPH, 141.208 ± 1.646 and 72.671 ± 5.963 µmol TE/g dw of FRAP, and 181.774 ± 1.513 and 75.541 ± 5.645 µmol TE/g dw of ABTS, respectively.

The use of UAE with DES/NaDES was also evaluated by Peng et al. [71], who reported that NaDES composed of betaine and maleic acid, combined with ultrasound, achieved a polyphenol extraction rate from *M. oleifera* leaves 1.56 times higher than that of ethanol solvent assisted by ultrasound, and by Saar-Reismaa et al. [74] in the quantification of phytochemicals from *Dipsacus fullonum* leaves, where they found that compound concentrations obtained with DES and UAE were 1.8 to 2.9 times higher than those obtained with 70% ethanol. This methodology's efficiency was also confirmed by Zhang et al. [84], who noted that rutin had the highest extraction rate of 281.1 µg/g with NaDES (choline chloride and lactic acid) combined with ultrasound, a yield 9.82 times greater than hot reflux extraction with ethanol. The authors also found that combining NaDES with microwaves increased phenolic compound extraction yield by 7.88 times compared to the traditional method (ethanol and reflux).

It is worth noting that some studies reported lower extraction yields for DES/NaDES compared to traditional solvents, such as Grudniewska and Popłoński [36], who obtained higher xanthohumol yields from hops using organic solvents—acetone (3.31 mg/g) and methanol (4.45 mg/g)—than with DES-based extraction (2.30 mg/g), and Xia, Li, and Jiang [35], who extracted 12.12 mg/g flavonoids with 70% ethanol, a slightly higher yield than with DES extraction (11.47 mg/g). However, other parameters should be considered when selecting the solvent, such as operational and environmental advantages, which will be discussed in Section Environmental Impact.

Factors such as antioxidant capacity and stability of extracted compounds were also assessed in selecting the most efficient solvent. Gomez-Urios et al. [88] found similar yields for two different NaDES, but one exhibited higher antioxidant activity. *Pontes* et al. [39] emphasized that extraction potential depends on the structure of solvent components. For instance, they compared two DES with the

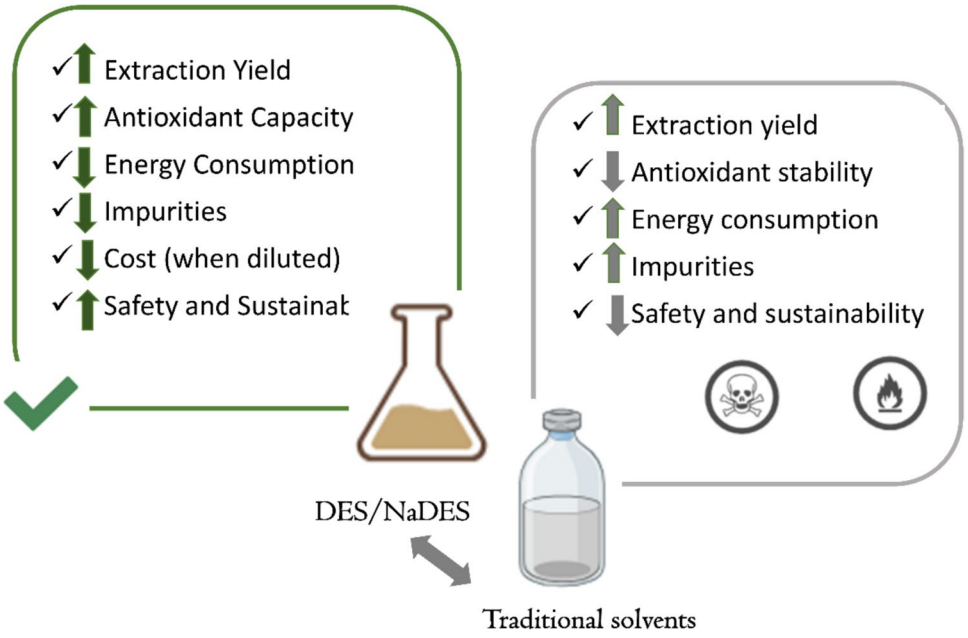

Fig. 4 Comparison of efficiency parameters between DES/NaDES and conventional solventes

best extraction performance and found that malonic acid–based DES extracted nearly 69% more than acetic acid–based DES, as malonic acid contains an additional carboxyl (-COOH) group.

Grudniewska and Popłoński [36] also observed that extraction efficiency depends on the physicochemical properties of the solvents. Among alcohol-based DES (choline chloride combined with ethylene glycol, glycerol, or propylene glycol), they found that choline chloride–glycerol exhibited the lowest extraction efficiency for xanthohumol, likely due to its high viscosity. Glycerol contains an additional hydroxyl (-OH) group, which increases hydrogen bond formation and consequently increases solvent viscosity. Similarly, González-Rivera et al. [43] found that lower yields were obtained in more viscous systems.

Benvenutti et al. [57] stressed that for industrial applications, costs must be considered in solvent selection, with NaDES costs ranging from 1.01 to 36.12 USD/100 mL. The cost of the solvent with the highest extraction yield, ChCl: Pro (1:2), was 10.26 USD/100 mL. Considering that these solvents are generally diluted in water to reduce viscosity and facilitate extraction, solvent costs would be reduced. They also noted that this solvent had the shortest preparation time, meaning lower energy consumption, and the lowest viscosity, which contributed to increased extraction efficiency. Given the above, Fig. 4 presents a comparison between DES/NaDES and conventional solvents.

Figure 4 presents a comparative summary of the solvents. It is noteworthy that good yields can be obtained with both; however, studies have reported that DES and NaDES provide greater stability to bioactives, prolonging their antioxidant activity period. The use of these new solvents generally results in lower energy consumption, as well as reduced impurity content. Moreover, these solvents are considered safer and more sustainable.

DES/NaDES with UAE or MAE Extraction efficiency can be enhanced using ultrasound-assisted extraction (UAE) or microwave-assisted extraction (MAE). Acoustic wave treatment (UAE) agitates plant cell walls, potentially breaking them and exposing bioactive compounds to the solvent, facilitating their extraction. Microwave treatment induces rotational movement in molecules, generating thermal energy that accelerates extraction [90]. Zhang et al. [85] highlighted that the heat and electromagnetic field effects generated by microwaves compromise the structure of cell walls, making them more porous and thereby increasing solvent penetration efficiency. The benefits of these combinations have been explored in recent review articles [109, 110], which demonstrated the potential of these technologies in the extraction of bioactive compounds.

The ultrasound power used in the selected studies ranged from 100 W [77] to 1200 W [42], with extraction times between 7.4 minutes [14] and 60 minutes [27]. Stupar et al. [95] used ultrasound at 52.5 W/cm^3 at 50 °C for 10 minutes to extract β-carotene from pumpkin (*Cucurbita maxima*), achieving a β-carotene concentration of 151.41 µg/mL.

Regarding MAE, Pavlović et al. [49] found that extraction yields were higher with DES/MAE than with DES alone. Liu et al. [46] observed that the DES composed of ChCl/1,4-butanediol (1:2) combined with MAE accelerated the extraction process, shortened extraction time, and increased efficiency compared to traditional extraction

methods. Vargas-Serna, Ochoa-Martínez, and Vélez-Pasos [50] extracted phenolic compounds from pineapple peel using MAE at a frequency of 2.55 MHz and approximately 250 W for 1 minute. The extraction with ChCl:glycerol yielded higher extraction rates than other DES and conventional solvents (water, ethanol, and methanol), reaching 7.78 mg eq GAE/g.

Stability of Samples During Storage The efficiency of bioactive compound extraction with DES/NaDES can be assessed by extraction yield, antioxidant activity, and compound stability. Dai et al. [108] and Stupar et al. [95] reported that NaDES enhance the stability of bioactive compounds due to the hydrogen bonds formed between solutes and solvent molecules. Zannou and Koca [33] explained that the strength of the interaction between NaDES and phenolic compounds is associated with the availability of these bonds. Gomez-Urios et al. [88] found that these solvents provided prolonged protection to bioactive compounds in orange peel extracts. This finding aligns with Alsaud, Shahbaz, and Farid [54], who highlighted that β-caryophyllene showed good stability in DES (menthol:lactic acid) over 9 days of storage, with a slight decrease in compound content from 10.83 to 10.27 mg/g, and with Zannou and Koca [86], who observed that total phenolics, flavonoids, DPPH radical scavenging, and FRAP activity in *A. tinctoria* root extracts demonstrated strong stability in NaDES during experimentation.

Separation of Solute and Solvent

The separation of solute from DES/NaDES can be achieved using macroporous resins [35, 48], antisolvents [36], or, in some cases, not performed at all. Some researchers, particularly those working with NaDES, argue that separation is unnecessary. For example, Carmona et al. [87] pointed out that NaDES residues remain intrinsically bound to the solute, making their removal costly due to low volatility, high viscosity, and strong molecular interactions with the substrate. They also emphasized that NaDES are non-toxic. Similarly, Liu et al. [111] noted that, like DES and ILs, NaDES have nearly zero vapor pressure, which makes its removal by evaporation difficult. Marinaccio et al. [68] evaporated the DES (menthol:thymol) using a vacuum vortex evaporator. However, their non-toxic nature suggests that removal is not always required.

Using antisolvents is a simple method for separating the solute from the solvent. However, as Grudniewska and Popłoński [36] highlighted, a suitable solvent must be selected in which the extracted compounds are insoluble. Water is often used as an antisolvent for solutes with low solubility. However, Liu et al. [111] cautioned that when NaDES components are soluble in polar or intermediate-polarity solvents, separation becomes difficult without the use of organic solvents. Liu et al. [47] emphasized the water-soluble nature of DES and the low water solubility of scutellarin, using the antisolvent method to recover scutellarin from the DES extract.

Other separation methods, such as solid-phase extraction (SPE) and the use of resins, are also employed for the purification of phytochemicals. SPE was used by Domínguez-Rodríguez et al. [63], who applied C-18 cartridges inserted into a vacuum manifold system, activated with methanol. The extract was added to the conditioned column and washed with water acidified with formic acid (0.35%, *v*/v) to elute the NaDES. Ethyl acetate was added twice to elute flavonols and flavones, followed by methanol acidified with formic acid (0.1%, v/v) twice to elute anthocyanidins. The flavonoid and anthocyanidin fractions were combined and concentrated under nitrogen, and finally, the extracts were redissolved in ethanol.

Meng et al. [69] used macroporous resins (NKA-9, HPD100, AB-8, DM301, D101, XAD761, and ADS-17) to treat flavonoid compounds in DES extracts, which were subsequently purified by macroporous adsorption chromatography (AB-8 resin). The sequential process involved washing with an aqueous phase, followed by stepwise elution with 60% ethanol to recover the target flavonoids.

Suresh et al. [76] also employed microporous resins to separate bioactives (steviol glycosides from stevia extracts) from NaDES. The resin used (HP-20) was able to adsorb the glycosides, while the NaDES components were eluted in the aqueous mobile phase (ammonium acetate buffer). They reported that, after elution of the NaDES, the glycosides were eluted with ethanol. Similarly, Tang et al. [77] used AB-8 macroporous resin to separate saponins from *Camellia oleifera* seed extract.

When recovered, DES/NaDES can be reused. Xia, Li, and Jiang [35] achieved a recovery rate of 93.98%, with the recycled DES extracting 10.78 mg/g slightly lower than the initial extraction yield of 11.47 mg/g. Grudniewska and Popłoński [36] demonstrated that, under their experimental conditions, DES could be recycled three times. Their recovery procedure involved vacuum evaporation of water from the aqueous DES solution. Suresh et al. [76] observed that the extraction efficiency using recovered NaDES decreased by 30.05% and 36.13% compared to the first extraction. They highlighted that, although the recovered NaDES exhibited lower extractability, they still extracted a considerable number of metabolites from the stevia biomass, and thus could be used to reduce NaDES production costs by employing them in multiple cycles.

Optimization of Experiments

In this review, 69.7% of the selected studies conducted extraction optimization, generally using independent variables such as the solid-liquid ratio, water content, extraction time, and temperature, while the dependent variable was the quantity of bioactive compounds extracted. As observed in Table 2, these parameters vary considerably depending on the matrix and solvent components, highlighting the importance of optimizing the extraction process.

Zannou and Koca [86] found that the levels of phenolics, flavonoids, and antioxidant activity (DPPH) in *A. tinctoria* were strongly influenced by the molar ratio and water content, with the highest responses obtained at a 1:4 ratio and 80% water content. Alañón et al. [40] observed that an increase in temperature had a positive effect on extraction efficiency. Pusty et al. [72] found that, among the process variables, the molar ratio had the greatest effect on extraction, followed by ultrasonication power, water content, and temperature. They further noted that the first three parameters had a positive influence on extraction, meaning they were directly proportional, whereas temperature had a negative effect.

Environmental Impact

Toledo Hijo et al. [21] emphasized that natural deep eutectic solvents (NaDES) and naturally derived ionic liquids obtained from non-toxic sources have emerged as a new generation of sustainable alternatives. Alañón et al. [40] highlighted that the use of DES aligns with several principles of green chemistry, including minimal reagent consumption, reduced waste generation, and safer solvents due to their low flammability and negligible vapor pressure. Koraqi et al. [44] argued that utilizing an alternative and stable extraction solvent is effective in preventing environmental and health hazards caused by industrial processes.

Santos-Martín et al. [94] stressed that NaDES combined with ultrasound represent an eco-friendly alternative for recovering phenolic compounds from plant materials and agricultural residues. Stupar et al. [95] noted that this approach is simple, easy to implement on an industrial scale, and has minimal impact on workers and the environment. Similarly, Vargas-Serna, Ochoa-Martínez, and Vélez-Pasos [50] asserted that DES (choline chloride-glycerol) and microwave-assisted extraction offer a green process for extracting phenolic compounds from pineapple peel, supporting the valorization of agricultural byproducts.

A review on the toxicity of deep eutectic solvents by Sharma and Lee [112] clarifies that the toxicity profile of DES varies according to concentration, viscosity, composition, and modes of interaction with living organisms. As an example, in a study where aqueous phosphonium-based DES was tested on *Artemia salina*, it was found that concentrated DES are more toxic than aqueous DES. Ni et al. [70] investigated the cytotoxicity of NaDES and NaDES extracts enriched with quercetin in Caco-2 cells and found no significant effect on cell viability in the range of 0 to 2000 mg/L compared to the control, confirming the low cytotoxicity of NaDES (choline chloride and citric acid) ($EC50 > 2000$ mg/L). Regarding the individual components of the NaDES, choline chloride promoted Caco-2 cell growth at relatively low concentrations (500–1000 mg/L), whereas citric acid inhibited cell growth at high concentrations (1000–2000 mg/L). A concentration of 2000 mg/L citric acid caused reduced cell viability, possibly due to its low pH. Conversely, Ferreira et al. [113] evaluated the toxicity of deep eutectic solvents in zebrafish and observed low toxicity of the DES composed of citric acid, trehalose, and water (2:1:3) at the tested concentrations. The enzymatic activity of glutathione transferase, catalase, and glutathione peroxidase, as well as total antioxidant capacity and lipid peroxidation, were determined, suggesting low toxicity of the solvent.

Taken together, the results indicate that DES/NaDES are versatile solvent systems and, in many cases, outperform conventional solvents, especially when combined with process-intensification techniques (UAE; MAE). From a chemical–structural perspective, the frequent use of choline chloride (HBA) and the strong performance of acidic HBDs suggest that dense hydrogen-bond networks and tunable polarity are key to solubilizing phenolics/flavonoids.

Operationally, the optimal formulation and processing windows (molar ratios 1:1–1:15; water addition ~3–75%; broad ranges of solid–liquid ratio and temperature/time) show that performance depends on balancing viscosity reduction (via water and temperature) with preservation of the eutectic microstructure; excessive water or high temperatures can disrupt the solvent or degrade thermosensitive compounds. The emphasis in 36,4% of the studies on agro-industrial residues underscores the environmental and economic advantages of these systems (lower energy use, fewer impurities, better bioactive stability), aligning extraction efficiency with sustainability in agri-food supply chains. In summary, rational selection of the HBA–HBD pair, fine control of water/temperature/time, and coupling with UAE/MAE are the pillars to maximize selectivity, yield, and process viability with DES/NaDES.

Conclusion

The studies analyzed in this review demonstrate that ionic liquids, deep eutectic solvents, and natural deep eutectic solvents have shown promising results in the extraction of bioactive compounds from plant sources. A decline in studies focusing on ionic liquids and an increase in research on DES were observed, which may be attributed to the cost and efficiency of these solvents. More than 30% of the studies conducted extractions from residues generated during vegetable processing, indicating the potential for utilizing these byproducts, which could help guide the sustainable development of agricultural supply chains. DES composed of choline chloride combined with lactic acid, malic acid, or oxalic acid, stood out in the extraction of phenolic compounds from plants.

The use of combined techniques, such as ultrasound and microwave-assisted extraction, has emerged as a promising alternative to enhance the efficiency of ionic liquids in plant matrices. The low environmental impact of NaDES has also been highlighted, attributed to their high biodegradability and low risk, as they are composed of naturally derived substances.

It is essential to emphasize the need for further research on the impact of sample preparation and extraction conditions on the yield and stability of phytochemical compounds. Considering the variety of substance combinations used to form these solvents, their toxicity and biodegradability should be more thoroughly investigated.

Investigations and optimization studies of extraction processes, with an emphasis on minimal reagent consumption and reduced waste generation, are also necessary.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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