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Review

Phytomass Valorization by Deep Eutectic Solvents—Achievements, Perspectives, and Limitations

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Abstract: In recent years, a plethora of extraction processes have been performed by a novel class of green solvents known as deep eutectic solvents (DESs), possessing several environmental, operational, and economic advantages proven by experience when compared to organic solvents and ionic liquids. The present review provides an organized overview of the use of DESs as extraction agents for the recovery of valuable substances and compounds from the original plant biomass, waste from its processing, and waste from the production and consumption of plant-based food. For the sake of simplicity and speed of orientation, the data are, as far as possible, arranged in a table in alphabetical order of the extracted substances. However, in some cases, the isolation of several substances is described in one paper and they are, therefore, listed together. The table further contains a description of the extracted phytomass, DES composition, extraction conditions, and literature sources. With regard to extracted value-added substances, this review addresses their pharmacological, therapeutic, and nutritional aspects. The review also includes an evaluation of the possibilities and limitations of using DESs to obtain value-added substances from phytomass.

Keywords: deep eutectic solvents; phytomass; valorization; extraction

1. Introduction

Biomass is considered to be any organic material produced by the growth of microorganisms, plants, or animals, involving also wastes and residues of organic nature [1,2]. Biomass is a renewable energy source, the second oldest source of energy following the Sun. Primary biomass and biowaste generated during its treatment, processing, and use are the source of a huge number of compounds and substances, referred to as value-added products, which can be extracted, recovered, and/or synthesized from biomass [3]. The ways of obtaining such value-added products are covered under the term valorization. The sum of the biomass across all taxa on Earth is approximately 550 gigatons of carbon, of which about 450 Gt C are plants, followed by bacteria (70 Gt C), fungi, archaea, protists, animals, and viruses, which together account for the remaining <10% [4].

Based on the composition of biomass, it is understandable that the attention of researchers and technologists is focused on plants and plant waste, which we will refer to as phytomass. The main mode of obtaining value-added products from phytomass and discussed in this review are extraction processes. In accordance with ecologically oriented developments in current chemistry and technology, we will deal with green extraction agents, specifically deep eutectic solvents.

This work is aimed at providing an overview of the obtained value-added products, their phytomass sources, used DESs, and conditions of valorization. The work is mainly devoted to results

achieved in the last few years and indicates the perspectives, but also the limitations of the development of this area.

2. Deep Eutectic Solvents

Over time, several types of extractants have been used to recover compounds and substances from phytomass. At the beginning, it was water, later on followed by organic solvents. At the end of the previous millennium, efforts to protect the environment and obtain cleaner products in higher yields in a less costly manner led to new kinds of extractants—ionic liquids. Probably the first room-temperature ionic liquid was described as early as 1914 [5]. Ionic liquids were utilized also in valorization of phytomass, specifically in obtaining some compounds from cellulose [6,7].

Some unfavorable characteristics of ionic liquids (sensitivity to humidity; toxicity; production, handling, and disposal costs; non-biodegradability; inflammability) have been overcome by a newer type of solvent—low-transition temperature mixtures (LTTMs). From the view of applicability, cost-relating factor is of key importance. The cost of producing a DES has been estimated to be 20% of that of an ionic liquid [8]. LTTMs are mixtures of two or more high-melting-point starting materials—hydrogen bond donor (HBD) and hydrogen bond acceptor (HB)—which can bond with each other to form a mixture having a final melting point that is lower than that of the starting components, becoming thus, usually liquids at room temperature. LTTMs are composed of inexpensive, recyclable, and non-toxic materials, frequently of natural origin (e.g., sugars, organic acids, and salts, etc.). In the field of these green solvents and extractants, along with the term LTTMs, various terms have been introduced, such as deep eutectic solvents (DESs), natural deep eutectic solvents (NADESs), and low-melting mixtures (LMMs). As pointed out by several scientific and industrial teams [9–15], it is obvious that these terms are interchangeable and there is no substantial difference in them. In this paper, we will stick to the term DESs coined by Abbott et al. in their pioneering paper [16] for liquids composed of natural high-melting-point starting materials.

It should be emphasized that despite the seemingly similar extraction effects of ionic liquids and DESs, there is a fundamental chemical difference between these types of extractants. Ionic liquids are ionic compounds; their components are ions attracted by the ionic bond. Components of DESs are bound by the hydrogen bond and van der Waals interactions; DESs are thus just mixtures. The fact that the composition of HBD and HBA is retained in the liquid phase after mixing allows for easy regeneration of DESs after use as a solvent.

Although many DESs are not eutectic mixtures in the exact sense of the word, the use of the acronym DES is constantly expanding, probably due to the fact that they are liquids at room temperature, they can be easily prepared without the need for complex and expensive cleaning procedures, are used in an environmentally friendly manner, and easily regenerate [15].

Based on Abbott's fundamental works and reflecting the nature of starting components, DESs are classified into five types [17,18]: Type I (quaternary salt and metal halide), Type II (quaternary salt and hydrated metal halide), Type III (quaternary salt and hydrogen bond donor), Type IV (metal halide and hydrogen bond donor), and Type V (non-ionic DESs composed only of molecular substances). Type V DESs were defined by Abranches et al. in 2019 [18], although the first non-ionic deep eutectic mixture was described by Usanovich as early as 1958 [19]. Such non-ionic DESs have found their application in polymer chemistry, medicine [20], and other application areas [21,22]. They have not been systematically used as extractants so far. When handling materials of biological origin, it is advantageous to avoid metal-containing compounds, and therefore, DESs of type III (and probably, Type V in the future) are preferred in the valorization of phytomass.

The basic properties of two- or more component DESs have been described by several authors [9,17,23–30]. The knowledge gained so far can be summarized as follows. DESs are biodegradable, cheap, easy to prepare, low toxic, fire resistant, miscible with water, have negligible vapor pressure, and are liquid in a wide temperature range. For most Type III DESs, their room-temperature viscosity (19–13,000 cP) and density (1.0 to 1.4 g/cm^3) are higher than that of water and their electrical conductivity is

rather low (<1 mS/cm). All of the mentioned physicochemical characteristics are temperature-dependent. Until recently, only hydrophilic DESs composed of typically hydrophilic materials were available [8–11]. The first data on hydrophobic DESs, stable in contact with water, were published in 2015 [10] and reviewed in 2019 [31].

Being multicomponents systems, DESs offer significant advantages over conventional solvents: their structure may be modified by the selection of solvent-forming components, as well as by the molar ratio of the components participating in hydrogen bond formation. That is why their properties (e.g., melting/glass transition temperature, viscosity, conductivity, refractive index, density, and pH) are significantly influenced by the DESs composition and can be purposefully modified to some extent. Given the high purity of their components, DESs can be prepared in the form of high purity mixtures in waste-free processes. One of the most attractive properties of DESs is their biodegradability, based on the use of natural precursors. All these characteristics caused DESs to be proposed instead of common organic volatile solvents, preventing, thus, a large-scale release of flammable vapors and emissions. In addition, the release of solvent during reaction processes, separation, and purification becomes limited.

3. Deep Eutectic Solvents as Extracting Agents

3.1. Requirements for Extracting Agents

DESs have been introduced as extractants in several areas. Their ability to function as denitrification agents was documented by Rogošic et al. [32]. Adjusting the HBA:HBD molar ratio, several DESs documented their advantage in analysis and separation of organic and inorganic compounds from food samples [33]. DESs composed of tetrabutylammonium bromide and long-chain alcohols were investigated as extracting solvents for headspace single-drop microextraction of more than 40 terpenes from six spices (cinnamon, cumin, fennel, clove, thyme, and nutmeg). Advantages in extraction of metals from mixed oxide matrixes were described by the team headed by Abbott [34]. Triaux and his coworkers [35] found that the most important factors for separation efficiency were extraction time and temperature. Along with their application in chromatography and biomass processing, some illustrative results of extraction of value-added compounds from biomass are described too [8,36–38].

The advantages of DESs as extractants over organic solvents and ionic liquids are mentioned in a nutshell above. To fulfil the main requirements of valorization, i.e., to obtain the highest possible amount of the desired compounds in the highest purity at the lowest total cost and adverse environmental impact, both the treated biomass and the extractant must meet optimal parameters. Among the properties of DESs, their thermal stability, liquid state temperature range, viscosity, polarity, and acidic basic properties are particularly important in the search for optimal DESs for the extraction of selected compounds. Other traditionally measured and published properties, such as electrical conductivity, refractive index, and density, are not decisive in selecting DESs for separation and extraction purposes.

3.2. Thermal Stability

Thermal stability is a key requirement of DESs in assessing the suitability of their use as extractants [11]. Thermal stability is defined either at the molecular level as the stability of a molecule when it is exposed to very high temperature or at the substance level as the resistance of a compound to decomposition and/or loss of mass at high temperatures [28]. From the viewpoint of practical application, thermal stability of a DES means a measure of how long the DES can hold before dissociating into its components and/or the breaking down by heat into smaller decomposition products which do not recombine on cooling. Thermal stability as part of thermal properties is usually monitored by thermogravimetric analysis. This technique allows researchers and technologists to determine temperature intervals of structural compositional changes of substances and weight loss. As far as DESs are concerned, their decomposition temperature is the highest temperature of their practical

use. It should be noted at this point that increasing the extraction temperature is limited not only by the thermal stability of the used DES but also by the processed biomass and extracted compounds.

3.3. Temperature Range of Liquid State

When evaluating possibilities of the use of organic solvents as extractants, the temperature range of their liquid state is one of the key parameters. However, this is not the case with DESs. Even in otherwise excellent papers and reviews devoted to DESs [9,11,17,23–30,39,40], instead of the temperature range of liquid state, only the melting/glass transition temperature is given. The reason for this situation is understandable since the boiling point of DESs usually is not measurable due to their decomposition at higher temperatures.

It should be pointed out also that published melting/glass transition temperatures must be taken with some caution. From the theoretical point of view, the significant melting point depression of a eutectic mixture compared to that of the pure HBA and HBD is due to several factors, such as charge delocalization (from, for instance, the halide anion (HBA) to the HBD, facilitated by hydrogen bond formation); a reduction in strength of several other cohesive interactions counterbalancing the increased strength of the H-bonds developed at a eutectic composition; the lattice energy of the HBA and HBD; the way the anion and HBD interact; and the entropy changes upon DES formation. From the practical point of view, problems lie in the fact that the mentioned temperatures depend to a large extent on the purity of the DES and the water content. The determined properties of DESs prepared from pure water-free components on a laboratory scale may not be identical to the properties of large-scale applied DESs.

3.4. Viscosity

To extract a desired compound from phytomass, there must be a contact of an extractant (DES, in our case) and an extractable compound. The penetration of DES into the body of phytomass strongly depends on DES viscosity. Generally speaking, the higher its extractant viscosity, the lower its extractive efficiency. Viscosity can be decreased in three main ways: by changing the molar ratio of the DES components (HBA and HBD); by adding water, organic solvent, or another additive; by rising the temperature. Viscosity data can be found in [11,17,23,26,41]. For several DESs, viscosity/temperature dependences are expressed by mathematical equations [11]; viscosity/DES composition dependences are individual for each DES. More details on viscosity issues are given in part "Factors limiting potential of deep eutectic solvents utilization and how to overcome them".

3.5. Polarity

The importance and effect of polarity in the separation of individual components from a multicomponent system are well-known in chromatographic methods. To express the polarity of chemical substances and their mixtures including DESs, several parameters are used. The classic, most frequently used quantities are relative permittivity εr (dielectric constant) [42], spectral parameter $E_T(30)$, and Kamlet–Taft π*, α, and β parameters. For pure organic solvents, several polarity parameters based on equilibrium, kinetic, and spectroscopic measurements are discussed in detail by Reichardt and Welton [43]. It should be pointed out that polarity is not an absolute property of the pure liquid and hence, there is no single correct value when comparing polarity scales. All polarity scales are relative and different scales give different polarities for the same solvent [44–46].

As far as the polarity of DESs is concerned, the literature is very sparse in data. Even in an excellent book on DESs [47], only a few lines are devoted to the polarity of DESs. Given the fact that DESs are composed of HBA and HBD, it can be expected that as the most suitable parameters characterizing DESs, Kamlet–Taft parameters π*, α, and β will be used preferentially. The parameters α and β express the H-bond acidity of HBD and basicity of HBA, respectively; π* is a measure of dipolarity/polarizability of the solvents.

Measurements of choline chloride (ChCl)-based DESs with urea, glycerol, acetic acid, malonic acid, glycolic acid, ethylene glycol, or levulinic acid, as well as those of DESs composed of tetrabutylammonium chloride and levulinic acid, indicate that their polarity is close to that of water [46,48]. The fact that the composition of two- or multicomponent DESs can be varied almost indefinitely in practice opens up the chance to prepare a DES with the required polarity suitable for the desired applications. The ability to modify polarity can be expected to be very important in the separation of lipophilic (non-polar) and hydrophilic (polar) nutrients from phytomass [37].

Taking the polarity aspect into account, it is worth pointing out the ability of some solvents to exhibit switchable polarity [49]. Switchable polarity solvents equilibrate between a higher polarity and a lower polarity when a trigger is applied. These solvents are particularly useful when two different polarities of the solvent are needed for two different steps. Up to now, mainly ionic liquids have been considered as belonging to the category of switchable polarity solvents; there is, however, no fundamental reason hampering the introduction of DESs into the same category. Despite the assumption of the importance of the polarity of DESs for their extraction properties, this phenomenon has not yet received the necessary attention.

3.6. Acid-Base Properties

The extractability of compounds from any raw materials, including phytomass, may depend, along with the nature of extracted compounds, to various extents on the acid-base properties of the DES used. In general, the acidity or basicity of DESs is determined mainly by the acidity/basicity constants and molar ratio of their components. It is, therefore, more or less predictable. Values of pH for the aqueous solutions of selected DESs range from basic DES with pH ≈ 13 (a DES containing glycerol and K_2CO_3, [50]), through nearly neutral DESs, to acidic ones containing an organic acid [28].

The predominance of acid-catalyzed reactions in synthetic chemistry has led researchers to focus more on acidic ionic liquids and DESs, as well as on unveiling modes of tailoring their properties. Two categories of acidic DESs were formulated, namely Brønsted acidic DESs displaying Brønsted acidity due to ionizable protons, and Lewis acidic DESs displaying Lewis acidity because of a deficiency in electron [39]. This categorization has not yet been introduced into the field of phytomass valorization by DESs.

As pointed out by Trajano and Wyman [51], along with advantages of some reactions performed at a lower pH (such as higher yields of desired compounds), there are also drawbacks concerning the necessity to use corrosion-proof equipment. Acidic DESs are able to react with some metals and dissolve their oxides. Moreover, the products must frequently be washed and neutralized.

4. Therapeutic Effects of Substances Extracted from Phytomass

Since the beginning of civilization, man has been associated with plants and herbs and has used their potential in the treatment of various diseases. Without knowing the plants' components, he learned what types are suitable for which diseases and how to prepare adequate preparations from these plants, which are used to protect or restore health, to alleviate disease manifestations but also to recognize the disease. The therapeutic potential of substances contained in medicinal plants has been historically proven [52]. The world's population (80%) is engaged in folk medicine based on the use of plants [53]. Secondary metabolites are the most successful source of potential drugs. Herbal-derived chemicals are known to decrease the risk of some severe disorders, including autoimmune and cardiovascular diseases, as well as neurodegenerative diseases [54].

Many plants contain a wide range of inhibitors of viral proteins and act against viral diseases. Plants can generally produce metabolites that have an inhibitory effect on the proliferation of enzymes, proteins, and viruses [55,56]. Natural products have the potential to form the basis of holistic healthcare. For some people, synthetic drugs cause harmful side effects and are expensive to buy compared to traditional herbal products [57], although "natural" does not automatically mean "harmlessness".

The therapeutic potential of herbal medicines was assessed in a variety of animal models, and their effect and mechanisms of action were investigated through neurochemical approaches [58].

There is scientific evidence and centuries of human empirical experience on the therapeutic superiority of plant extracts over individual isolated ingredients, as well as their biological equivalence with synthetic drugs. The results of various studies on the effects of multicomponent extracts are summarized in the Wagner study [59]. In recent decades, pharmaceutical research and industry have sought to uncover the causes of the pharmacological and therapeutic superiority of many natural multi-ingredient products over individual compounds. One of the explanations is that plant extracts may contain bioactive natural products in the form of prodrugs, and in some cases, these compounds may optimize the effects of individual substances to achieve therapeutic goals. An illustrative example was provided by David et al. [57] documenting that in plants, many natural products exist in the form of conjugates with saccharide moieties (called glycosides). Many of the glycosides are activated upon cell disruption to yield highly active therapeutic compounds (e.g., glucosinolates and cyanogenetic glycosides). Thus, the glycosides themselves are not active directly; however, they can become active and efficient upon metabolization.

Another explanation lies in the existence of a synergistic therapeutic effect of several active substances in natural extracts. Flavonoids have a wide variety of biological activities and therapeutic potential [60]. Ginkgolide A and B can serve as examples. It is known that the combination of ginkgolide A and B acts on antiplatelet-activating factors in ginkgo biloba phytopharmaceuticals. The synergistic effect of the combination of these ginkgolides in the preparation of ginkgo biloba was confirmed by Wagner [61]. The extracts may contain several bioactive compounds with different specific activity. Polyphenols extracted by DESs such as curcumin, ferulic acid, proanthocyanidin, quercetin, quercetin-3-O-glucoside, isorhamnetin, kaempferol, rutin, p-coumaric acid, gallic acid, caffeic acid, catechin, epicatechin, catechinic acid, chlorogenic acid, syringic acid, vanillic acid, and others have shown antioxidant, anti-inflammatory properties [62]. Aromatic phytochemical constituents have analgesic, anticarcinogenic, antidiabetic, antifungal, cardioprotective, hepatoprotective, and neuroprotective properties [52,54,62]. The potential of the 237 extracted substances from phytomass for orally bioavailable therapeutics by predicting a number of ADME (Absorption, Distribution, Metabolism, and Extraction)-related properties was published in the work Jablonsky et al. 2017 [62]. When using such multicomponent extracts, several therapeutic effects of their individual components may be exerted. In order to isolate the desired secondary plant metabolites, it is possible to utilize various extraction techniques. Based on the chosen extraction method, it is subsequently possible to yield various types of substances in various quality and composition.

The interest in natural products or obtaining active substances from plants also has an economic background. This is based on society's efforts and beliefs about the benefits of returning to traditional medicine. This had the effect that herbal phytopharmaceuticals reached USD 60 billion, with annual growth rates of 5–15% [63].

5. Valorization of Phytomass by Deep Eutectic Solvents

Extraction Techniques

To date, a number of papers have been published on the extraction and separation of value-added compounds and substances from phytomass. In order to achieve the maximum yield, purity, and selectivity of such substances, their extraction from phytomass is carried out by purposefully selected methods. Their choice depends predominantly on the processed phytomass and required target compounds. Along with classical auxiliary techniques (heating, centrifugation, shaking), the application of DESs becomes associated with advanced extraction techniques, such as ultrasound-assisted extraction (UAE), negative pressure cavitation (NPC), enzyme-assisted extraction (EAE), hydrodiffusion extraction (HDE), supercritical fluid extraction (SFE), and microwave-assisted extraction (MAE). The mentioned techniques are thoroughly evaluated in the review published by Cunha and Fernandes [64]. The extraction of value-added compounds is often associated with

the pretreatment of phytomass, which means the treatment of the inputted raw phytomass, e.g., by mechanical milling prior to the action of DES as extractants to facilitate the penetration of DES into the processed phytomass and to improve the contact of DES with the extracted components by disrupting the solid impermeable structures of the natural polymers [8].

6. Extracted Value-Added Compounds

The achievements in obtaining value-added compounds by phytomass valorization with a focus on the last 5 years are shown in Table 1. For clarity and convenient orientation, the data are arranged, as far as possible, in alphabetical order of the extracted compounds.

Table 1. Value-added compounds extracted from phytomass by Type III DESs and extraction conditions.

Compounds	Sample	Solvent	Ratio	Extraction Conditions; Analytical Methods	Ref.
Acacetin-7-diglucuronide Apigenin-7-O-diglucuronide, Campneoside, Cistanoside F, Dimethyl quercetin, Durantoside I, Eukovoside, Forsythoside A, Gardoside, Chrysoeriol-7-diglucuronide, Isoverbascoside, Ixoside, Lippioside, Lippioside I derivative, Lippioside II, Luteolin-7-diglucuronide, Martynoside, Oxoverbascoside, Teucardoside, Theveside, Verbascoside, β-hydroxyverbascoside/β-hydroxy-iso verbascoside, Total phenolic compounds	*Lippia citriodora*	ChCl:lactic acid ChCl:tartaric acid ChCl:1,3-batanediol ChCl:ethylene glycol ChCl:xylitol ChCl:1,2-propanediol ChCl:fructose.water ChCl:sucrose.water ChCl:maltose ChCl:glucose:water ChCl:urea	1:2 2:1 1:6 1:2 2:1 1:2 2:1:1 4:1:2 3:1 2:1:1 1:2	Microwave-assisted extraction 200 mg powder, 2 mL DES (with 25% water), 65 °C, 20 min, 700 W, 18 bar spectrometric analysis HPLC-ESI-TOF-MS	[65]
Aglycone, Demethyloeuropein, Hydroxytyrosol, Oleacein	Olive leaves, ripened olive drupes	ChCl:urea ChCl:glycerol ChCl:Lactic acid ChCl:ethylene glycol ChCl:citric acid	1:2 1:1 1:1 1:1 1:1	MAE at 100 W, S/L 1:2.5 (g/mL) with 0 or 20% water, 10 or 30 min at 80 °C, HPLC	[66]
Amentoflavone, Quercitrin, Hinokiflaveno, Myricitrin	*Platycladi Cacumen*	ChCl:levulinic acid ChCl:ethylene glycol ChCl:N,N′:dimethylurea ChCl:D-glucose Betaine:levulinic acid Betaine:ethylene glycol Betaine:1-methylurea Betaine:D-glucose L-proline:levulinic acid L-proline:glycerol L-proline:acetamide L-proline:D-glucose	1:2 1:2 1:1 1:1 1:2 1:2 1:1 1:1 1:2 1:2.5 1:1 1:1	Ultrasound 200 W, 50 °C, 30 min, centrifugation 20 min (16,200 G), suspension diluted eight times with 50% acetonitrile, HPLC-UV, The optimized DES extraction conditions: 30 min; S/L 1:4 (mg/mL) for ChCl:Levulinic Acid (90%) (1:2)	[67]
Apigenin rutinoside, Luteolin, Luteolin di-glycoside, Luteolin glucoside, Luteolin rutinoside, Oleuropein	Olive (*Olea europaea*) Leaves	Glycerol:sodium-potassium tartrate tetrahydrate:water	7:1:2	Powder leaves, 10 mL LTTM, ultrasonic power of 140 W, concentration of the LTTM in an aqueous solution (50 and 80%, *w*/*v*), S/L (1:15; 1:45 (g/mL)) and temperature (50 to 80 °C), LC-DAD-MS, total polyphenol, and flavonoid yield, antioxidant activity	[68]

Table 1. *Cont.*

Naringenin, Oleuropein, Caffeic acid, (±) catechin hydrate, Cinnamic acid, Gallic acid, Quercetin dehydrate, Luteolin, p-coumaric acid, Rutin hydrate, Trans-ferulic acid, Tyrosol, 3-hydroxytyrosolapigenin	olive cake, onion seed, and by product from tomato and pear canning industry	Lactic acid:glucose + 15% of water and 0.1% (*v*/*v*) formic acid	5:1	Ultrasound time (15, 35, 60 min), S/L 1:15, 1:45, 1:75 (mg/mL) and water dilution of the optimal DES (0%, 40% and 75%), temperature 40 °C. Optimization: S/L 1:75 (mg/mL) and homogenized by a vortex during 15 s. Ultrasound treatment (200 W output power, 20 kHz frequency), 60 min, 40 °C, HPLC-DAD analysis	[69]
Artemisinin	*Herba Artemisiae Scopariae*	$[N(Me)(Oc)_3]Cl$:ethylene glycol	1:2	S/L 1:10 (g/mL), 250 rpm, 30 °C, 15 min, HPLC-UV	[70]
		$[N(Me)(Oc)_3]Cl$:1-propanol	1:2		
		$[N(Me)(Oc)_3]Cl$:1,3-propanediol	1:2		
		$[N(Me)(Oc)_3]Cl$:glycerol	1:2		
		$[N(Me)(Oc)_3]Cl$:1-butanol	1:2		
		$[N(Me)(Oc)_3]Cl$:1,2-butanediol	1:2		
		$[N(Me)(Oc)_3]Cl$:hexyl alcohol	1:2		
		$[N(Me)(Oc)_3]Cl$:capryl alcohol	1:2		
		$[N(Me)(Oc)_3]Cl$:decyl alcohol	1:2		
		$[N(Me)(Oc)_3]Cl$:dodecyl alcohol	1:2		
		$[N(Me)(Oc)_3]Cl$:1-tetradecanol	1:2		
		$[N(Me)(Oc)_3]Cl$:cyclohexanol	1:2		
		$[N(Me)(Oc)_3]Cl$:DL-menthol	1:2		
		$[N(Me)(Oc)_3]Cl$:1-butanol:1-propanol	1:1:3 1:2:2 1:3:1 1:4:0		
		$[N(Me)(Oc)_3]Cl$:1-butanol:hexyl alcohol	1:1:3 1:2:2 1:3:1 1:4:0		
		$[N(Me)(Oc)_3]Cl$:1-butanol:capryl alcohol	1:1:3 1:2:2 1:3:1 1:4:0		
		$[N(Me)(Oc)_3]Cl$:1-butanol:1,2-propanediol	1:1:3 1:2:2 1:3:1 1:4:0		
		$[N(Me)(Oc)_3]Cl$:1-butanol:1,3-butanediol	1:1:3 1:2:2 1:3:1 1:4:0		
		$[N(Pr)_4]Br$:1-butanol:1-propanol	1:1:2 1:1.5:1.5 1:2:1 1:3:0		
		$[N(Pr)_4]Br$:1-butanol:hexyl alcohol	1:1:2 1:1.5:1.5 1:2:1 1:3:0		
		$[N(Pr)_4]Br$:1-butanol:capryl alcohol	1:1:2 1:1.5:1.5 1:2:1 1:3:0		
		$[N(Pr)_4]Br$:1-butanol:1,2-propanediol	1:1:2 1:1.5:1.5 1:2:1 1:3:0		
		$[N(Pr)_4]Br$:1-butanol:1,3:butanediol	1:1:2 1:1.5:1.5 1:2:1 1:3:0		
		$[N(Bu)_4]Br$:1-butanol:1:propanol	1:0.5:1.5 1:1:1 1:1.5:0.5 1:2:0		
		$[N(Bu)_4]Br$:1-butanol:hexyl alcohol	1:0.5:1.5 1:1:1 1:1.5:0.5 1:2:0		

Table 1. *Cont.*

		$[N(Bu)_4]Br$:1-butanol:capryl alcohol	1:0.5:1.5 1:1:1 1:1.5:0.5 1:2:0		
		$[N(Bu)_4]Br$:1-butanol:1,2-propanediol	1:0.5:1.5 1:1:1 1:1.5:0.5 1:2:0		
		$[N(Bu)_4]Br$:1-butanol:1,3-butanediol	1:0.5:1.5 1:1:1 1:1.5:0.5 1:2:0		
		$[N(Bu)_4]Br$:1-butanol $[N(Me)(Oc)_3]Cl$:1-butanol $[N(Me)(Oc)_3]Cl$:1-butanol:capryl alcohol	1:2 1:4 1:3:1	Extraction by air-bath shaking at 250 rpm and 30 or 60 °C, water-bath shaking at 150 rpm and 30 or 60 °C, magnetic stirring at 150 rpm and 30 or 60 °C, heating at 60 °C and 0 rpm, or ultrasonication at 200 W and 30 or 60 °C.	
		$[N(Me)(Oc)_3]Cl$:1-butanol	1:4	S/L (from 1:10 to 1:20 g/mL), ultrasonic powers (120 to 200 W), Temperature (40–60 °C), particle sizes (20 to 80 mesh), time (40–80 min)	
Astragalin, Benzoic acid, Caffeic acid, Catechinic acid, Epicatechin, Gallic acid, Gentisic acid, Hyperin, Chlorogenic acid, Quercetin Rutin, Syringic acid, Vanillic acid	*Morus alba* L.	ChCl:urea ChCl:ethylene glycol ChCl:glycerol ChCl:citric acid ChCl:malic acid Betaine:levullinic acid Betaine:lactic acid Betaine.glycerol Proline:malic acid Proline:glycerol Proline:levullinic acid Proline:lactic acid	1:2 1:2 1:2 2:1 1:1 1:2 1:1 1:2 1:1 2:5 1:2 1:1	0.2 g powder, 4 mL (DES:water 3:1 v/v) sonicated at 40 °C, 30 min, centrifuged 120 rpm for 10 min HPLC-UV	[71]
Astrazon orange G, astrazon orange R, chrysoidine	Red chili peppers	ChCl:ethyl glycol ChCl:1,2 butanediol ChCl:glycerol ChCl:1,3 butanediol ChCl:1,4 butanediol	1:3 1:3 1:3 1:3 1:3	S/L 1:10 (g/mL), temperature: 30 °C, time: 20 min, and ultrasonic power: 75 W, HPLC-UV	[72]
Baicalein, Baicalin, Scutellarin, Wogonoside, Wogonin	*Radix scutellatiae*	ChCl:glycerol ChCl:glycol ChCl:1,2-propylene ChCl:1,4-butanediol ChCl:lactic acid ChCl:malic acid:water ChCl:glucose:water L-proline:glycerol L-proline:glucose:water L-proline:fructose:water Citric acid:fructose:water Citric acid:glucose:water	1:4 1:4 1:4 1:4 1:4 1:1:3 1:1:2 1:4 5:3:8 1:1:5 1:1:3 1:1:5	50 mg powder, 42 min, 1.2 mL DES (66.7% DES and 33.3% water), vortexed 5 min, ultrasonification 42 min, HPLC	[73]
Bergapten, Caffeoylmalic acid, Rutin, Psoralen Psoralic acid-glucoside	*Ficus carica L.*	Glycerol:xylitol:D-(−)-fructose	1:3:1 1:3:2 1:3:3 2:3:1 2:3:2 2:3:3 3:3:1 3:3:2 3:3:3	DES-MAE, S/L 1:20 (g/mL), temperature 55 °C, time 10 min, microwave power 250 W, HPLC	[74]

Table 1. *Cont.*

		Glycerol:L-proline:D-(-)-fructose	3:3:3	DES-UAE, water concentration 20%, S/L 1:20 (g/mL), temperature 60 °C, time 20 min, ultrasonic power 250, 700 W, HPLC	
		ChCl:D-(+)-Galactose ChCl:L-proline ChCl:DL-malic acid ChCl:xylitol ChCl:glycerol ChCl:D-(+)-Glucose ChCl:citric acid ChCl:sucrose ChCl:D-(−)-fructose	1:1 2:1 1:1 5:2 1:1 1:1 2:1 1:1 1:1	DES-MAE, S/L 1:20 (g/mL), temperature 55 °C, time 10 min, microwave power 250 W, HPLC	
		Glycerol:L-proline:D-(−)-fructose	3:3:3	DES-MAE, water concentration 10–40%, S/L 1:5, 1:15, 1:25 (g/mL), temperature 40–80 °C, time 20–60 min, microwave power 250 W, HPLC	
Biochanin A, Daidzein, Daidzin, Genistein, Genistin	spike samples	ChCl:(+)-glucose ChCl:L(+)-tartaric acid ChCl:citric acid ChCl:saccharose ChCl:glycerine ChCl:D(+)-xylose Urea:ChCl Urea:L(+)-tartaric acid Glycerine:D(+)-glucose Glycerine:L(+)-tartaric acid Glycerine:citric acid Urea:citric acid ChCl:citric acid:glycerine ChCl:citric acid	2:1 1:1 1:1; 2:1; 1:2 2:1 1:2 1:1; 2:1 1:1 2:1 2:1 1:1 2:1 2:1 1:1:1; 2:2:1 1:1	water content 30%, S/L 1:3 (g/mL), extraction time 60 min, extraction temperature 60 °C, ultrasonic power 616 W, UHPLC-UV	[75]
		ChCl:citric acid	1:1	Central composite design: time 40–120 min, temperature 30–80 °C, ultrasonic power 264–616 W, S/L 1:3 (g/mL), 30% water content	
Caffeic acid, Catechins, Epicatechin, Protocatechuic acid	Palm bark	ChCl:ethyleneglycol ChCl:glycerol ChCl:xylitol ChCl:formic acid ChCl:citric acid ChCl:oxalic acid ChCl:malonic acid ChCl:phenol	1:1 1:1 1:1 1:1 1:1 1:1 1:1 1:1 1:1, 1:2, 1:3, 1:4, 1:5	0.5 g of the palm powder was soaked in 7.5 g of the DES and 2.5 g of H_2O in a 50 mL round-bottom flask. The mixture was refluxed at 40 °C for 6 h in a water bath for extraction. HPLC-MS	[76]
Caffeic acid, Hydroxytyrosol, Luteolin, Rutin, Vanillin Total phenolic content	Olive pomace	ChCl:citric acid ChCl:lactic acid ChCl:maltose ChCl:glycerol	1:2 1:2 1:2 1:2	Homogenate-assisted extraction 2 g olive pomace, 25 mL NADES, 30 min, 40 or 60 °C, homogenization 4000, 12,000 rpm Microwave-assisted extraction 2 g olive pomace, 25 mL NADES, 200 W, 40 or 60 °C, 30 min. Ultrasound-assisted extraction 2 g olive pomace, 25 mL NADES, 60 kHz, 280 W, 40 or 60 °C, 30 min. High hydrostatic pressure-assisted extraction 2 g olive pomace, 25 mL NADES, 300 or 600 MPa, 5 and 10 min, HPLC-DAD, spectrometric analysis	[77]

Table 1. *Cont.*

Caffeine, Catechin, Catechin gallate, Epicatechin, Epigallocatechin, Epicatechin-3-gallate, Epigallocatechin-3-gallate Gallatecatechin, Gallic acid, Gallocatechin	Green tea	Betaine:glycerol:glucose	4:20:1	Power irradiation 500 W, ultrasonic irradiation time 6.4–73.6 min, content of DES in the extraction solvent 24.7–100% w/w, volume of the extraction solvent per 100 mg of green tea powder 0.6–0.8 mL, LC-UV	[78]
Chlorogenic acid, (+)-catechin Gallic acid, trolox Total phenolic content, Total flavonoid content, Antioxidant activity	Coffee grounds	ChCl:urea ChCl:acetamide ChCl:glycerol ChCl:sorbitol ChCl:ethylene glycol ChCl:1,4-buatnediol ChCl:1,6-hexanediol ChCl:malonic acid ChCl:citric acid ChCl:fructose:water ChCl:xylose:water ChCl:sucrose:water ChCl:glucose:water	1:2 1:2 1:2 1:2 1:2 1:2 1:2 1:2 1:2 5:2:5 2:1:2 4:1:4 5:2:5	50 mg grounds, 0.85 mL DES irradiated at ambient temperature for 45 min, centrifuged at 12,300 g for 20 min, UPHLC-Q-TOF-MS	[79]
Chlorogenic acid, 3,4-di-O-caffeoylquinic acid, 3,5-di-O-caffeoylquinic acid, 4,5-di-O-caffeoylquinic acid	*Artemisia argyi* leaves	ChCl:malic acid ChCl:urea ChCl:glutaric acid ChCl:malonic acid ChCl:ethylene glycol ChCl:glycerol	1:1 1:2 1:1 1:1 1:3 1:2	20 mg powder, 1 mL solvents, ultrasonic 200 W, 40 kHz, 30 min, HPLC	[80]
		ChCl:malic acid:glutaric acid ChCl:malic acid:ethylene glycol ChCl:malic acid:glycerol ChCl:malic acid. urea ChCl:malic acid:malonic acid	2:1:1,2:2:1, 1:2:0.5, 2:2:1 1:2:0.5, 2:2:1 2:1:1, 2:2:1, 2:1:2 2:1:1, 2:2:1, 1:1:1, 2:1:2		
Chlorogenic acid, Quercetin-3-O-glucoside, Quercetin-O-pentoside	*Juglans regia* L.	ChCl:acetic acid ChCl:propionic acid ChCl:butyric acid ChCl:valeric acid ChCl:glycolic acid ChCl:lactic acid ChCl:phenylacetic acid ChCl:3-phenylacetic acid ChCl:malic acid ChCl:glutaric acid ChCl:citric acid ChCl:3-phenylpropionic acid ChCl:3-phenylbutyric acid ChCl:3-phenylvaleric acid	1:2 1:2 1:2 1:2 1:2 1:2 1:2 1:2 1:1 1:1 2:1 1:2 1:2 1:2	0.15 g powder, 5 mL DES with 20% (w/w) of water, 50 °C, 1 h, 600 rpm, HPLC	[81]
Chlorogenic acid	blueberry leaves	ChCl:ethylene glycol ChCl:glycerin ChCl:1,3-butanediol ChCl:citric acid ChCl:oxalic acid ChCl:glucose ChCl:maltose ChCl:sucrose	1:2 1:3 1:4 1:5 1:6 1:7 1:8 1:9	NPCE-DES-ATPS, temperature 60 °C, S/L 1:20 (g/mL), water concentration 20% (v/v) in DES, time 30 min and negative pressure −0.07 Pa, HPLC	[82]
		ChCl:1,3-butanediol	1:4	S/L 1:15; 1:25 (g/mL), the extraction temperature (50–70 °C) and extraction time (20–40 min), HPLC	
Cinnamyl alcohol, Rosavin, Rosin, Salidroside, Tyrosol	*Rhodiola rosea L.*	Lactic acid:glucose:water Lactic acid:fructose:water	6:1:6 5:1:1, 5:1:5	S/L 1:20 (g/mL), sonification 50 W, 35 kHz, 60 min, 36 °C, HPLC	[83]
Coumarin, trans-cinnamaldehyde	*Cinnamomum burmannii* (cinnamon bark)	ChCl:glycerol ChCl:sorbitol ChCl:xylitol ChCl:lactic acid ChCl:malic acid ChCl:citric acid Betaine:lactic acid Betaine:malic acid Betaine:citric acid	1:2 1:2 4:1 1:1 1:1 1:1 1:1 1:1 1:1	Ultrasound-assisted extraction, S/L 1:10 (g/mL)	[84]

Table 1. *Cont.*

Coumarin, trans-cinnamaldehyde	*Cinnamomum burmannii* (cinnamon bark), *Caesalpinia sappan* heartwoods	ChCl:glycerol		Ultrasonic extraction: 35 W, 42 Hz, S/L 1:66–1:93.75(g/mL), water content 10–80%, different ratio of glycerol to ChCl (66–20%), HPLC	[85]
Curcumin	herbal tea, turmeric drug (food supplement), turmeric powder	ChCl:phenol	1:2 1:3 1:4	VAS-DES-ELLME, HPLC, UV-VIS methodology	[86]
Epigallocatechin-3-gallate	Green tea	Betaine:glycerol:glucose	4:20:1 4:15:1 4:10:1 4:5:1	S/L 1:10 (g/mL), 45 min, irradiation power 500 W, room temperature, LC-UV	[78]
		Betaine:maltitol Betaine:urea Betaine:glycerol Betaine:citric acid Betaine:glucose Betaine:maltose Betaine:sucrose Betaine:D-sorbitol Betaine:Xylitol Citric acid:Xylitol Citric acid:maltitol Citric acid:fructose Citric acid:glycerol Citric acid:glucose Citric acid:maltose Citric acid:sucrose Citric acid:D-sorbitol Glycerol:D-sorbitol Glycerol:fructose Glycerol:galactose Glycerol:urea Glycerol:glucose Glycerol:maltose Glycerol:sucrose Glycerol:maltitol Glycerol:xylitol Citric acid:glycerol:glucose Citric acid:glycerol:maltose Citric acid:glycerol:maltitol Betaine:glycerol:glucose Betaine:glycerol:urea Betaine:glycerol:maltitol Betaine:glycerol:citric acid Betaine:glycerol:maltose Urea:glycerol:maltose Urea:glycerol:maltitol Urea:glycerol:glucose	4:1 1:2 1:1 1:1 4:1 4:1 4:1 2:1 4:1 1:1 2:1 1:1 1:2 1:1 2:1 1:1 1:1 2:1 3:1 3:1 1:1 3:1 3:1 3:1 3:1 2:1 1:2:1 2:4:1 2:4:1 4:4:1 1:1:2 4:4:1 1:1:1 4:4:1 3:3:1 3:3:1 2:2:1		
Epimedin A, Epimedin B, Epimedin C, Icariin	*Epidemium pubescens* Maxim.	ChCl:1,4-butanediol ChCl:ethylene glycol ChCl:1,2-propanediol ChCl:lactic acid ChCl:glycerol	1:5, 1:6 1:3, 1:4, 1:5, 1:6 1:4, 1:5, 1:6 1:2, 1:3, 1:6 1:1, 1:2, 1:3, 1:4, 1:5, 1:6	0.02 g of *E. pubescens* powder, 3 mL extractant, vortexing 10 min., and ultrasonic radiation at 25 °C for 20 min, and supernatant was mixed water, molar ratio 1:1 (DES/water *v*/*v*), HPLC-UV	[87]
Epimedin A, Epimedin B, Epimcedin C, Icariin Icarisid II	*Herba Epimedii*	ChCl:urea ChCl:ethylene glycol ChCl:1,4-buatnediol ChCl:glycerol ChCl:glucose:water ChCl:malic acid ChCl:citric acid ChCl:lactic acid L-proline:1,2 propylene glycol L-proline:glycerol L-proline:ethylene glycol ChCl:1,2-propylene glycol	2:1 1:2, 1:3 1:3 1:4 2:1:1 1:1 1:1 1:2 1:3 1:4 1:3, 1:4, 1:5, 1:6 1:2, 1:3, 1:4, 1:5, 1:6	0.2 g powder, 4 mL solvent (DES:water 7:3, *v*/*v*), mixed by vortex 5 min, ultrasonic extractionat room temperature for 45 min. HPLC	[88]
Flavonoids	*Carthamus tinctorius*	ChCl:oxalic acid ChCl:ethylene glycol ChCl:1,3-butanediol ChCl:1,6-hexanediol	1:1	Ultrasonic treatment: 0.5 g powder, solvents 10–35 mL, 45 °C, 20 min, 150 W Other ultrasonic treatment: different conditions, change the parameters: 10–60 min, 60–240 W, 25–45 °C Spectrometric analysis	[89]

Table 1. *Cont.*

Ginkgolide A	Ginkgo biloba	ChCl:glycerol ChCl:gthylene glycol Xylitol:levulinic acid 1, 2-propanediol:levulinic acid 1, 3-butanediol:levulinic acid Betaine:ethylene glycol Betaine:levulinic acid Betaine:glycerol ChCl:urea ChCl:levulinic acid ChCl:glycolic acid ChCl:glutaric acid ChCl:D-sorbitol ChCl:xylitol ChCl:1, 3-butanediol ChCl:1,2-propanediol	1:2 1:2 1:1 1:1 1:1 1:3 1:3 1:2 1:2 1:2 1:1 1:1 1:1 1:1 1:3 1:2	UAE, 70% (*w*/*w*) aqueous solution at 100 W and 25 °C for 10 min, S/L 1:15 (g/mL), colorimetric method	[90]
		Betaine:ethylene glycol + water	6:4	Magnetic stirring at 45 °C for 20 min, colorimetric method	
				UAE at 45 °C and 100 W for 20 min, colorimetric method	
Bilobalide Ginkgolide A, Ginkgolide B, Ginkgolide C	Ginkgo biloba	Betaine:ethylene glycol + water ChCl:urea + water	1:2 1:2	DES containing water 0–100% *w*/*w*, S/L 1:15 (g/mL) with ultrasound at 100 W and 25 °C for 10 min., colorimetric and HPLC-ELSD method	[90]
		Betaine:ethylene glycol + water ChCl:urea + water	1:2 1:2	Water 40% *w*/*w*, S/L 1:15 (g/mL) with ultrasound at varied temperature (25–60 °C) and 100 W for 10 min., colorimetric and HPLC-ELSD method	
		Betaine:ethylene glycol + water	1:3	Water 40% *w*/*w*, S/L (1:7.5, 1:10, 1:12.5, 1:15, 1:20, 1:30, and 1:50 (g/mL)), with ultrasound at 45 °C and 100 W for 10 min., colorimetric and HPLC-ELSD method	
		Betaine:ethylene glycol + water	1:3	S/L 1:10 (g/mL) with ultrasound at 45 °C and 100 w for different time 5–40 min., colorimetric and HPLC-ELSD method	
Glycyram, Licuroside	*Glycxyrrhizae* roots	Sorbitol:malic acid:water	1.1:3	S/L 1:10 (g/mL), 24 h, 25 °C, RP HPLC	[91]
Hespederin	*Mandarin peels*	ChCl:acetamide ChCl:1,4-butanediol ChCl:citric acid ChCl:ethylene glycol ChCl:glycerol ChCl:lactic acid ChCl:levulinic acid ChCl:malonic acid ChCl:malic acid ChCl:N-methyl urea ChCl:oxalic acid ChCl:sorbitol ChCl:urea ChCl:thiourea ChCl:xylitol	1:2 1:2 1:1 1:1 1:2 1:1 1:1 1:1 1:1 1:3 1:1 1:1 1:1 1:1 1:1	50 mg powder, 1 mL solvent (DES with 20% (*v*/*v*) water), stirring 50 °C for 30 min, HPLC-DAD	[92]
Indole-3-acetic acid, 1-naphtaleneacetic acid	Fruit juice	Benzyltriethylammonium chloride:thymol $[N(Me)(Oc)_3]Cl$:butanol $[N(Me)(Oc)_3]Cl$:isoamyl alcohol $[N(Me)(Oc)_3]Cl$:octanol	1:4 1:4 1:4 1:4	Fruit juice samples diluted with in ratio 1:10, VA-DES-DLLME, HPLC	[93]
Levofloxacin	Green bean	Betaine:ethyleneglycol:water	1:2:1	SPE-HPLC	[94]
Lignin content in delignified biomass	oil palm biomass residues, empty fruit bunch	Malic acid:ChCl-water	2:4:2 (L-malic acid)	S/L 1:20 (*w*/*w*), 85 °C, overnight	[95]
		Malic acid:ChCl-water	2:4:2 (cactus)		
		Malic acid:monosodium glutamate:water	3:1:5 (L-malic acid)		
		Malic acid:monosodium glutamate:water	3:1:5 (cactus)		

Table 1. *Cont.*

Oxyresveratrol	*Morus alba* Roots	Urea:glycerin	1:1, 1:2, 1:3	1 g powder, 20 mL NADES, ultrasonic treatment 10, 15, 20 min, HPLC	[96]
Pectin	pomelo (*Citrus grandis (L.) Osbeck*) peels	Lactic acid:glucose:water Lactic acid:glycine Lactic acid:glucose Lactic acid:Glycine:water	6:1:6, 5:1:3 9:1 5:1 3:1:3	S/L 1:20 (g/mL), 60 min, 50 °C, 500 rpm S/L 1:20 (g/mL), 45 min, 70 °C, 55 rpm	[97]
Phlorotannin content	Brown algae: *Fucus vesiculous* L., *Ascophyllum nodosum* L.	ChCl:lactic acid ChCl:malic acid. Water Glucose:lactic acid:water Betaine:malic acid:water Betaine:lactic acid:water Betaine:malic acid:glucose Betaine:glycerin:glucose	1:1, 1:2, 1:3 1:1:1, 2:1:1 1:5:3 1:1:1 1:2:1 1:1:1 1:5:1	20 g algae, 100 mL solvents (pure DES or with water content 50–70%), 120 min, 50 °C, spectrometric analysis	[98]
Polyprenyl acetates	*Ginkgo biloba* leaves	[N(Me)(Oc$_3$]Cl:hexanoic acid [N(Me)(Oc$_3$]Cl:octanoic acid [N(Me)(Oc$_3$]Cl:capric acid [N(Me)(Oc$_3$]Cl:lauric acid [N(Me)(Oc$_3$]Cl:myristic acid [N(Me)(Oc$_3$]Cl:palmitic acid [N(Me)(Oc$_3$]Cl:octadecenoic acid [N(Me)(Oc$_3$]Cl:ricinoleic acid [N(Me)(Oc$_3$]Cl:1-propanol [N(Me)(Oc$_3$]Cl:1-butanol [N(Me)(Oc$_3$]Cl:hexyl alcohol [N(Me)(Oc$_3$]Cl:capryl alcohol [N(Me)(Oc$_3$]Cl:decyl alcohol [N(Me)(Oc$_3$]Cl:dodecyl alcohol [N(Me)(Oc$_3$]Cl:1-tetradecanol [N(Me)(Oc$_3$]Cl:1-hexadecanol [N(Me)(Oc$_3$]Cl:cyclohexanol [N(Me)(Oc$_3$]Cl:DL-menthol [N(Me)(Oc$_3$]Cl:capryl alcohol:octylic acid	1:2 1:2 1:2 1:2 1:1 1:1 1:2 1:2 1:2 1:2 1:2 1:2 1:2 1:1 1:2 1:2 1:2 1:2 1:2:3	80 mg of Ginkgo biloba leaves powder was extracted with 0.80 mL of the DES by heating at 60 °C and 0 rpm, stirring at 150 rpm and 25 or 60 °C, water-bath shaking at 150 rpm and 25 or 60 °C, air-bath shaking at 250 rpm and 25 or 60 °C, ultrasonic treating at 200 W and 25 or 60 °C, HPLC-DAD	[99]
Proanthocyanidin	*Gingko biloba* leaves	ChCl:glycerol ChCl:ethylene glycol ChCl:propylene glycol ChCl:1,3-buatnediol ChCl:sorbitol ChCl:xylitol ChCl:1,5-pentanedioic acid ChCl:glycolic acid ChCl:malonic acid ChCl:malic acid ChCl:levulinic acid ChCl:lactic acid ChCl:citric acid ChCl:tartaric acid ChCl:urea ChCl:oxalic acid	1:2 1:2 1:2 1:3 1:1 1:1 1:1 1:1 1:1 1:1 1:1 1:2 1:1 1:1 2:1 1:1	100 mg powder, 1 mL DES with 30% water, shaking at 250 rpm, 25 °C, 5 min, centrifugation at 10,000 rpm for 10 min, spectrometric analysis	[100]
Protein	Brewer's spent grain	Sodium formate:urea Potassium acetate:urea Sodium acetate:urea	1:2, 1:3 1:2, 1:3 1:2, 1:3	90 wt% carboxylate salt—urea DESs at 10 wt% consistency, 90 °C and time 4 h	[101]
		ChCl:urea Sodium acetate:urea	1:2 1:2	consistency 5 or 10% wt, defat samples, 80 °C, 20 h extraction	
Protein	Bamboo shoots and sheath	ChCl:levulinic acid	1:2, 1:3, 1:4, 1:5, 1:6	S/L 1:30 to 1:60; Temperature 20–40 °C, water content 5–30%	[102]
Quercetin	Ginkgo biloba	ChCl:glycerol ChCl:ethylene glycol ChCl:1,4-butanediol	1:2, 1:3, 1:4, 1:5 1:2, 1:3, 1:4, 1:5 1:2, 1:3, 1:4, 1:5	powder (2.0 g) was dissolved in 40 mL methanol, ultrasonic treated (60 W), 30 min, HPLC	[103]
Quercetin, Quercetin-3-O-glucoside, Isorhamnetin, Kaempferol, Rutin	Sea buckthorn leaves	ChCl:citric acid ChCl:malic acid ChCl:lactic acid ChCl:ethylene glycol ChCl:1,3-butanediol ChCl:1,4-butanediol ChCl:1,6-hexanediol ChCl:1,2-propanediol ChCl:glycerol ChCl:glucose ChCl:fructose ChCl:sucrose	1:1 1:1 1:1 1:1 1:1 1:1 1:1 1:1 1:1 1:1 1:1 1:1	microwave-assisted extraction, 1.0 g of leaves, 20 mL DES with 20% (*v*/*v*) water, 600 W, 17 min, HPLC	[104]

Table 1. *Cont.*

Quercetin, Isorhamnetin, Kaempferol, Naringenin	*Pollen Typhae*	ChCl:1,4-butanediol ChCl:glucose ChCl:glycerol ChCl:1,4-buatnediol:glycerol L-proline:glycerol ChCl:lactic acid ChCl:ethylene glycol ChCl:1,2-propanediol	1:4 1:4 1:4 1:2:2 4:11 1:4 1:4 1:4	100 mg powder, 2 mL DES, vortexed 5 min, and ultrasonic irradiation 35 min, centrifugation at 4200 rpm for 25 min, HPLC-UV	[105]
Quercetin, Isorhamnetin, Naringenin, Kaempferol, Myrecetin,	*Flos Sophorae*	ChCl:malic acid ChCl:citric acid ChCl:malonic acid ChCl:methylurea ChCl:urea ChCl:N,N-dimethylurea ChCl:1,3-butanediol ChCl:ethylene glycol ChCl:glycerol	1:1, 1:3 1:1, 1:3 1:1, 1:3 1:1, 1:3 1:1, 1:3 1:1, 1:3 1:1, 1:3 1:1, 1:3 1:1, 1:3	200 mg powder, 1 mL DES, and short homogenization, AP/MALDI-MS	[106]
Rosmarinic acid, Rutin	*Satureja montana L.*	ChCl:urea ChCl:sorbitol ChCl:1,4-butanediol ChCl:lactic acid ChCl:levulinic acid	1:2 1:1 1:2 1:2 1:2	50 mg leaves, 1 mL solvents (DES + water (10, 30, 50% of water, *v*/*v*), stirring at 1500 rpm, 30, 50, 70 °C for 60 min, HPLC	[107]
Rutin	tartary buckwheat hull	ChCl:1,2-propanediol ChCl:glycerol ChCl:glucose ChCl:sucrose ChCl:xylitol ChCl:sorbitol Glycerol:L-proline Glycerol:L-alanine Glycerol:L-histidine Glycerol:L-threonine Glycerol:L-lysine Glycerol:L-arginine	1:1 1:1 2:5 1:1 1:2 2:5 3:1 3:1 3:1 3:1 4.5:1 4.5:1	40 mg of tartary buckwheat hull powder, 1.0 mL solvent, 40 °C, 60 min, UAE power 200 W,	[108]
Total flavonoids and polyphenols, and total polyphenols at saturation tentative identity: Apigenin C-glycoside, Chlorogenic acid, Quercetin diglycoside, Quercetin glycoside, Quercetin glycoside derivative, Quercetin rhamnoside derivative, Quercetin malonylglycoside derivative, Kaempferol glycoside derivative, Kaempferol malonylglucoside, Multiflorin B	Moringa *oleifera Lam.* leaves	Glycerol:sodium acetate	4:1 5:1 6:1	2.5 g of lyophilized leaves was mixed with 50 mL of aqueous LTTM mixture and stirred at 600 rpm for 180 min, at 50 °C, LC–DAD–MS, total flavonoids and polyphenols	[109]
Total phenolic and anthocyanin content	*Hibiscus sabdariffa*	Citric acid:glycerol Citric acid:ethylene glycol	1:4 1:4	Microwave-assisted extraction, 60 to 150 s, power 250, 350, 450, 550, 600 W, spectrometric analysis antioxidant activity determined	[110]
Total polyphenolic and flavonoid contents, Chlorogenic acid, chlorogenic acid isomer, Quercetin glucoside, quercetin malonylglycoside derivate, Kaempferol glucoside, kaempferol malonylglucoside, Multiflorin B, Neochlorogenic acid	*Moringa oleifera L.*	Glycerol:nicotinamide	5:1	Ultrasonic pretreatment: 0.57 g plant, 20 mL solvent (70% *w*/*v* aqueous solution), 50 Hz, 550 W, acoustic energy density 78.6 W/L, 23 °C, 5–40 min Batch stirred-tank extraction: 0.57 g plant, 20 mL solvent (70% *w*/*v* aqueous solution), 50 °C, 150 min, spectrometric analysis, HPLC antiradical activity, reducing power	[111]

Table 1. *Cont.*

Total phenolic content	*Ruta graveolens L.*	ChCl:citric acid	2:1	50 mg leaves, 1 mL solvent with different content of water (10–30%), stirring at time 30, 52, 60, 90 min, 30, 50, 70 °C, RP-HPLC	[112]
Total phenolic content	Spruce bark	ChCl:lactic acid:water ChCl:lactic acid:water ChCl:lactic acid:water ChCl:lactic acid:water ChCl:lactic acid:1,3-propanediol:water ChCl:lactic acid:1,3-propanediol:water ChCl:lactic acid:1,3-propanediol:water ChCl:lactic acid:1,3-propanediol:water ChCl:lactic acid:1,3-propanediol:water ChCl:lactic acid:1,3-propanediol:water ChCl:lactic acid:1,3-butanediol:water ChCl:lactic acid:1,3-butanediol:water ChCl:lactic acid:1,3-butanediol:water ChCl:lactic acid:1,3-butanediol:water ChCl:lactic acid:1,3-butanediol:water ChCl:lactic acid:1,3-butanediol:water ChCl:lactic acid:1,4-butanediol:water ChCl:lactic acid:1,4-butanediol:water ChCl:lactic acid:1,4-butanediol:water ChCl:lactic acid:1,4-butanediol:water ChCl:lactic acid:1,4-butanediol:water ChCl:lactic acid:1,5-pentanediol:water ChCl:lactic acid:1,5-pentanediol:water ChCl:lactic acid:1,5-pentanediol:water ChCl:lactic acid:1,5-pentanediol:water ChCl:lactic acid:1,5-pentanediol:water	1:2:0.96 1:3:0.97 1:4:0.99 1:5:0.98 1:1:1:0.92 1:2:1:0.95 1:3:1:0.91 1:4:1:0.92 1:5:1:0.91 1:1:1:0.93 1:2:1:0.92 1:3:1:1 1:4:1:1 1:5:1:1 1:1:1:0.96 1:2:1:0.92 1:3:1:0.92 1:4:1:0.91 1:5:1:0.91 1:1:1:0.87 1:2:1:0.98 1:3:1:0.90 1:4:1:0.90 1:5:1:0.96	0.5 g powder, 10 mL DESs, stirring at 60 °C for 2 h, spectrometric analysis antioxidant activity determined	[113]
Total phenolic content, boldine, 9 alkaloids and 22 phenolic compounds	*Peumus boldus* leaves	ChCl:1,2-propanediol ChCl:glycerol ChCl:lactic acid ChCl:levulinic acid L-proline:citric acid L-proline:oxalic acid L-proline:levulinic acid	1:3 1:2 1:2 1:1 1:2 1:1 1:1	Plant 0.1 g, 10 mL NADES (80% aqueous solution), vortexed 30 s, stirring extraction 60 °C, 50 min, 340 rpm Ultrasound extraction: room temperature, 20 min, 140 W, 37 Hz HPLC-PDA-ESI-IT/MS, HPLC-ESI-QTOF-MS	[114]
Total polyphenolic and flavonoid contents	Thyme (*Coridothymus capitatus*, *Thymus vulgaris*), Oregano (Origanum vulgare hirtum), Greek sage (*Salvia fruticosa*), Sage (*Salvia officinalis*)	Lactic acid:nicotinamide Lactic acid:ChCl Lactic acid:sosium acetate Lactic acid:ammonium acetate Lactic acid:glycine Lactic acid:L-alanine:	7:1 7:1 7:1 7:1 7:1 7:1	0.57 g of dried plant material, added 20 mL solvent, S/L 1:30 (g/mL), treated UAE, 37 Hz, 140 W, extraction time 60 min, 55 °C, extraction by aqueous DES solutions (75% *v*/*v*), other extraction β-cyclodextrin was added to the mixture (1.5% *w*/*v*), antiradical activities, reducing power determined	[115]
Total polyphenolic and flavonoid contents Chlorogenic acid, Di-caffeoylquinic acid, di-p-coumaroylquinic acid derivate, Isoquercetin, Quercetin, Narcissin, neochlorogenic acid, rutin	*Sambucus nigra flowers*	Lactic acid:glycín	5:1, 7:1, 9:1, 11.1, 13:1	Ultrasonic pretreatment: 0.57 g plant, 20 mL solvent (70% *w*/*v* aqueous solution), 50 Hz, 550 W, acoustic energy density 75.3 W/L, 22 °C, 5–40 min Batch stirred-tank extraction: 0.57 g plant, 20 mL solvent (70% *w*/*v* aqueous solution), 50 °C, 150 min, spectrometric analysis, HPLC-DAD, LC-DAD-MS antiradical activities, reducing power determined	[116]

Table 1. *Cont.*

Vanillin	Vanilla pods (*Vanilla planifolia*)	Betaine:citric acid Lactic acid:1,2-propandiol Lactic acid:fructose Fructose:glucose		15 mg of vanilla pods were extracted 1 mL NADES, water content (90:10, 75:25, 60:40, 40:60 (*v*/*v*)), HPLC-DAD	[117]
Vanillin	Vanilla pods (*Vanilla planifolia*)	ChCl:citric acid:water ChCl:malic acid:water ChCl:glycerol Fructose:glucose:water Malic acid:glucose:water Betaine:sucrose:water Betaine:citric acid:water Betaine:malic acid:glucose:water Citric acid:fructose:glucose:water Malic acid:glucose:fructose:water L-Serine:malic acid:water B-alanine:citric acid:water Lactic acid:1,2-propanediol Lactic acid:fructose	1:1:6 1:1:6 1:1 1:1:6 1:1:6 2:1:6 1:1:6 1:1:1:9 1:1:1:9 1:1:1:9 1:1:6 1:1:6 1:1 5:1	50 mg of vanilla pods were extracted 50 °C, 1 h, HPLC-DAD	[117]

Choline chloride—ChCl; methyl trioctyl ammonium chloride—$[N(Me)(Oc)_3]Cl$; tetrabuthylammonium bromide—$[N(Bu)_4]Br$, tetrapropylammonium bromide—$[N(Pr)_4]Br$.

7. Assessing the Main Opportunities of Using Phytomass for Extraction of High Value-Added Components by Deep Eutectic Solvents

Today's level of chemical synthesis makes it possible, in principle, to prepare any chemical compound at the laboratory and industrial scale. The properties of chemical compounds, including those of biological origin, do not depend on the method of their preparation. The advantage of compounds and substances isolated from natural sources over synthetically prepared ones lies in several factors. One of them is the cost related to their obtaining, which in the case of renewable natural resources can be significantly lower. Possible causes of different therapeutic effects are given in the section "Therapeutic effects of substances extracted from phytomass". As in most cases of groups of related compounds (polyphenols, flavonoids, etc.) being separated from phytomass by DESs, we will use the term value-added substances in the following text. In addition, the most suitable case is a situation where entire extracts (i.e., DESs + extracted substance) can be used directly without their prior separation.

When the impact of obtaining substances from biological materials on the environment is also taken into account, it is logical that methods with a minimal adverse effect will be preferred. Thus, the extraction methods will preferably be those using green solvents, including DESs. Discussing the properties of substances referred to as value-added ones, we will focus on those exhibiting therapeutic effects and applied in the food sector.

In studies published mainly during the few last years, numerous value-added substances were obtained using various extraction techniques and green solvents. The attention was focused predominantly on phytomass containing a relevant amount of substances, denoted usually as bioactive compounds. Taking the potential of renewable phytomass processing into account, the investigation of extraction was directed to isolation of such substances in the highest possible yield. The value-added substances isolated from phytomass, its waste, and food waste can be classified based on their biological properties, structural or chemical class of compounds, actual or potential applicability, etc. Many of the value-added substances can be isolated from different sources using various extraction techniques and green solvents. The mentioned factors essentially make it impossible to unambiguously classify the extracted value-added compounds. The spectrum of the properties of these compounds is really wide (anticoagulative, anti-inflammatory, antioxidant, hepatoprotective, antihypertensive, antitumor, antimicrobial, anticancer, antidiarrheal, antiallergic, antiatherosclerotic, estrogenic, insecticidal, antimutagenic, pharmacokinetic, antiproliferative, neuroprotective, antiangiogenetic, antagonist, and others) and, therefore, their application is possible in different areas [62,118–120].

The most important potential use of these compounds isolated using DESs includes pharmaceutical and biomedical applications, and last but not least, application in the food industry such as additives and functional substances, nutraceuticals used in the food industry and to enhance food quality.

In the following, we will focus on individual types of extracted substances based on published data. Most of them are phenolic compounds, where groups of substances (total polyphenols), their subgroups (flavonoids), or even individual compounds (rutin) have been isolated and determined.

From the following data, it is clear that the extraction experiments were performed at a laboratory scale. The yield parameters of large-capacity extractions may vary due to different operating conditions.

7.1. Total Polyphenols

Polyphenols—organic compounds found in plants—include more than 8000 compounds. Particular attention is devoted mainly to curcumin, resveratrol, catechins, anthocyanins, and flavonoids. Interest in these substances stems from their vital role in health through the regulation of metabolism, weight, chronic disease, and cell proliferation. In vitro and in vivo studies indicate that polyphenols have antioxidant and anti-inflammatory properties that could have preventive and/or therapeutic effects for cardiovascular disease, neurodegenerative disorders, cancer, and obesity [121]. Thus, it is natural that polyphenols are often separated not only by DESs but also by other solvents.

A comparison of the extraction efficiency of green and other solvents, polyphenols, and flavonoids determined the antioxidant activity and reducing power from Olive (*Olea europaea*) leaves, using five different solvents (water, 60% methanol, 60% ethanol, 9% (*w*/*v*) aqueous glycerol, and 50% (*v*/*v*) DES). In accordance with the results by Georgantzi et al. [115], it was found that to efficiently extract flavonoids, conventional solvents (methanol, ethanol, or aqueous glycerol) should be preferred. The antioxidant activity and reducing power was lowest when working with DESs, which was ascribed to a lower amount of extracted flavonoids. The same conclusion can be found also in an older paper published by Lee et al. [122]. Glycerol and sodium acetate in various molar ratios, acting as DESs [109], were used for extraction of *Moringa oleifera Lam.* leaves. The content of extracted polyphenols and flavonoids, antioxidant activity, and reducing power were compared to results obtained using ethanol (80% *v*/*v*). In spite of a higher yield of polyphenols (51.69 mg GAE/g dw (dry weight)) and flavonoids (16.48 mg RtE/g dw) against the conventional solvent (30.05 mg GAE/g dw; 13.76 mg RtE/g dw), antioxidant activity of DESs was lower. This disagreement is explained by the authors as a result of synergism or antagonism among the polyphenolic constituents. This conclusion was supported also by Philippi et al. [123].

UAE-DES extraction of olive cake, onion seed, tomato, and pear by lactic acid:glucose (5:1), 15% water, and 0.1% (*v*/*v*) formic acid was evaluated for different byproducts [69] with the aim to determine the yield of various phenolic compounds (Table 1). As a result of the optimization, lyophilized material and DES were homogenized by a vortex during 15 s and the suspensions were processed by ultrasound (200 W, 20 kHz) for 60 min at 40 °C.

Ruta graveolens L. as a rich source of phytochemicals has been used to extract polyphenolic substances using ChCl and citric acid (2:1). The extracts obtained at 30 °C with 20% water content and at a time of 90 min with DES extract content (13.3 g/mL) reached the highest polyphenol content 38.24 mg GAE/g dry matter and the highest antioxidation activity 72.53%. The extracts had antibacterial properties, especially against Gram-negative bacteria *P. aeriginosa* [112].

Extraction of different types of phenolic substances [80] using six binary DESs was applied to a traditional Chinese medicinal plant of the genus Artemisia (*Artemisia argyi*). In addition, the effect of ternary DESs, which contained ChCl, malic acid, and a third component (urea, ethylene glycol, glycerol, glutaric acid, and malonic acid), was investigated. Ternary DESs containing ChCl, malic acid, and urea (2:1:2) showed higher extraction yields for phenolic acids compared to conventional organic solvents and other DESs. The optimal conditions for achieving the highest yield of phenolic compounds for this system were: extraction time 23.5 min; liquid to substrate ratio 57.5 mL/g dry plant material; water content 54%.

The extraction of polyphenols from *M. oleifera* leaves with a new type of DES, which contained glycerol and nicotinamide, was performed by ultrasonic pretreatment. The result was the optimization of the process in which the highest yield of polyphenols (82.87 mg GAE/g dry biomass) was obtained after 30 min of ultrasonic pretreatment [111]. Ultrasonic pretreatment was also used by Kaltsa et al. [116]

who extracted polyphenols from the flowers of the black elder (*Sambucus nigra*). In this case, the effect of ultrasound was confirmed, which ensured a higher yield of the polyphenols of interest using the DES containing lactic acid and glycine.

DESs containing water based on ChCl with lactic acid, 1,3-propanediol, 1,3-butanediol, 1,4-butanediol, and 1,5-pentanediol, with different molar ratios, were used as extractants for the extraction of polyphenols from spruce bark [120]. The content of polyphenols in the extracts ranged from 177.6 to 596.2 mg of GAE per 100 g of dry bark. In addition to the content of polyphenols, antioxidant activity was also evaluated. Differences in radical scavenging activity (RSA) indicate that each DES preferentially dissolved a different type of extractant with a different reactivity to $DPPH^{\bullet}$. The RSA values of the extracts (i.e., containing the DES system and the extracted substances) ranged from 81.4% to 95%. Lower antioxidant activity (RSA 86.4%) was observed for extracts obtained with ChCl:lactic acid:water (1:2:0.96), and for the system containing ChCl:lactic acid and various diols in a molar ratio of 1:1:1, namely 82.4% for 1,3-propanediol; 84.2% for 1,3-butanediol; 85.4% for 1,4-butanediol; 81.4% for 1,5-pentanediol. ChCl:lactic acid:1,3-butanediol:water extracts (1:5:1:1) exhibited the highest antioxidant activity (RSA 95%), and this extract also had the highest polyphenol content (596.2 mg GAE/100 g dry bark).

Bioactive substances such as trans-cinnamaldehyde and coumarin were extracted using DESs by Sakti et al. [85] and Aryati et al. [84]. Cinnamon bark (*Cinnamomum burmannii*) was used as a source of these substances. Both studies examined the effect of ultrasound extraction in combination with DESs. Sakti et al. [85] applied ChCl and glycerol; Aryati et al. [84] ChCl (six kinds) and betaine (three kinds). It has been shown that higher yields of the extracted substances can be reached under suitable conditions using the DESs than by application of conventional methods such as reflux, Soxhlet, or maceration using an organic solvent (96% ethanol) [84].

7.2. Phlorotannins

Phlorotannins are a class of polyphenol compounds exhibiting a variety of biological activities, and are used as antifungal, antimicrobial, antioxidant, anticoagulant, antiallergic, antihyperlipidemic, algicidal, and enzyme-inhibitory agents [124–126]. Obluchinskaya et al. [98] used DESs to extract phlorotannin from brown algae (*Fucus vesculosus* L., *Ascophyllum nodosum* (L.) *Le Jolis*). The extraction efficiency of polyphenols is evaluated using 10 DESs containing ChCl, betaine, and glucose in different molar ratios. The extraction was performed as maceration at 120 min, 50 °C with a phytomass to extractant ratio of 1:5. When 50–70% aqueous solutions of DESs (ChCl with addition of lactic or malic acid and also malic acid and betaine) were applied, the maximum extraction efficiency of phlorotannin reached 60–72%.

7.3. Flavonoids

Flavonoids are a class of polyphenolic plant and fungus secondary metabolites. Flavonoids are of interest due to their antioxidant properties antioxidative, anti-inflammatory, antimutagenic, and anticarcinogenic properties coupled with their capacity to modulate key cellular enzyme functions [127,128]. Of all flavonoids, anthocyanins, quercetin, kaempferol, rutin, and their derivatives are the most studied in terms of DESs extraction. Quercetin and derivates are plant flavonoid pigments and have a wide range of biological actions including anticarcinogenic, anti-inflammatory, and antiviral activities, as well as attenuating lipid peroxidation, platelet aggregation, and capillary permeability [129,130]. The extraction of flavonoids such as quercetin, kaempferol, naringenin, and isorhamnetin from *Pollen Typhae* by ultrasound-assisted deep eutectic solvents extraction was realized by Meng et al. [105]. DESs showed greater extraction efficiency of flavonoids comparing with conventional solvents such as water, ethanol, methanol, and 75% of aqueous ethanol. The highest extraction efficiency was achieved by application of ChCl and 1,2-propanediol (1:4) with water (30%).

This conclusion was supported also by Cui et al. [104]. The extraction of quercetin, quercetin-3-O-glucoside, isorhamnetin, kaempferol, and rutin from sea buckthorn leaves using the selected 12 DESs was more efficient

than that performed by 70% ethanol. Target flavonoids reached the yield of 20.82 mg/g for optimized conditions [104].

The genus Epimedium is rich in terms of flavonoids, of which icariin, epimedin A, epimedin B, and epimedin C are known especially to be biologically active, such as antitumor, an immunoenhancing effect, and improvement in the function of the cardiovascular, nervous, and immune systems [131,132].

ChCl in combination with 1,2-propanediol, 1,4-butanediol, glycerol, or lactic acid in various molar ratios has been used to extract substances such as epimedin A, B, C, and icariin from the Chinese medicinal herb *Epidemium pubescens Maxim*. The highest extraction efficiency of prenylated flavonol glycosides was achieved using the DES composed of ChCl and lactic acid (1:2) [87]. Kulturbas and coworkers [110] used microwave extraction of Sudanese hibiscus (*Hibiscus sabdariffa*) by the DESs containing citric acid and glycerol or ethylene glycol. Parameters such as yield of polyphenols, anthocyanates, and antioxidant activity were monitored. A system containing citric acid and ethylene glycol (35 mL DES, including 50% water, microwave power 550 W) was evaluated as the most suitable and efficient. Guo et al. [88] applied ultrasonic extraction in combination with DES and evaluated the extraction efficiency of substances such as: epimedin A, epimedin B, epimedin C, icariin, and icariside II. A screening evaluation of 12 types of DES for the extraction of the mentioned substances from a plant known as Chinese viagra (*Herba Eminedii*) was performed. Based on the screening evaluation, the DES containing L-proline and ethylene glycol in a molar ratio (1:4) was selected and used in the planned experiment. Optimal conditions for extraction of flavonoids are: 0.2 g of substrate in powder form and ultrasonic extraction for 45 min using 4.00 mL of a 70% aqueous solution of the mentioned DES. Comparing the extraction of icariin with the traditional method described in the *Chinese Pharmacopoeia* (2015 edition), solvent consumption was reduced by 80% and extraction time was shortened by 25%.

7.4. Catechins

Catechins (flavan-3-ols) belong to the group of polyphenols, and with other catechin flavonoids have antioxidant and anti-inflammatory properties, and affect the molecular mechanisms involved in angiogenesis, extracellular matrix degradation, the regulation of cell death, and multidrug resistance in cancers and related disorders [133].

Jeong et al. [78] tested the impact of 42 DESs on the ultrasonic-assisted extraction of catechin from green tea (Table 1) and compared extraction efficiency with that obtained using water, methanol, ethanol, 70% methanol, and 70% ethanol. The authors found that all the DESs are more suitable to extract epigallocatechin-3-gallate than water or ethanol. Moreover, they verified possibilities to apply ternary systems composed of betaine:glycerol:glucose in various molar ratios. The performed screening evaluation and comparison with water, methanol, ethanol, 70% methanol, or ethanol led to the conclusion that the ternary systems exhibited a higher extraction power. When applying the optimized system with the following variables: ultrasonic irradiation time 6.4–73.6 min, content of DES in the extraction solvent 24.7–100% *w*/*w*, volume of the extraction solvent per 100 mg of green tea powder 0.6–0.8 mL, and the mentioned ternary 4:20:1 system, the maximum yield of epigallocatechin-3-gallate was 102.3 mg/g, and that of total catechins 217.7 mg/g (optimal conditions: 81% DES, room temperature, 6.5 min) was reached. UAE with DES was identified as being the best system for catechins compounds extraction, followed by stirring (50% ethanol, room temperature, 150 min—165.9 mg/g); heating (water, 80 °C, 30 min—101.5 mg/g); UAE (water, 60 °C, 40 min—100.7 mg/g) and heating + stirring (water, 80 °C, 40 min—93.3 mg/g). It can be concluded that Jeong et al. [78] documented a possibility of the use of green solvents to extract catechin substances, while combination with UAE allows the reaching of high extraction yield in a relatively short time without the necessity to heat the solvent. Fu et al. [76] compared the effect of methanol and eight different types of DESs (Table 1) following the extraction of polyphenols from palm bark. They also documented, in accordance with Jeong et al. [78], that extraction using the selected DESs was more efficient than that performed by methanol.

Fu et al. [76] pre-treated palm bark samples by ChCl with ethyleneglycol, glycerol, xylitol, phenol, formic acid, citric acid, oxalic acid, and malonic acid. DES-modified adsorbent and DES-effluent was used for solid-phase extraction. The extractability of bioactive compounds such as protocatechuic acid, catechins, epicatechin, and caffeic acid were monitored. Results showed that the eco-friendly extraction has high potential degree to be introduced to the area of new analytical and extraction methods. Georgantzi et al. [115] found that when using DESs as extractants, higher yields of extracted polyphenols were reached than those using water in all cases (Table 1). An analogous result was obtained when applying 60% ethanol. Comparing extraction yield reached by DESs enriched by 1.5% *w/v* cyclodextrin showed that in majority cases the extractant containing cyclodextrin was more effective than water or a water-ethanol mixture. On the other hand, to extract flavonoids from various plants, the results obtained using water or water-ethanol mixture as extractants led to a higher yield than those obtained by pure or cyclodextrin-enriched DESs. The authors investigated also influence of agents to antiradical activity and reducing power of the extracts and found that the results depended on the kind of extracted matrices.

The flavonoid constituents such as amentoflavone, quercitrin, myricitrin, and hinokiflavone have diverse pharmacological properties [134,135]. The paper of Zhuang et al. [67] is devoted to the extraction of myricitrin, quercitrin, amentoflavone, and hinokiflavone from *Platycladi Cacumen*. They found that by applying 12 tested DESs, the yield of myricitrin and quercitrin was higher than that reached using water or methanol as extractants. For the other compounds, the yield was similar. In addition, it was observed that the extraction efficiency is strongly influenced by the viscosity of the used DESs. Saccharides-based DESs showed lower extraction efficiency than that obtained by acid-, amide-, and/or alcohol-based DESs.

7.5. Curcumin

Curcumin is a key active yellow polyphenolic constituent of Curcuma longa; it has various pharmacologic effects including anti-inflammatory, antioxidant, antiproliferative, and antiangiogenic activities [54,136,137]. In traditional medicine (Ayurvedic therapy), it is used to treat stomach disorders, blood cleaning, and skin diseases, as well as disorders of bile production, anorexia, rhinitis, liver functions, and rheumatism or cough [137].

Aydin et al. [86] reported a powerful microextraction method (vortex-assisted DESs emulsification liquid–liquid microextraction) for target compounds curcumin in turmeric drug (food supplement), turmeric powder, and herbal tea. It was shown that this method has the most positive impact at the following conditions: pH (optimal 4), molar ratio (the best results for choline chloride:phenol (1:4)), ratio of DES to tetrahydrofuran (1:1), vortex time (2 min), centrifugation time (5 min at 4500 rpm), and preconcentration factor 12.5. The negative effect of ions in the matrix on efficiency of extraction was confirmed.

7.6. Caffeoylquinic Acids

Caffeoylquinic acids and their derivatives are biologically active dietary polyphenols, playing therapeutic roles such as antioxidant activity, antibacterial, hepatoprotective, cardioprotective, anti-inflammatory, antipyretic, neuroprotective, antiobesity, antiviral, antimicrobial, antihypertension, free radicals scavenger, and a central nervous system stimulator [138,139].

A DES (choline chloride:1,3 butanediol), coupled with the aqueous two-phase system for the negative pressure cavitation extraction, was investigated as a new system for blueberry leaves extraction. Response surface methodology was used to find the best extraction conditions. The target compound (chlorogenic acid) reached the yield of 46.88 mg/g for optimized conditions [82]. In addition, the effects of other techniques such as heat reflux extraction (HRE, 60 °C, 3 h), NPCE (59 °C, 24 min), UAE (60 °C, 60 min, 250 W), and microwave-assisted extraction (MAE, 60 °C, 20 min, 700 W) were compared. The most suitable of the techniques from the viewpoint of chlorogenic acid extraction was NPCE, followed by MAE, HRE, and UAE.

7.7. Isoflavones

Isoflavones such as genistein, daidzein, and biochanin A are widely consumed phytoestrogens. Bajkacz and Adamek [75] investigated the impact of 17 different DESs on the extraction of substances such as genistein, daidzein, genistin, biochanin A, and daidzin from soy products. Stemming from the screening evaluation, choline chloride:citric acid (1:1) was identified as the best of the tested DESs. The influence of different solid to solvent ratios (S/L) and water content was followed, and central composite design on the determination of optimum conditions of extraction was used. The work is unique also due to the fact that the authors compared the extraction efficiency for 10 extraction techniques using several conventional solvents such as methanol, ethanol, different ethanol/methanol mixtures, dimethyl sulphoxide:acetonitrile:water, acetone:hydrochloric acid (5:1 *v*/*v*). Soxhlet extraction and UAE and MAE methods coupled with HPLC-DAD provided lower yields with higher relative standard deviations in comparison with the DES-UHPLC-UV.

7.8. Rutin

Rutin is the glycoside combining the flavonol quercetin and the disaccharide rutinose. It is a citrus flavonoid found in a wide variety of plants including citrus fruit. It has been explored for a number of pharmacological and nutraceutical effects [140].

Huang et al. [108] investigated the possibilities to apply UAE extraction using 13 DESs (Table 1), and compared the yield of rutin from tartary buckwheat hulls with conventional solvent (80% wt methanol). The ChCl-based DESs with sucrose, sorbitol, and glycerol:glycine, L-histidine:glycerol achieved a lower extraction efficiency than the mentioned conventional solvent. In addition, the authors performed tests on DESs biodegradation and found that all the DESs underwent biodegradability higher than 70% until 28 days.

ChCl with urea, sorbitol, 1,4-butanediol, lactic acid or levulinic acid was used to extract rutin and rosmarinic acid from *Satureja montana* [107]. The amount of rutin obtained was 1.40 to 17.29 mg/g per plant and 0.21 to 7.84 mg of rosmarinic acid/g per plant. Of the solvents, ChCl and lactic acid (1:2) and ChCl:levulinic acid (1:2) were the most suitable for rutin extraction. For rosemary acid, a urea-containing DES proved to be the most suitable. The analysis of the main components showed that increasing the extraction temperature and decreasing the amount of water can increase the extraction of secondary metabolites of the monitored substances.

As documented by screening tests, the extraction of caffeoylmalic acid, psoralic acid-glucoside, rutin, psoralen, and bergapten from *Ficus carica* L. (leaves) was more effective using methanol than eight DESs (Table 1). However, when applying ternary DESs mixtures of glycerol:xylitol:D-(−)-fructose with varying content of individual saccharide components, extraction efficiency exceeded that reached using methanol. It was also documented that, along with extractants, extraction techniques play a significant role in extraction efficiency. Comparing the results obtained by DES-UAE, DES-MAE, methanol-UAE, and methanol-MAE techniques, DES-MAE was identified as the most suitable. The differences in extraction yield were ascribed to differing penetration of the extractant to the matrix [74]. Under optimal conditions (glycerol:xylitol:D-(−)-fructose; extraction temperature 64.46 °C, S/L 1:17.53, and ultrasonic time 24.43 min) the extraction yield of caffeoylmalic acid, psoralic acid-glucoside, rutin, psoralen, and bergapten was 6.482, 16.34, 5.207, 15.22, and 2.475 mg/g, respectively. It is worth mentioning the number of significant figures of the values of the given quantities is the result of optimization by the response surface methodology, not of an experiment.

7.9. Hesperidin

The antioxidant hesperidin, a major flavonoid in orange and lemon, has many pharmacological effects, such as antioxidation, anticancer, antiviral, antibacterial, and anti-inflammatory. The neuroprotective potential of this flavonoid is mediated by the improvement of neural growth factors and endogenous antioxidant defense functions, diminishing neuro-inflammatory and apoptotic pathways [141,142].

Jokic et al. [92] screened the effect of 15 ChCl-based DESs and monitored extraction efficiency from shards of different mandarin varieties (*Okitsu*, *Chahara*, *Kuno*, and *Zorica rana*). The yield of hesperidin ranged from 1.4 to 112 mg/g material. In addition to the screening evaluation, the work focused on determining the optimal conditions for the extraction of hesperidin for these varieties using ChCl and acetamide (1:2). For the *Okitsu* variety, the optimal conditions for hesperidin extraction were 90 min, temperature 68.14 °C, and water content 13.83%; for the variety *Chahara*, it was 45.40 min, 69.70 °C, and a water content of 10.67%, while for the varieties *Kuno* and *Zorica rana*, it was: 88.79 and 54.72 min, 55.02 and 69.66 °C, and 19.73 and 14.86% water, respectively, for extraction of hesperidin with ChCl and acetamide in a molar ratio of 1:2.

7.10. Terpenes

Terpenes are classified according to the number of isoprene units into monoterpenes, sesquiterpenes, diterpenes, and triterpenes. A broad range of the biological activities of plant terpene metabolites are described, including cancer chemopreventive effects, antimicrobial, antifungal, antiviral, antihyperglycemic, anti-inflammatory, and antiparasitic activities [143,144].

7.11. Ginkgolides

Ginkgolides are biologically active terpenic lactones. Su et al. [90] compared the extraction efficiency of 16 DESs (Table 1) and conventional solvents (water, ethanol) for extraction of *Gingko Biloba* leaves (UAE, 70% (*w*/*w*) aqueous solution at 100 W and 25 °C for 10 min with a solid to solvent ratio of 1:15). Using a colorimetric method (determination of ginkgolide A), they determined the extraction yield and found that in the case of ChCl:urea and betaine:ethylene glycol, the extraction yield (1.06 mg/g) and (1.15 mg/g), respectively, exceeded that reached using ethanol (1.04 mg/g). Moreover, they followed the influence of water content in the two DESs, and the best extraction was achieved using 40% water content for both DESs. Their paper brings also results from the viewpoint of comparison with other extraction techniques: boiling reflux (60 min, methanol, yield 1.51 mg/g; ethanol, 1.72 mg/g; methanol:water (7:3 *v*/*v*), 2.02 mg/g; ethanol:water (7:3 *v*/*v*), 2.15 mg/g); betaine:ethyleneglycol + water (6:4, *w*/*w*, UAE, 45 °C, 100 W, 20 min, 2.36 mg/g); magnetic stirring (45 °C, 20 min, 2.25 mg/g); and ethanol:water (7:3 *v*/*v*, UAE, 45 °C, 100 W, 20 min, 1.84 mg/g). Based on the results obtained, it was concluded that betaine:ethylene glycol represented the most suitable extraction system both in association with UAE and with magnetic stirring. It should be pointed out that the extraction yields are very similar; however, when working at a large scale, the economic benefits may not be negligible.

7.12. Glycyrrhetinic Acid

Glycyrrhetinic acid is a triterpenoid derivative and has different pharmacological properties with possible antiviral, antifungal, antiprotozoal, and antibacterial activities [145]. Sorbitol-based DESs have been used to extract biologically active substances (glycyrrhetinic acid, licuroside) from liquorice root (*Glycyrrhizae*) [91]. Simple maceration was used in this study, and substances such as malic acid, water, and glycerin were used as additional components of DESs.

7.13. Artemisinin

Artemisinin is a sesquiterpene lactone and its derivatives are essential components of antimalarial treatment [146]. Artemisinin is effective also in treating other parasitic diseases, some viral infections, and various neoplasms [147].

Cao et al. [70] realized a screening test of the influence of various methyl trioctyl ammonium chloride-based 13 DESs on the extraction of *Artemisia annua* leaves. The extraction yield ranged from 1 to 1.62 mg/g. Moreover, the impact of molar ratio of 3 two-component (in total, 48 extractants differing in composition) and 15 ternary DESs (in total, 60 extractants) on extraction efficiency was followed (Table 1). The yield ranged from 1.1 to 2.2 mg/g. In particular, the yield of extractive compounds for three different DESs was determined by applying various extraction techniques, namely extraction at

30 or 60 °C by air-bath shaking at 250 rpm, water-bath shaking at 150 rpm, magnetic stirring at 150 rpm, ultrasonication at 200 W, and heating at 60 °C and 0 rpm. The highest yield was reached using UAE at 30 or 60 °C for all tested DESs. Of course, the higher temperature supports penetration of extractant due to lowering its viscosity and, slightly also, its density into the matrices. Subsequently, through an RSM optimization procedure, the influence of such parameters as solid to solvent ratio, ultrasonic power, temperature, particle size, and time of extraction for DES (methyl trioctyl ammonium chloride:1-butanol (1:4)) was evaluated. At optimum conditions (S/L 1:15.5; ultrasonic power 180 W; particle size 80 mesh; temperature 45 °C; time 70 min), the yield reached 7.99 mg/g. It was, thus, confirmed that the UAE method with a selected DES is more efficient than extraction by petroleum ether.

7.14. Polyprenol Acetates

Polyprenol acetates are important lipids with many bioactive and pharmacological activities [148]. Leaves of Gingko biloba were extracted by DESs by Cao et al. [99]. Hydrophobic DESs (15 different DESs) were rated based on polyprenyl acetates extraction. Three of the most effective DESs: methyl trioctyl ammonium chloride:hexyl alcohol; methyl trioctyl ammonium chloride:capryl alcohol; methyl trioctyl ammonium chloride:decyl alcohol were subjected to a more detailed investigation, varying the molar ratio from 1:1 to 1:8. For all selected DESs, the best results were obtained at the 1:5 ratio. Along with the mentioned two-component DESs, ternary systems methyl trioctyl ammonium chloride/capryl alcohol with different second hydrogen bonding donors at different molar ratios (Table 1) were studied. The best DES of them (methyl trioctyl ammonium chloride:capryl alcohol:octyl acid (1:2:3)) was subsequently evaluated from the viewpoint of extraction yield with different extraction methods (25, 60 °C). The gradual decrease in extraction yield for both temperatures was as follows: stirring, UAE, air-bath shaking; water-bath shaking, and heating. Applying RSM, analysis of optimum conditions for the mentioned best DES (84.11 mg/g) was performed and compared to those for other extractants (ethyl acetate (84.17 mg/g); n-hexane (75.48 mg/g), petroleum ether (71.39 mg/g)).

7.15. Proteins

Proteins—large biomolecules consisting of one or more long chains of amino acid residues—play many critical roles in all living organisms. They are an irreplaceable part of food. Their use in medical therapy requires their isolation in pure form [149]. Wahlström et al. [101] extracted Brewer´s spent grain using four eutectic mixtures (sodium formate: urea; potassium acetate: urea; sodium acetate:urea in molar ratios 1:2 or 1:3, and ChCl: urea (1:2)). As a product, proteins composed of amino acids, predominantly serine, arginine, aspartic acid, threonine, alanine, valine, and leucine were isolated. The authors pointed out an advantage of applying a breakthrough technology suitable for the extraction of proteins from various kinds of protein-rich biomass.

8. Factors Limiting the Potential of Deep Eutectic Solvents Utilization and How to Overcome Them

The data in Table 1 and in the previous section documented the pros in the use of DESs for the extraction of value-added substances from phytomass. However, it should be admitted that DESs are not perfect and their use has its limitations. This section deals with the cons of applying DES for extraction purposes and valorization of phytomass.

The use of DESs in the field of biomass pretreatment or extraction of value-added substances has significantly expanded in the 21st century [11]. However, the process of applying faces several limitations from an experimental and commercial point of view.

8.1. Purity

It is natural that the process of developing new types of solvents and their application at a laboratory scale takes place in glass and using analytical grade chemicals. One of the main limits of subsequent commercial application is the possibility of using chemicals with purity lower than

analytical grade. Here, however, problems can arise in terms of the stability of the created system. Even though a DES is formed, crystallization may occur due to long-term storage (sometimes, only a few hours). This effect may be exacerbated by impurities that would be present in the starting chemicals and could initiate crystallization. The reason for using chemicals with lower purity is, of course, that their prices are lower than that of pure chemicals. On the other hand, it should be noted that if the DESs application process is commercialized and expanded, the cost of producing DESs will decrease significantly [40]. In this respect, and given the relatively easy and simple preparation, lower costs would help to expand the use of DES as a new way of exploiting the potential of biomass or biowaste. However, it should be noted that the cost of some conventional organic solvents may be lower.

8.2. Viscosity

A significant limiting factor associated with the application of DESs is viscosity. Due to the formation and interaction of hydrogen bonds in the DES structure, the viscosity of DESs is relatively high, being 100–1000 times higher than that of water or conventional organic solvents [150]. On the one hand, viscosity presents the limit for penetration into the substrate, and on the other hand, from the point of view of commercial application, there is a problem in terms of the technological steps associated with the preparation of DESs themselves. This is mainly related to handling, mixing, filling, or transportation. Naturally, there are strategies that can partially eliminate this shortcoming, but the price associated with these measures and the consequent effectiveness of the use of DESs in the required operation with it (the goal of using DESs) play an important role here. The easiest way, although not the cheapest, is to increase the temperature and thus, achieve a decrease in viscosity. Another possibility of a simple solution is to add another reagent to the system, either water or another solvent, that will ensure a decrease in viscosity (e.g., alcohols, [113]). However, whether it is water or another type of solvent, it is necessary to realize that from this point of view, there is a change in the whole system, because the addition of another component also changes the behavior of DES. The addition of water into DESs in the process of their formation causes the incorporation of water molecules into the structure of DESs and their fixation by hydrogen bonds; this water can hardly be later fully removed by, e.g., a rotary evaporator. A small addition of water may result in a decrease in viscosity, temperature lowering, and shorter time needed for DES preparation. Water as another component plays an important role for the formation of hydrogen bond donors and acceptors in the DES structure [151,152]. If DES systems contain water or other organic substances as solvents, it is necessary to take water (for example, organic solvents are automatically taken into account) into account as another component of the DES. Therefore, binary systems need to be characterized as ternary.

8.3. Hygroscopicity

Another challenge or limiting factor is the hygroscopicity of DES. As already mentioned, the addition of water affects the nature of DES in terms of the structure and bonds they form, and water also affects the polarity and ability of DES to extract or solubilize target groups of substances isolated from phytomass. The hygroscopicity of DES must, therefore, not be neglected in the case of ensuring the technological process and its laboratory or commercial use. A more detailed description effect of water vapor from the surrounding air and of these facts is discussed elsewhere [153].

8.4. Long-Term Stability

In order to ensure better handling, mixing, and transport from DES, we have introduced as one of the options an increase in temperature. Regardless of the economic side of things, however, it should be noted that exposure of DES to higher temperatures for a long time can have adverse consequences [11].

8.5. Acid-Base Properties

Acidity or alkalinity are other important factors influencing the applicability of DES. Some DESs have significantly low pH, which significantly limits the choice of materials for their commercial use. Laboratory experiments are usually performed in glass, where this effect can be neglected. When using materials containing different types of metals and their compounds, these can cause an undesirable color change and affect the effect of DESs. The absorption of metallic components from the operating equipment is one of the key problems of the commercial use of DESs. Eliminating this problem may require the use of more expensive materials to transport, mix and apply the DESs themselves, which clearly increases input costs and may potentially discourage potential operators from commercializing the use of DESs. In addition, impurities can destabilize DESs and cause them to crystallize, thereby altering their stability.

8.6. Toxicity

Among the most common issues of research teams, scientists, but also practice and control bodies is the toxicity and recyclability of DES. As for toxicity: at the beginning of the research and application of DESs in 2003, it was very often said that DESs are non-toxic. Over time and the natural evolution of the composition of DESs, this concept has gradually disappeared and currently, DESs are characterized as having low or acceptable toxicity to various biological systems. The toxicity of DESs depends mainly on the toxicity of the starting components, but some DESs may be more toxic than their starting components [153]. The answer to this question about toxicity is a bit unclear. The shortcomings of DESs are gradually emerging, especially in terms of their impact on organisms and the environment; however, the boundaries of the terminology of the impact of DESs and its toxicity are gradually shifting. In general, the toxicity of a substance to organisms and the environment depends on the dose (concentration) and duration of its action. Related to this are the issues of biocompatibility and biodegradability of DESs before applying them to commercial purposes.

8.7. Adsorbable Organic Halides

A question or possibility of other research activities that still arises from published works or relevant project activities is the ability of chlorine-containing DESs to react with a substrate matrix or extractables, leading to adsorbable organic halides. This issue is extremely important in view of the need to limit the use of these halides and even to reject them on the basis of the 12 principles of environmental chemistry in the field of green technologies. However, it should be emphasized that in assessing the possible negative impacts of chlorine compounds, a distinction must be made between "inorganic, ionic" chlorine in the form of Cl^- anions and chlorine bound to a carbon atom in organic compounds. This distinction is important e.g., in waste incineration.

8.8. Recycling

Given the ongoing research and commercial implementation of DESs processes, recyclability issues also need to be answered. Based on the information from the works that dealt with the careful application of DESs, the following conclusion can be drawn. The most common technique in regenerating DESs is to use an anti-solvent to remove (precipitate) the component from the system in operation, and then, evaporate the anti-solvent from the system, and reuse the DESs. Regeneration and reuse aspects are crucial in assessing sustainability and environmental protection, as well as in reducing the costs of the process [11].

9. Future Trends and Concluding Remarks

The excellent properties of DESs, such as sustainability, biodegradability, pharmaceutical acceptable toxicity, negligible volatility, and high extractability of compounds with diverse polarity, highlight their potential as green extractants. Several comparisons of the isolation value-added

substances from phytomass performed by DESs and organic solvents have clearly demonstrated, along with ecological advantages, also a higher yield of extracted substances using DESs and thus, cost-related benefits. It can be expected that the valorization of phytomass in the future will focus mainly on the extraction of therapeutically important substances, nutrients, and food supplements. The selection and composition of DESs will be optimized so that whole extracts can be used in practice, without prior separation of DESs and extracted value-added substances. It can be assumed that in the field of research of DESs themselves, mixtures with lower viscosity, predetermined polarity, and acid-base properties, capable of specifically extracting targeted value-added substances, will be sought.

Despite the considerable number of phytomass kinds valorized using DESs, there is still a huge amount of primary phytomass itself, waste of its processing, and food-related waste, which have not been studied from the point of view of isolating value-added substances. Expanding resources is a challenge for both laboratory and industrial workers and can bring many surprising and useful results in the future.

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Abbreviations

$[N(Me)(Oc)_3]Cl$	methyl trioctyl ammonium chloride
$[N(Bu)_4]Br$	tetrabutylammonium bromide
$[N(Pr)_4]Br$	tetrapropylammonium bromide
ChCl	choline chloride
DES	deep eutectic solvent
dw	dry weight
EAE	enzyme-assisted extraction
GAE	gallic acid equivalents
HBA	hydrogen bond acceptor
HBD	hydrogen bond donor
HDE	hydrodiffusion extraction
HPLC-ESI-TOF-MS	high performance liquid chromatography coupled to electrospray ionization time-of-flight mass spectrometry
HPLC-PDA-ESI-IT/MS	high-performance liquid chromatography coupled to photo diode array detector and electrospray ion-trap mass spectrometry
HPLC-ESI-QTOF-MS	high-performance liquid chromatography coupled to electrospray ionization quadrupole time-of-flight high-resolution mass spectrometry
HPLC-ELSD	high performance liquid chromatography-evaporative light scattering detector method
LC-DAD-MS	high performance liquid chromatographic method coupled with diode-array detection and mass spectrometry

LTTMs	low-transition temperature mixtures
LMMs	low-melting mixtures
MAE	microwave-assisted extraction
NADES	natural deep eutectic solvent
NPC	negative pressure cavitation
PLE	pressurized liquid extraction
RSM	response surface methodology
RtE	rutin equivalents
S/L	solid to solvent ratio
SFE	supercritical fluid extraction
VA-DES-DLLME	vortex assisted deep eutectic solvent dispersive liquid-liquid microextraction
UAE	ultrasound-assisted extraction
UPHLC-Q-TOF-MS	ultra-high performance liquid chromatography-quadrupole time-of-flight mass spectrometry

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