sustainability

MDPI

Review

Use of Natural Deep Eutectic Solvents (NADES) in Food Science and Food Processing

Rana Alsaidi and Thies Thiemann *

Department of Chemistry, College of Science, United Arab Emirates University, Al Ain P.O. Box 15551, United Arab Emirates; 201770305@uaeu.ac.ae
* Correspondence: thies@uaeu.ac.ae

Abstract: Natural deep eutectic solvents (NADESs) are a new class of solvent systems with applications in the food industry. Due to their reduced toxicity and their enhanced biodegradability over traditional fossil-fuel based solvents, NADESs are seen as environmentally friendly, "green" solvents. The review covers their use in the extraction of nutritionally valuable molecules, including biopolymers from plants and from agricultural and food wastes. NADESs are used in the preservation of fruits and vegetables, in active packaging or direct produce coating. They also play a role in flavor and food enhancement applications and can be used in food analysis. Current limitations as to recovery methods of the target compounds from the extracts, the scale-up of operations, costs and regulations are discussed in the review. Some of the start-up companies are introduced that develop DES/NADES solvents for the market, thereby accelerating the shift from petroleum-based solvents to green solvents.

Keywords: natural deep eutectic solvents; extraction; biomass; food wastes; food preservation; food packaging

check for updates

Academic Editor: Raffaele Cucciniello

Received: 7 December 2024
Revised: 4 March 2025
Accepted: 4 March 2025
Published: 6 March 2025

Citation: Alsaidi, R.; Thiemann, T. Use of Natural Deep Eutectic Solvents (NADES) in Food Science and Food Processing. *Sustainability* **2025**, *17*, 2293. https://doi.org/10.3390/su17052293

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Recently, there has been a research focus on utilizing deep eutectic solvent systems (DES) and specifically natural deep eutectic solvents (NADESs) in food chemistry and food processing. As the components of NADESs are deemed natural and as frequently NADESs exhibit a higher biodegradability and lower toxicity than conventional solvents, they are often seen as green, sustainable alternatives to conventional solvents. They are employed to extract from biomass valuable natural products that can be used as food additives. Because NADESs can help stabilize biomolecules, they have been found to be useful in food preservation. Also, NADESs can be constituents of sustainable food packaging.

Deep eutectic solvents (DESs) are solutions of Lewis and Brønsted acids with bases, forming eutectic mixtures LADES (Lewis acidic deep eutectic solvents) and BADES (Brønsted acidic deep eutectic solvents), respectively. While their individual components can be solids or liquids, the eutectic mixtures are often liquid at room temperature. Many of these eutectic mixtures rely on hydrogen bonding, where one component is the hydrogen bond donor (HBD) and the other is the hydrogen bond acceptor (HBA). Oftentimes, the hydrogen bonds are directed towards a halide as the actual hydrogen bond acceptor. Therefore, many of the organo-ammonium chloride salts as well as the anhydrous metal halides used in DESs act as HBA (see compounds **1**–**11**, Figure 1). This can lead to cases where a molecule under certain conditions acts as a hydrogen bond donor (HBD), while the hydrochloride salt of the molecule will act as HBA. Proline and its hydrochloride salt **11** is such an example

(Figure 1). Figure 1 shows molecules that can be HBA or HBD, depending on the interacting partner. Typical examples are decanoic acid (**12**) and menthol (**10**).

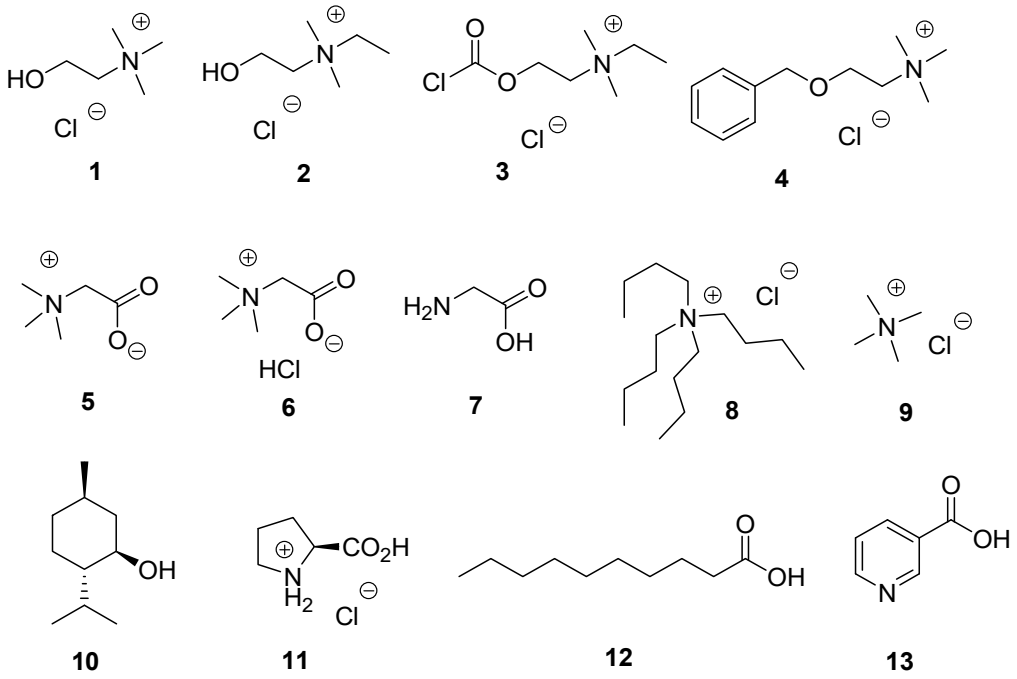


Figure 1. Natural product-derived hydrogen bond acceptor (HBA) used in NADESs [Choline chloride (**1**), (2-hydroxyethyl) ethyldimethylammonium chloride (**2**), choline chloride chloroformate (**3**), *O*-benzyl choline chloride (**4**), betaine (**5**), betaine hydrochloride (**6**), glycine (**7**), tetrabutylammonium chloride (**8**), tetramethylammonium chloride (**9**), menthol (**10**), proline hydrochloride (**11**), decanoic acid (**12**), nicotinic acid (**13**)].

DESs exhibit low volatility, their viscosity can be tailored, and they possess water miscibility. Some are biodegradable after use, and some of them are recyclable. Traditionally, DESs have been divided into four sub-categories [1], according to the type of acid and base used (Table 1). Type I DESs are made through a combination of an organic salt and a metal salt of Zn, Sn, Fe, Al, Ga, and In. This category encompasses the classical ionic liquids. A typical example of type 1 DESs is the combination of 1-ethyl-3-methylimidazolium chloride and anhydrous $AlCl_3$ [2]. In type 2, DESs metal halide hydrates are used as hydrogen bond donors. Here, recently a DES prepared from choline chloride (ChCl) and $CuCl_2{\cdot}2H_2O$ was forwarded as a conditioner for waste-activated sludge [3]. In DESs of type IV, metal halides, many of them transition metal halides, are utilized as hydrogen bond acceptors [4,5]. An example is a system created with a mixture of zinc nitrate [$Zn(NO_3)_2$] and urea for the preparation of ZnO nanoparticles [6]. Type III DESs form arguably the most diverse DESs sub-category [1]. These are metal-free deep eutectic solvents. Their use is manifold and includes electrodeposition and metal extraction in the metal processing industry. More recently, a new class was defined from the observation of the strong interaction stemming from the acidity difference of phenolic and aliphatic hydroxyl moieties [7]. Here, the interactions between HBAs and HBDs are of a non-ionic nature, and the deep eutectic solvent consists of a non-ionized molecular assembly [8]. The type III subcategory of deep eutectic solvents includes the natural deep eutectic solvents (NADESs) [9]. NADESs are mixtures of two or more compounds that are plant-based primary metabolites or their close derivatives [10,11]. Figures 1 and 2 show typical examples of HBDs and HBAs used in NADESs. As we will see later, oftentimes water is added to the deep eutectic solvents when these are used as extracting agents. Addition of 10–30 vol% water to a DES (NADES) reduces the viscosity of the solution, improving mass transfer and extraction efficiency [12].

Adding too much water to the DES solution, however, is detrimental to the extraction efficiency, most likely because of partial destruction of the microstructure of the DES, which may weaken the interactions between the DES and the solutes [13,14].

Table 1. Categories of deep eutectic solvents (DESs).

Type I	Organic salt (mostly organic ammonium salt)/metal salt (mostly metal halide)
Type II	Organic salt (mostly organic ammonium salt)/metal salt hydrate (mostly metal halide hydrate)
Type III	Organic salt (mostly organic ammonium salt)/hydrogen bond donor
Type IV	Metal salt hydrate (mostly metal halide hydrate)/hydrogen bond donor
Type V (recently added)	Alkanols/phenols

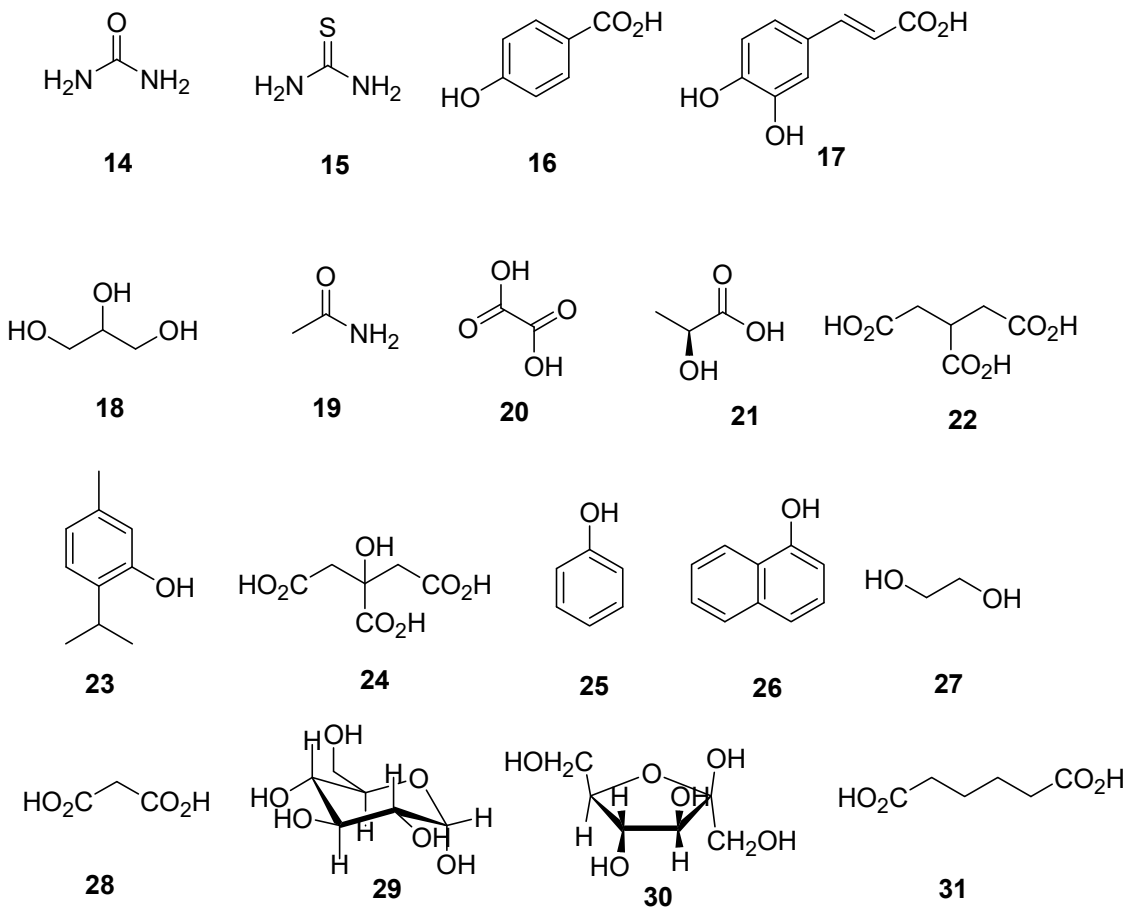


Figure 2. Natural product-derived hydrogen bond donor (HBD) used in NADES [Urea (**14**), thiourea (**15**), 4-hydroxybenzoic acid (**16**), caffeic acid (**17**), glycerin (glycerol, **18**), acetamide (**19**), oxalic acid (**20**), lactic acid (**21**), propane-1,2,3-tricarboxylic acid (**22**), thymol (**23**), citric acid (**24**), phenol (**25**), α-naphthol (**26**), ethylene glycol (**27**), malonic acid (**28**), β-D glucose (**29**), fructose (**30**), adipic acid (**31**)].

A focus of many published studies on DES, specifically on NADESs, is on the ability of the deep eutectic solvents to solubilize and extract biomolecules of value from plant material [15] such as flavonoids [16–18], including flavonoid glycosides [18,19], anthocyanins [20–22], pectins [23–25], polyphenols [26–28] and proteins [29].

Food wastes and wastes stemming from the fruit and vegetable processing industry are a significant resource of biomolecules such as phenolic compounds that cover our alimentary needs. Both the direct extraction of nutraceuticals and other valuable biomolecules from food wastes [30] as well as the bioconversion of biomass from food waste [31], e.g., by fermentation, are known. Pomace, a solid waste obtained by pressing fruits, vegetables

and their containing peel, remnant pulp, seeds and stones is considered a source of dietary fiber (ca. 50% of dry weight) and phenolics (1200–4000 mg/kg dry weight), including flavanols (catechin **32**, epicatechin **33**, procyanidins **34**), flavonols **35**, hydroxycinnamates **17**, and dihydrochalcones such as **36** [32,33], shown in Figure 3. To have an indication of the amount of biowastes available, for every 1000 kg of processed olives, around 800 kg of olive pomace are produced [34,35]. For the moment, non-DES extraction techniques dominate the field [32], such as supercritical fluid extraction utilizing supercritical CO_2 with and without co-solvents such ethanol [36] and conventional solid-liquid extraction with aqueous alcohol, mostly ethanol [37]. Morgana et al. [35], and others started looking at the effect of different NADESs, especially of food-grade NADESs, on the extraction of valuable biomolecules from important agricultural wastes such as olive and grape pomace. Often, phenols such as flavonoids, anthocyanins (e.g., **37**), and phenolic acids (e.g., **16**) show excellent recovery rates from these pomaces in NADES extractions. These processes were complemented by the use of NADES to extract sugars from dates and to obtain protein extracts from plant wastes. As NADESs composed of food-grade ingredients do not have to be removed before use, food-grade NADESs can be seen as a possible constituent of novel food bio-additives [35], delivering with them a wide range of valuable nutraceuticals. Sometimes, NADESs have been found to enhance the bioavailability of the extracted biomolecules. It has been stressed by a number of authors [38–40] that polyphenolic extracts prepared in NADES can be considered ready-to-use in the food and pharmaceutical industries, without the need for demanding and expensive downstream purification steps. Radošević et al. [41] have evaluated the toxicity of choline chloride based DES/NADES. It must be noted that choline chloride exhibits a very low acute oral toxicity with an LD_{50} in rats of 3.15–5.00 g/kg and is used as an additive in chicken feed. Choline itself is an essential nutrient for mammals, including humans as it is required to produce the neurotransmitter acetylcholine (**38**) and *S*-adenosylmethionine (**39**) (Figure 4). Nevertheless, the toxicity of many other DES and NADES constituents and especially the interaction of DES/NADES with cellular membranes will still need to be investigated in greater detail [42].

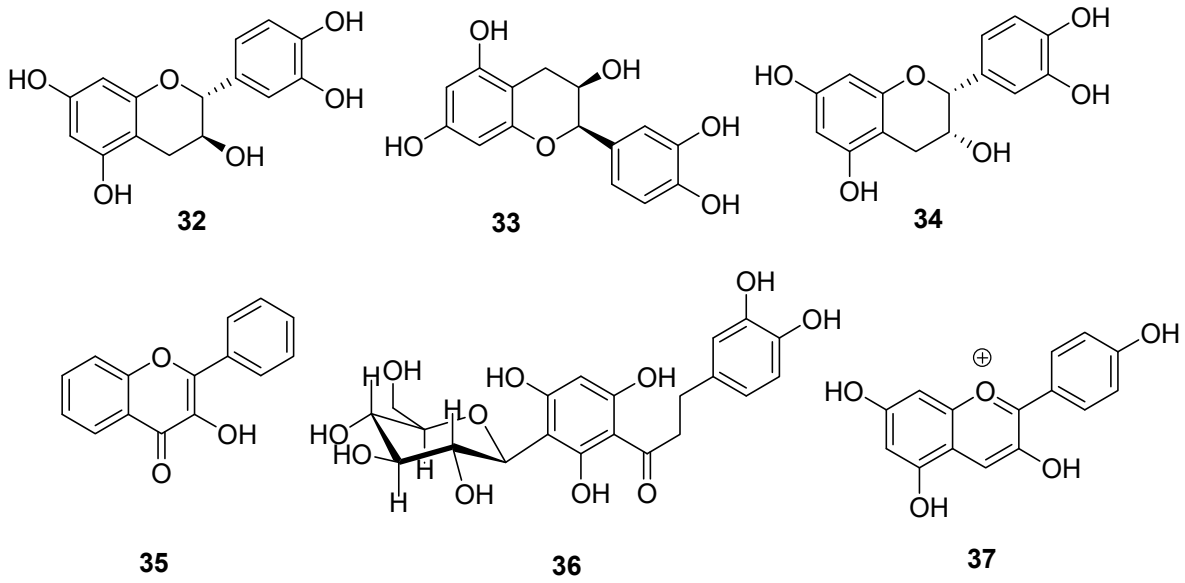


Figure 3. Typical compounds of interest in the extraction of biomass with DES/NADES [catechin **32**, epicatechin **33**, procyanidin **34**, favonol **35**, dihydrochalcone [aspalathin, **36**], and anthocyanin [pelargonidin, **37**]].

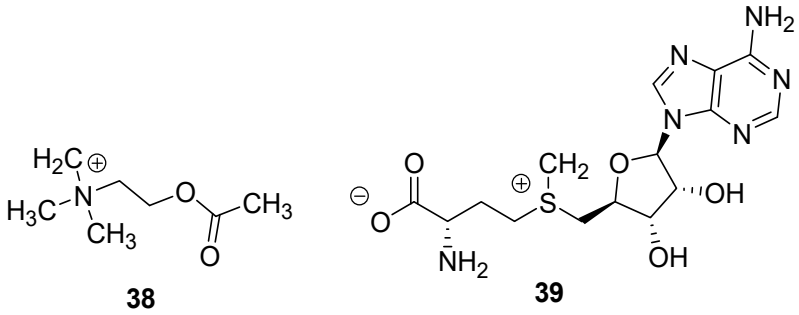


Figure 4. Structures of acetylcholine (**38**), and *S*-adenosylmethionine (**39**).

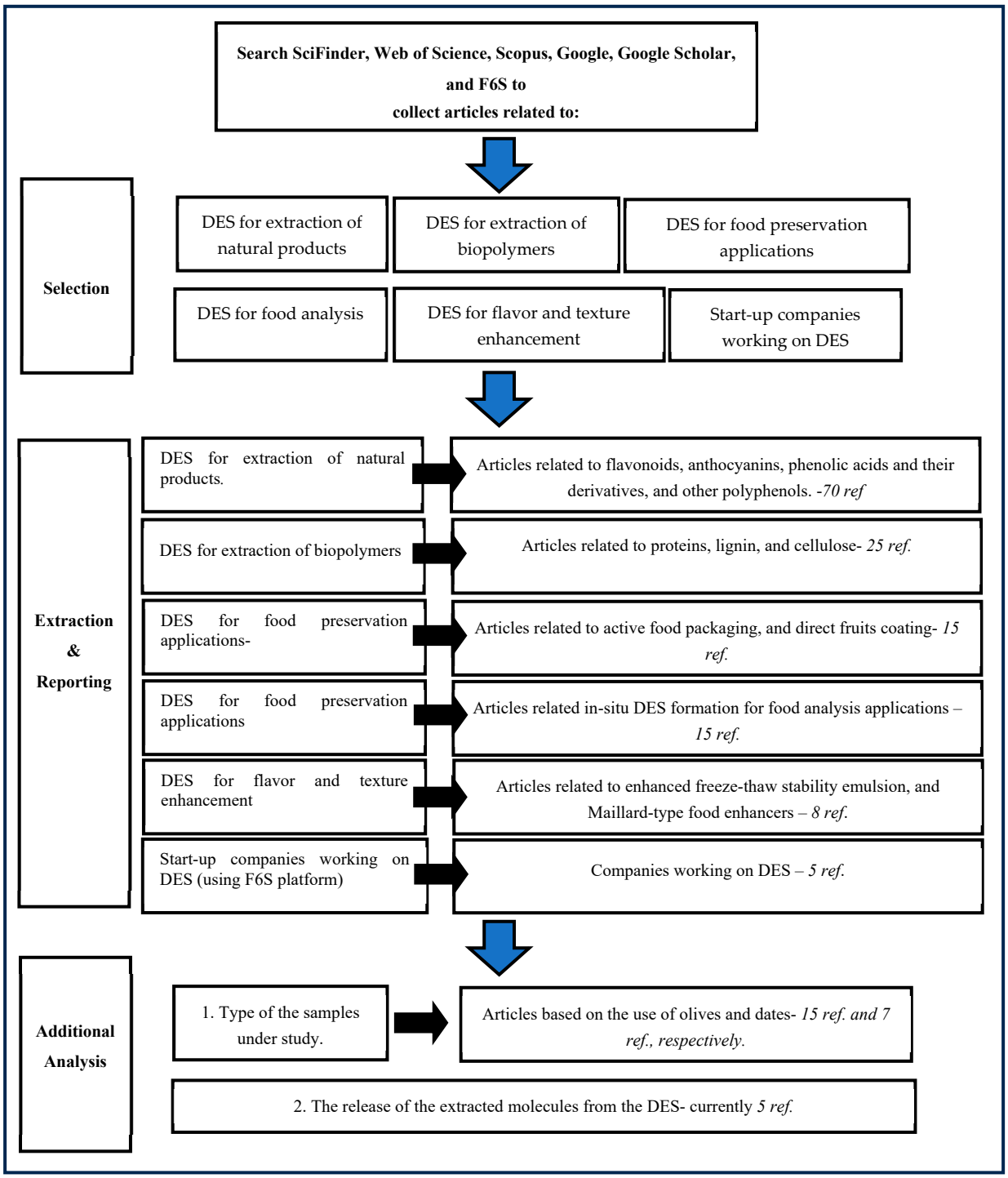
In this review, we will discuss several applications of DESs in the area of food science and food processing. Though DESs and especially NADESs can be used to extract important biomolecules and biopolymers from food sources such as fruits, vegetables, and their waste products, there are yet few methods to separate the extracted biomolecules from DES cost-efficiently on a large scale that would lead to for instance a facile isolation of large amounts of pure flavonoids or anthocyanins. Therefore, if the addition of nutritional compounds of value extracted with the help of DES is to be used to enhance food, then the used DES components would need to be included in the food processing. NADESs can be used in food packaging, preservation, and analysis as shown in this review. Also, reports will be discussed which show that NADESs can be used as a reaction medium for the synthesis of flavor-enhancement compounds and for food texture-enhancement applications. Finally, we present some of the start-up companies that started the development of DESs.

Limitations on the commercialization of NADES in the food industry sector are also discussed. Currently, these include an economically viable scale-up of operations, government regulations that include NADESs as acceptable solvent systems in the food industry, easy separation of extracts from NADES systems and a facile recyclability of NADES systems. Furthermore, more detailed toxicological studies on the more commonly utilized NADESs are needed.

2. Methodology

There are a number of prior reviews on the application and use of NADESs in the food industry [15,43–45] as well as on the use of NADESs for the extraction of classes of compounds from biomass (flavonoids: [46]). In the current review, we focus on articles that have practical and promising applications of DESs that can pave the way for a more sustainable and green food industry and food research. We followed a narrative review approach. Scheme 1 shows the methodology the authors followed while writing the manuscript. Several search engines and platforms were used, including SciFinder, Scopus, Web of Science, google scholar, google, and F6S. The search was conducted according to Scheme 1.

The following work was given preference: (1.) publications that introduce new NADES systems that can be utilized in food science and food processing; (2.) publications that report on the exact chemical composition of NADES extracts from biosources; (3.) papers that disseminate information on the use of NADES in food preservation and food packaging. Work that investigated overall antioxidant activity or total phenolic content without analyzing the molecular composition of the extracts was often excluded.



Scheme 1. The methodology of the performed literature research for this review.

3. Extraction of Biomolecules of Alimentary and Nutritional Value

3.1. Applications of Deep Eutectic Solvents in the Extraction of Phenols

Polyphenols are a diverse group of compounds, naturally occurring in plants. They have successfully been extracted from agricultural by-products, such as wine lees, red grape pomace, onions, olives, tomatoes, pear, and lemon-waste peels [21,47,48]. Polyphenols can be classified into flavonoids and non-flavonoids, where the non-flavonoid polyphenols comprise of phenolic acids **40**, tannins **41**, hydroxylated stilbenes **42**, polyphenol amides **43**, and lignins (**44**, **45**), among others ([49], Figure 5).

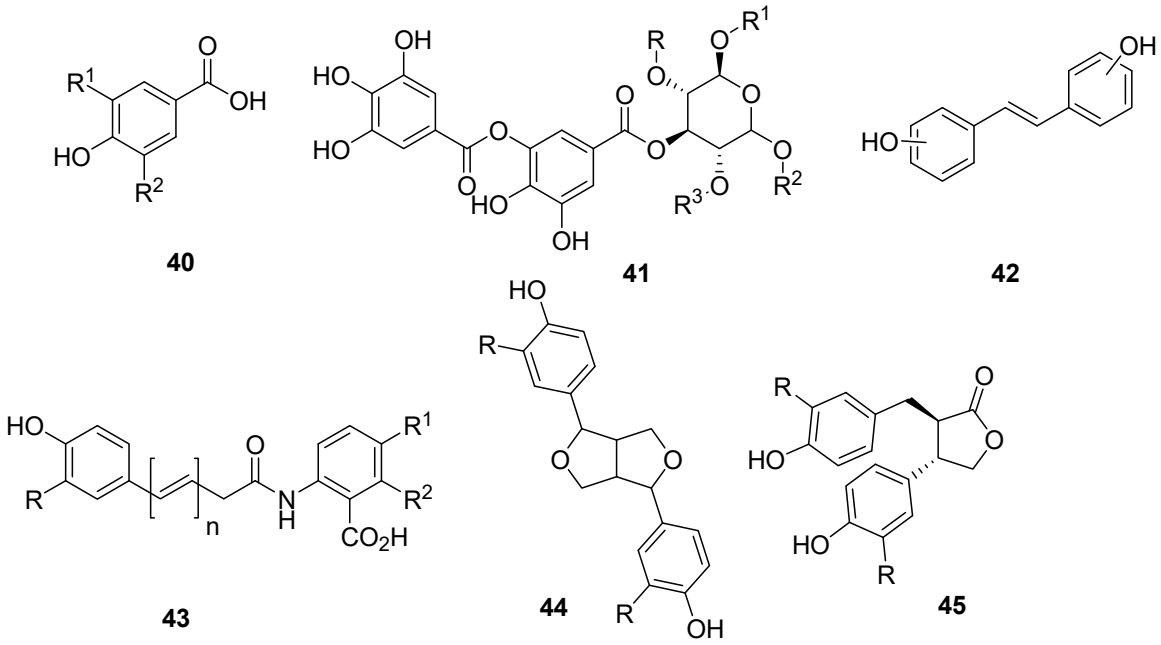


Figure 5. Different groups of non-flavonoid polyphenols.

3.1.1. Extraction of Flavonoids: Flavones, Flavanones, Flavanols, and Flavanonols

Structurally, flavonoids can be classified into flavones (**46**), flavanones (**47**), flavanols (**35**), flavanonols (**48**), isoflavonoids (**49**,**50**), and anthocyanins (**51**) (Figure 6). With their free-radical scavenging capacity, many flavonoids have anti-oxidative activity. Fruits, vegetables, tea, and wine are some of the dietary sources of flavonoids [50]. Ali et al. [51] utilized a eutectic mixture of choline chloride and *p*-toluene sulfonic acid (1:2M) to extract flavonoids from the fruits of the Chinese wolfberry (*Lycium barbarum* L.) under ultrasonic irradiation. The flavonols myricetin (**52**) (57.2 mg/g), morin (**53**) (12.7 mg/g), and rutin (**54**) (9.1 mg/g) were obtained in high yield (Figure 7). In 2018, Bajkcz and Adamek [16] published a larger study in which they reported on the extraction of cranberries, fruits of *Lycium barbarum* L., grapes, plums, orange peels, onions and broccoli, as well as mustard, rosemary, and black pepper. The targeted flavonoids were rutin (**54**), hesperidin (**55**), neohesperidin (**56**), naringenin (**57**), naringin (**58**), quercetin (**59**), hesperetin (**60**), and chrysin (**61**) (Figure 7). The effect of 17 types of NADES based on choline chloride (**1**), acetylcholine chloride (**38**·**HCl**), choline tartrate (**62**), betaine (**5**), and carnitine (**63**) as HBAs and citric acid (**24**), malic acid (**64**), tartaric acid (**65**) and lactic acid (**21**) as HBDs was compared [16] (Figure 8). A 30% aq. solution of acetylcholine chloride/lactic acid ratio (2:1) was found to be the ideal solvent for extraction. All target flavonoids were observed in *Lycium barbarum* L. fruits. Naringenin (**57**) and quercetin (**59**) were most abundant in *Lycium barbarum*, naringin (**58**) in orange peels. The results were based on the extraction of a 200 mg biomass sample mixed with 600 µL of NADES, stirred at 60 °C for 45 min at 1400 rpm. Thereafter, the extract was centrifuged, the supernatant was diluted with methanol (1:1) and centrifuged again. The analysis of the sample was carried out on an UHPLC system with UV detection, using a Poroshell 120 EC-C18 analytical column for separation. Older work comes from Bi et al. [52], who optimized conditions for the extraction of myricetin (**52**) and amentoflavone (**66**) (Figure 9) from the Hinoki cypress (*Chamaecyparis obtusa*), utilizing aq. mixtures of choline chloride (**1**) with alcohols ethylene glycol (**27**), glycerol (**18**), 1,2-butanediol (**67**), 1,3-butanediol (**68**), 1,4-butanediol (**69**), 2,3-butanediol (**70**), and 1,6-hexanediol (**71**) (Figure 10). Optimized conditions could be obtained when using 35 vol% of water in choline chloride/1,4-butanediol (1/5) at 70 °C for 40 min and a solid/liquid ratio of 1 g sample/10 mL solvent, where 0.031 mg myricetin (**52**) and 0.518 mg of amentoflavone (**66**, Figure 9) could be extracted from 1 g sample [52]. Amentoflavone (**66**)

is a biflavonoid which exhibits a whole host of physiological activities including antimalarial as well as anticancer activity. Also, it inhibits the actions of CYP3A4 and CYP2C9, enzymes responsible for the metabolism of more than 50% of the drugs currently on the market [53]. It is also an inhibitor of human cathepsin B, which plays an important role in intracellular proteolysis [54]. The combination of choline chloride with the diol triethylene glycol (**72**), was used to extract rutin (**54**) from buds of the Japanese pagoda tree (*Sophora japonica*, *Styphnolobium japonicum*). Here, 194.17 ± 2.31 mg·rutin per g of biomass could be obtained with a ChCl/triethylene glycol solution containing 20% water [55].

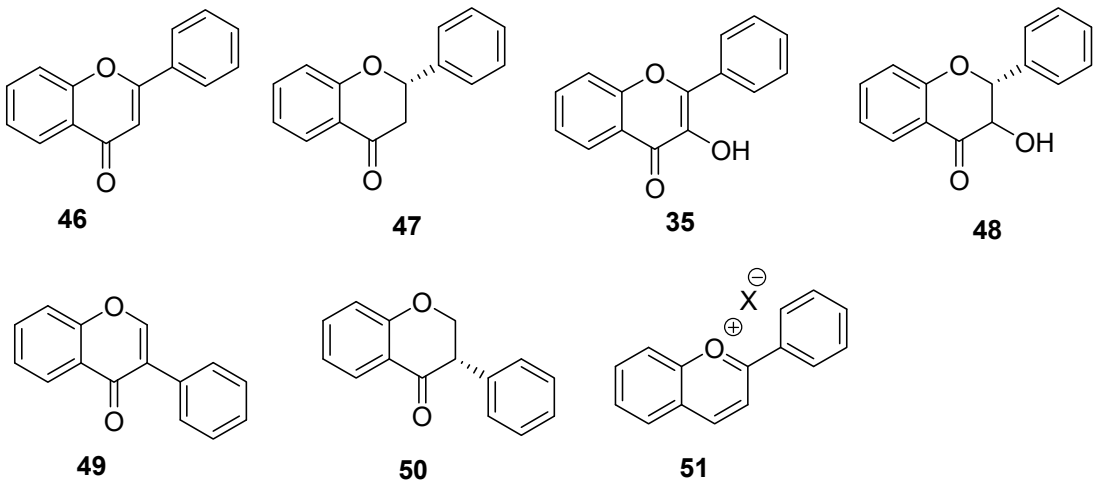


Figure 6. Classes of flavonoids.

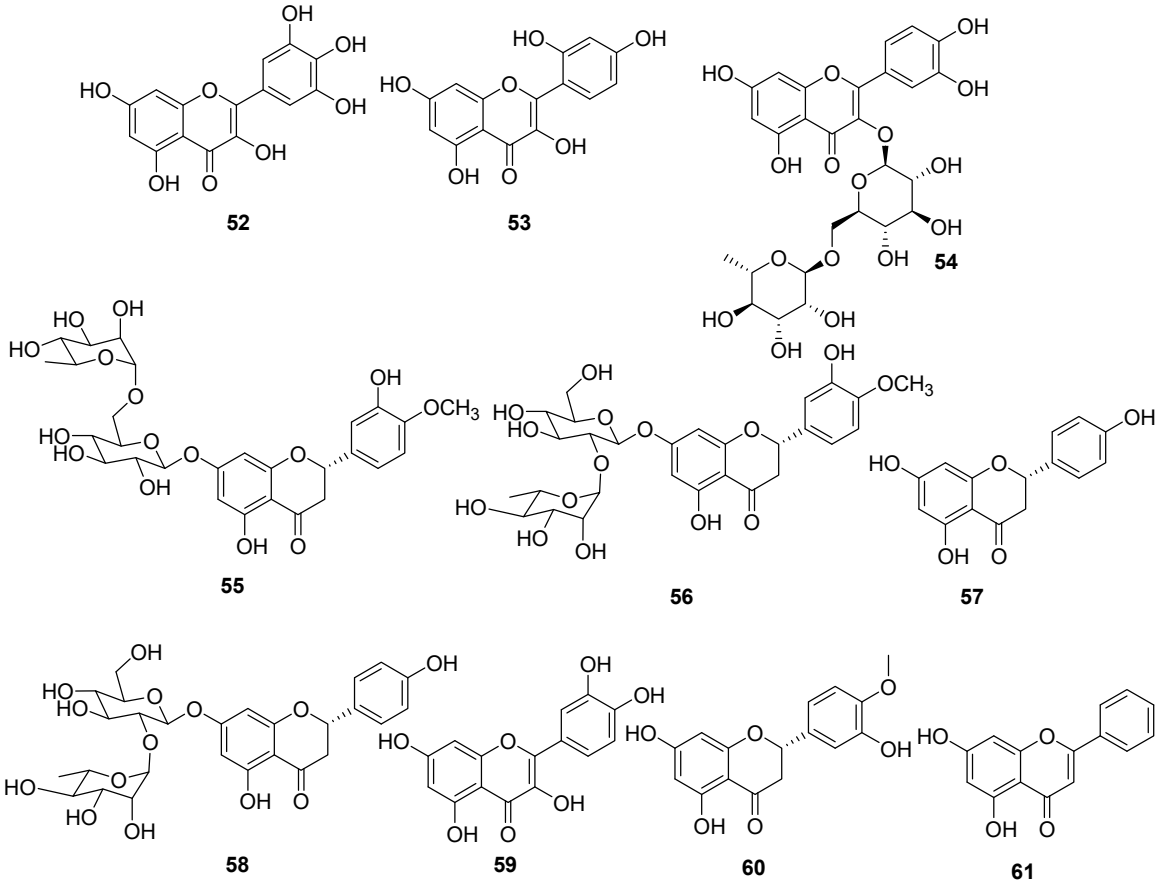


Figure 7. Typical flavonols of high value that can be extracted with DES/NADES.

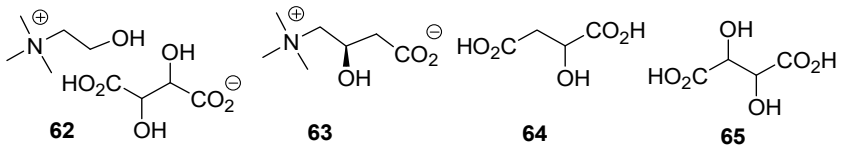


Figure 8. Further DES/NADES components used as HBA (**62** and **63**) and HBD (**64** and **65**) [16].

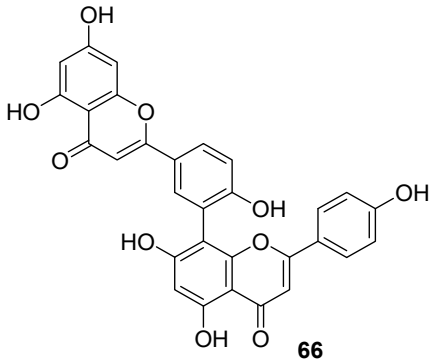


Figure 9. Structure of biflavonoid amentoflavone (**66**).

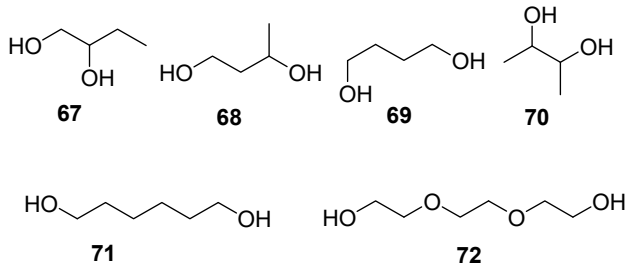


Figure 10. Alcohols used as co-solvents in NADES formulations.

Citrus peel wastes have been found to be an excellent source of flavonoids [56]. Typical flavonoid derivatives in citrus peel include polymethoxylated flavones nobiletin (**73**) and tangeretin (**74**), flavones apigenin (**75**), luteolin (**76**), and diosmetin (**77**), flavanones naringin (**58**), hesperidin (**55**), and naringenin (**57**), and flavanols quercetin (**59**) and rutin (**54**) (Figure 11). Xu et al. designed five ternary DESs [57] to extract polymethoxylated flavonoids (PMFs) and glycosides of flavonoids (GoFs) of varying polarity from citrus peel. Choline chloride (**1**)–levulinic acid (**78**)–*N*-methyl urea (**79**) with a water content of 20% (Figure 12) proved to be an efficient DES, showing the highest extraction yield of total flavonoids, at 18.75 mg PMFs and 47.07 mg GoFs per g material [57].

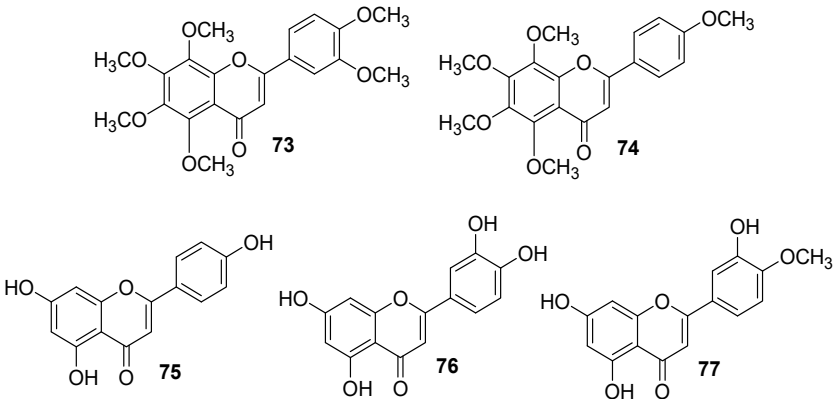
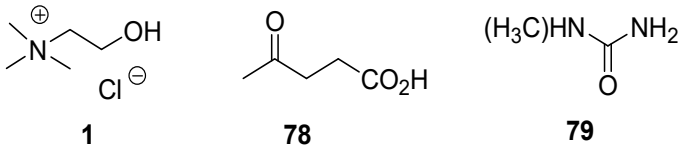


Figure 11. Polyhydroxylated and polymethoxylated flavones **73**–**77** from citrus peel.



1 **78** **79**

Figure 12. Choline chloride (**1**)–levulinic acid (**78**)–*N*-methyl urea (**79**) as an efficient DES for the extraction of polyhydroxylated and polymethoxylated flavones from citrus peel [57].

Herbs are a further source of flavonoids, and herb extracts obtained with NADES have been studied extensively. One such example is the extraction of Baikal/Chinese skullcap (*Scutellaria baicalensis*) with β-alanine–citric acid and with proline–citric acid [58]. The authors chose to evaluate the extraction of the 8 flavonoids baicalein (**80**), baicalin (**81**), scutellarein (**82**), wogonin (**83**), wogonoside (**84**), scutellarin (**85**), oroxylin A (**86**), and oroxyloside (**87**) (Figure 13) with the two different NADES, where addition of 40–50% water (*w*/*w*) to β-alanine–citric acid and 60% water (*w*/*w*) to proline–citric acid gave the highest extract yields, with 39.4 ± 9.5 µg and 32.0 ± 1.3 µg baicalin (**81**)/g biomass and 73.3 ± 0.9 µg and 82.4 ± 2.1 µg wogonoside (**84**)/g biomass, respectively [58]. T.P. Vo et al. [59] looked at the extraction of flavonoids from Dangshen (*Codonopsis pilosula* Franch), a perennial species of flowering plant in the bellflower family found in East Asia. Its roots are used in traditional Chinese medicine. Among 6 tested NADES, the authors found lactic acid–glucose (2:1) to be the most effective. An ultrasonic-microwave-assisted extraction was used, leading to a yield of 24.36 ± 0.48 mg rutin equivalent per g of dry substance. Wang et al. [60] extracted the leaves of the edible Korean perilla *Perilla frutescens* (L.) Britt., a plant from the mint family, with glucose-glycerol. The three flavonoids luteolin (**76**), apigenin (**75**), and 5,7,2′,5′-tetrahydroxyflavones (**88**) and the five flavonoid derivatives luteolin-7-*O*-diglucuronide (**89**), apigenin-7-*O*-diglucuronide (**90**), luteolin-7-*O*-glucuronide (**91**), apigenin-7-O-glucuronide (**92**), and quercetin-3-*O*-β-D-glucuronide (**93**) as well as the two anthocyanin compounds shisonin (**94**) and malonylshisonin (**95**) were identified in the extracts by UPLC-Q-TOF-MS (Figure 14). It was interesting to note that stability tests revealed a total flavonoid loss rate of the NaDES extract after four weeks that was by 37.75% lower than that of the concurrently obtained ethanol extract.

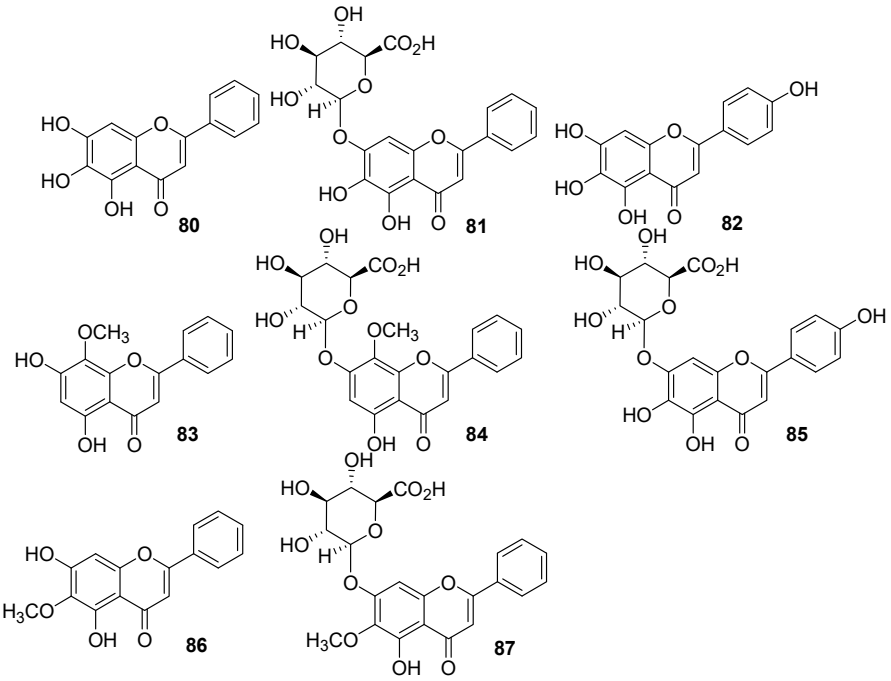


Figure 13. Flavonoids isolated from *Scutellaria baicalensis* [58].

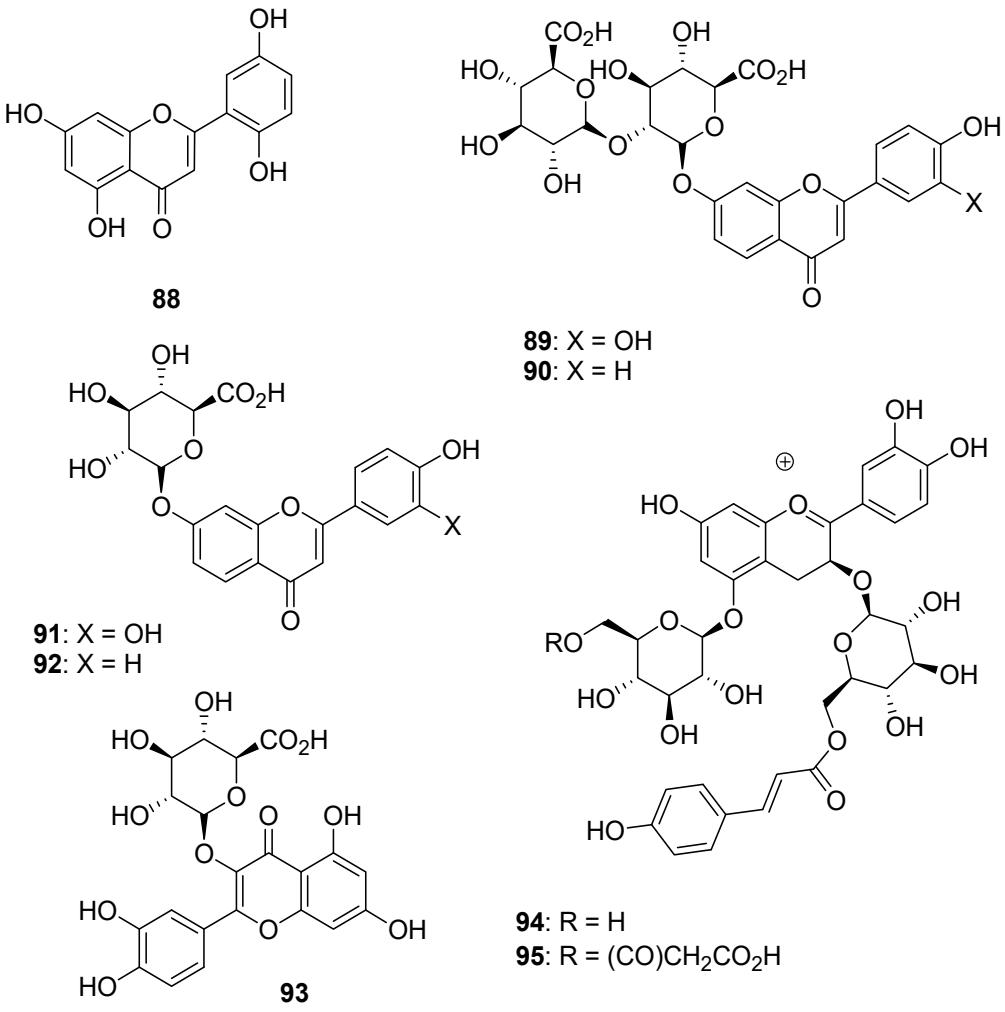


Figure 14. Flavonoids and anthocyanins extracted from Korean perilla *Perilla frutescens* (L.) [60].

3.1.2. Extraction of Anthocyanins

Anthocyanins are a class of water-soluble flavonoids. In plants, they often act as vacuolar pigments. There is as of yet no non-equivocal evidence of the effect of anthocyanins on human health. They have been found to have an anti-oxidative effect in vitro, but this effect has not yet been proven in vivo [61]. Nevertheless, the anti-inflammatory, neuroprotective, anti-obesity, anti-diabetic, anticarcinogenic, and cardioprotective properties of anthocyanins have been reported in the literature [62]. In the European Community (EC), some anthocyanins have been approved as food and beverage colorants [63]. The extraction of anthocyanins from different types of biomass has been studied extensively [64]. Thus, Guo et al. [65] utilized choline chloride-citric acid-glucose with a water content of 30% to obtain 6.05 mg anthocyanins per g fresh mulberry fruit, which is 1.24 times the yield obtained with the highest yielding traditional organic solvents (Figure 15, Table 2). Also, the stability of the anthocyanins was found to be higher in NADES than in traditional organic solvents. Panić et al. [38] tested 8 different NADES in their efficacy to extract anthocyanins from grape pomace. Among them were combinations of proline/malic acid, betaine/malic acid, and ternary mixtures such as malic acid/glycerol/glucose. The most effective combinations were found to be choline chloride/citric acid (ChCl-Cit) and choline chloride/proline/malic acid. The extractions were carried out under ultrasonication, microwave irradiation and under a combination of both. Four anthocyanin-3-*O*-monoglucosides **96**–**99** of delphinidin, petunidin, peonidin, and malvidin, respectively, two acylated derivatives (malvidin- and peonidin-3-acetylmonoglucosides, **100** and **101**)

and two coumaroyl derivatives (peonidin- and malvidin-3-(6-O-p-coumaroyl) monoglucosides **102** and **103**) were identified, with malvidin-3-O-monoglucoside (**98**) as the most abundant. The anthocyanins were separated from the ChCl-Cit extracts by resin adsorption on a glass column. ChCl-Cit was eluted from the column with water. Subsequently, the anthocyanins were recovered from the column by elution with ethanol. The NADES ChCl-Cit was recycled by evaporation of the water under vacuum. The extracted anthocyanin profile was analyzed by high performance liquid chromatography (HPLC). The extractions were carried out in up to half-liter batches [38]. It must be noted that the direct extraction of the pomace with either ethanol or methanol did not give any detectable amounts of anthocyanin monoglucosides or their derivatives. Silva and coworkers [66] extracted anthocyanins from blueberries using different mixtures of ChCl, glycerol (gly) and citric acid. They found ChCl-gly-citric acid (0.5:2:0.5), diluted with 25% water, to be the most suitable NADES, giving a yield of 599 mg cyanidin-3-glucoside (**104**, cy-3-glc) equivalent per 100 g blueberry powder [66]. The individual extracted anthocyanins were identified by HPLC-DAD-MS^n to be malvidin-3-galactoside (**105**) > delphinidin-3-galactoside (**106**) ∼ malvidin-3-arabinoside (**108**) > petunidin-3-glucoside (**96**) ∼ delphinidin-3-arabinoside (**109**) > petunidin-3-arabinoside (**110**). Zannou and Koca [67] found that the three eutectic solvent systems choline chloride–glycerol (1:2) [98.81 ± 1.48 mg epicatechin equivalent (ECE)/100 g], choline chloride–ethylene glycol (1:2) [104.72 ± 5.17 mg ECE/100 g], and choline chloride and butane-diol (1:2) [102.26 ± 4.07 mg ECE/100 g], all in the presence of 20% H_2O could extract more flavonoids per g dry weight of blackberry pomace than conventional polar protic solvents could such as methanol [96.35 ± 4.20 mg ECE/100 g], ethanol [72.30 ± 2.56 mg ECE/100 g] and H_2O [53.02 ± 4.11 mg ECE/100 g] [67]. The highest values of anthocyanin recovery were found for the NADESs choline chloride–acetic acid [115.37 ± 0.43 mg cyanidin-3-glucoside equivalent (CGE)/100 g], choline chloride–ethylene glycol [114.88 ± 5.29 mg CGE/100 g], choline chloride–citric acid [112.67 ± 3.90 mg CGE/100 g), choline chloride–glycerol [110.04 ± 2.34 mg CGE/100 g], choline chloride—glucose [109.06 ± 2.32 mg CGE/100 g], lactic acid—sorbitol [103.10 ± 6.42 mg CGE/100 g], choline chloride—sorbitol [101.56 ± 4.44 mg CGE/100 g], and choline chloride—xylitol (Figure 16) [101.49 ± 2.78 mg CGE/100 g]. This compares well with the anthocyanin recovery shown with water as solvent [62.14 ± 2.81 mg CGE/100 g], with methanol [89.73 ± 3.93 mg CGE/100 g] and with ethanol [81.27 ± 0.32 mg CGE/100g] [67]. The extractions were carried out under ultrasonication (20 min, 25 °C). The anthocyanins were determined by HPLC (Agilent 1260), where the anthocyanins were separated on an Inertsil ODS-4 column. The four anthocyanins cyanidin-3-glucoside (**104**), cyanidin-3-rutinoside (**111**), cyanidin chloride (**112**) and pelargonidin-3-glucoside could be identified in all the solvents used. The most abundant anthocyanin in the blackberry was found to be cyanidin-3-glucoside (**104**), followed by cyanidin-3-rutinoside, cyanidin chloride (**112**) and pelargonidin-3-glucoside (**113**). Fu and coworkers [68] have looked at the use of the NADES mixture of choline chloride–oxalic acid (Ch-Ox) for the extraction of anthocyanins from blackberry pomace. The extraction was carried out under pulsed ultrasonication [68]. The best extraction results were obtained after 3.2 min ultrasonication (325 W of ultrasonic power) at 76 °C with a 60 mL/g solvent to solid ratio. The crude anthocyanins were purified by solid-phase extraction (SPE), where the crude extracts were loaded onto a SPE C-18 cartridge after activation with methanol and reconditioning with acidic water [69]. After the polar components were eluted with acidic water and ethyl acetate, anthocyanins were eluted using acidic ethanol. The extracted anthocyanins were analyzed with a Waters HPLC system. Ten different anthocyanins were found in the extracts of Ch-Ox: Delphinidin-3-galactoside [**106**, 82.82 mg/g purified dried extract (PDE)], delphinidin-3-glucoside [**97**, 19.09 mg/g PDE], delphinidin-3-arabinoside [**109**, 70.90 mg/g PDE], cyanidin-3-glucoside [**104**, 3.17 mg/g PDE], petunidin-3-glucoside [**96**, 8.62 mg/g PDE], petunidin-

3-arabinoside [**110**, 8.63 mg/g PDE], petunidin-3-galactoside [**107**, 25.44 mg/g PDE], malvidin-3-galactoside [**105**, 28.45 mg/g PDE], malvidin-3-glucoside [**98**, 11.83 mg/g PDE], and malvidin-3-arabinoside [**108**, 63.90 mg/g PDE]. It was found that the amount of water added to the choline chloride–oxalic acid mixture has a profound effect on the anthocyanin yield, where the initial addition of water increases the yield, most likely due to a better mass transfer of the anthocyanins from the biomass material into the solvent due to a decrease in the viscosity of the solvent [70]. Excessive water disrupts the HB-HA interaction within the NADES and decreases the interaction of the solvent with the anthocyanins to be extracted. The highest total anthocyanin content (TAC) in the blackberry extracts was found with choline chloride–oxalic acid in the presence of 30% H_2O [68].

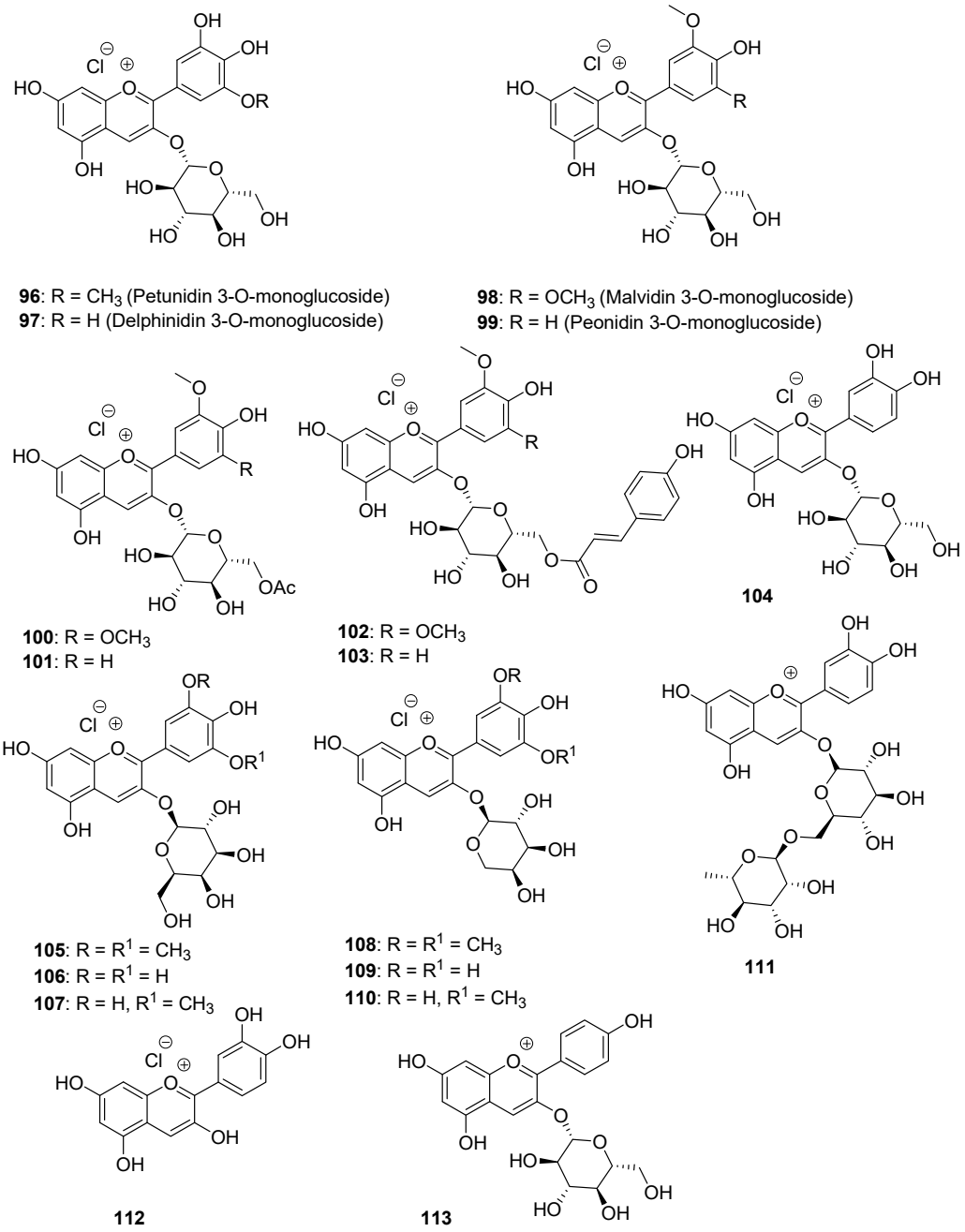


Figure 15. Anthocyanines isolated from grape pomace.

Table 2. Extraction of anthocyanins from fruits.

Sample	NADES Mixture	Extraction Method	Reference
Mulberry (*Fructus mori*)	Choline chloride/citric acid/glucose (1:1:1) with 40% H_2O	High-speed homogenization/cavitation-burst extraction	Guo et al. [65]
Grape pomace (*Vitis vinifera* cv)	Choline chloride/citric acid	Simultaneous ultrasonication/microwave irradiation	Panić et al. [38]
Grape pomace (*Vitis vinifera* cv)	Choline chloride/proline/malic acid	Simultaneous ultrasonication/microwave irradiation	Panić et al. [38]
Pomace of the Brazilian grape-tree (*Myrciaria cauliflora*) fruit	Choline chloride/propyleneglycol Choline chloride/citric acid	50 °C	Benevutti et al. [23]
Blueberry (O'Neal and Florida cultivars)	Choline chloride/glycerol/25% H_2O	Ultrasonication 40 kHz, at room temperature for 50 min.	Silva et al. [66]
Blueberry pomace	Choline chloride/oxalic acid	Pulsed ultrasonication	Fu et al. [68]
Blackberry (*Rubus* spp.)	Choline chloride/glycerol/20% water	Ultrasonication at 25 °C for 20 min.	Zannou and Koca [67]
Blackberry (*Rubus* spp.)	Choline chloride/butanediol/20% water	Ultrasonication at 25 °C for 20 min.	Zannou and Koca [67]
Blackberry (*Rubus* spp.)	Choline chloride/ethyleneglycol/ 20% H_2O	Ultrasonication at 25 °C for 20 min.	Zannou and Koca [67]

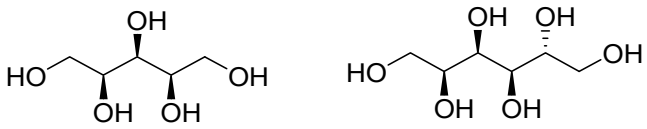


Figure 16. Xylitol (**114**) and sorbitol (**115**), two reduced sugars used as components in NADES for the extraction of anthocyanins from grape pomace.

Fu and coworkers [68] have noted that especially at higher pH values, the extracted anthocyanins are more stable in NADES than in aqueous and in aqueous ethanolic solvents. Independently, it has been reported that antioxidants extracted from the wastes of the wild mango fruit (*Mangifera pajang*) exhibit better stability in the NADES (choline chloride-ascorbic acid) than in aqueous solutions [71].

3.1.3. Extraction of Phenolic Acids and Their Derivatives

Chlorogenic acid (**116**), an intermediate in lignin biosynthesis, is the ester of caffeic acid (**17**) and (−)-quinic acid. It offers significant protection against cardiovascular diseases (CVDs), type 2 diabetes, and inflammation-related conditions [72]. Therefore, it is the target of extractions from numerous plant sources, in which it is abundantly available. Thus, under ultrasonication, Park et al. [73] were able to extract chlorogenic acid (**116**, 5-caffeoylquinic acid, 9.36 mg/g) and caffeic acid (**17**, 0.31 mg/g) from *Artemisia scopariae herba*, a plant commonly used in traditional Chinese medicine against liver diseases. For this, Park et al. [73] used a 50% mixture of a synthesized DES from tetramethyl ammonium chloride and urea (1:4) and methanol/water (60:40, *v*/*v*). After calculations using the polarizable continuum model (PCM) [74,75], Yue et al. [76] chose proline–malic acid as the most suitable NADES to extract chlorogenic acid (**116**) from *Artemisia scopariae herba* (at 3.7 mg/g). Yuniarti et al. [77] looked at different ratios of choline chloride (**1**) and sorbitol to extract chlorogenic acid (**116**) as well as caffeine (**117**) from green coffee beans and found that in a 60 min extraction a molar ratio of 4:1 choline chloride-sorbitol at a liquid-solid ratio of 1:30 g/mL yielded 5.87 mg/g of caffeine (**117**) and 12.24 mg/g of chlorogenic acid (**116**). Maimulyanti et al. [78] found

choline chloride–proline (1:1) to be the most suitable NADES solvent to extract phenolics from coffee husk waste with a yield of 10.07 mg GAE (gallic acid equivalent)/g and a polyphenol concentration of 671.4 mg/L. The extract included members of the chlorogenic acid family. Fanali et al. [79] used ChCl-betaine to extract chlorogenic acid (**116**) from spent coffee grounds. In addition, 3-*O*-caffeoylquinic acid (**120**), 5-*p*-coumaroylquinic acid (**118**), 4-*O*-caffeoylquinic acid (**119**), 4-feruloylquinic acid (**121**), 1,5-γ-quinolactone (**122**), 3-feruloylquinic acid (**123**), 3,4-dicaffeoylquinic acid (**124**), and 3,5-dicaffeoylquinic acid, (**125**) were isolated from the extracts. Sunflower meal can also be a source of chlorogenic acid (**116**). This was shown by Bezerra et al. [80] who found lactic acid-glucose the best solvent for extraction with 1.79 g chlorogenic acid (**116**) contained in 1L of extract. In comparison, 40% aq. ethanol gave 1.31 g chlorogenic acid per L of extract. Yu et al. [81] have estimated that a daily intake of chlorogenic acid of 13.5–500 mg/d is conducive to human health. Chlorogenic acid (**116**) plays a role in the glucose and lipid metabolisms. No tolerable upper intake level for chlorogenic acid has been formulated thus far.

Spent coffee grounds were also extracted by Silva et al. [82] with two different NADES, namely with citric acid–mannitol and with lactic acid–glucose. It was found that in both cases a ratio of 9:1 DES-H_2O gave the highest yield of total phenolic compounds extracted with 756.70 ± 8.57 GAE/L and 612.78 ± 4.52 GAE/L, respectively. The exact composition of the extracts was not analyzed (Silva et al., 2024) [82] (Figure 17).

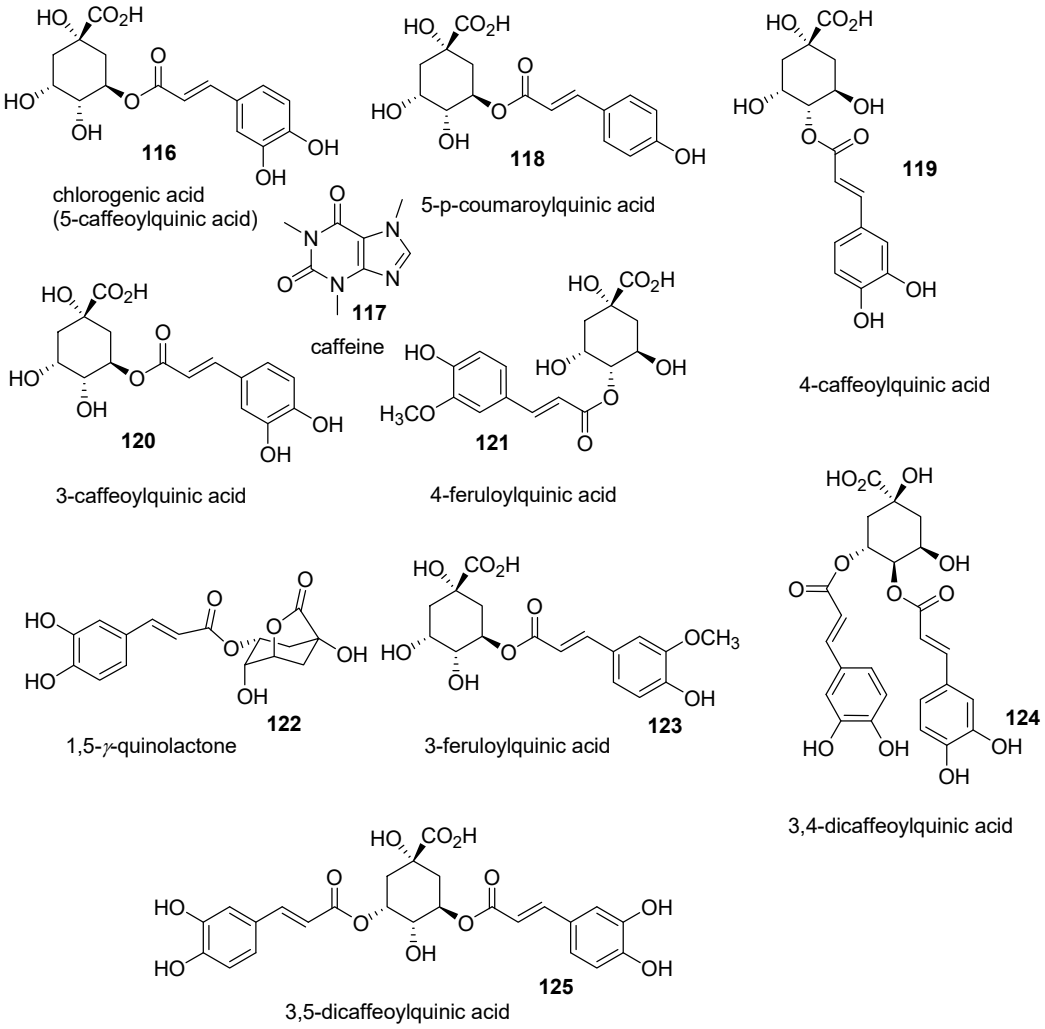


Figure 17. Phenolic acids and derivatives extracted from coffee husk wastes and spent coffee grounds.

3.1.4. Extraction of Polyphenols Other than Flavonoids and Phenolic Acids and Derivatives

A number of groups have looked at the extractability of curcuminoids from turmeric (*Curcuma longa*), a flowering plant in the ginger family Zingiberaceae, which is native to the Indian subcontinent and South East Asia. The curcuminoids include the heptanoid curcumin (**126**), a phenolic pigment, and its derivatives desmethoxycurcumin (**127**) and bisdesmethoxycurcumin (**128**) (Figure 18). Curcumin (**126**) was extracted by Le et al. from *C. longa* wastes with DES. The best result was obtained with ChCl-Pro (2:1) at a 20% water content, with an extraction yield of 54.2 mg curcumin per g waste. This was 1.31 times higher than yields found for the methanolic extraction of the wastes. Curcumin (**126**) could be isolated from DES by dilution of the extract with water [83]. Liu et al. [84] found that at 50 °C and 30 min extraction time, NADES made of a 1:1 citric-acid-to-glucose ratio with 15% water content gave the best results for the extraction of curcuminoids **126**–**128** from *C. longa*. S. Patil et al. [85] could extract 77.13 mg curcuminoids per g *C. longa* with choline chloride–lactic acid (1:1) with 20% water content utilizing power ultrasound. Afterwards, the extract was precipitated upon addition of water, resulting in 42.0% recovery of curcuminoids with 82.2% purity. Interestingly, natural deep eutectic solvents (NADES) have been shown to be good bioavailability promoters. Curcuminoids are known for their rather limited bioavailability in humans, especially due to their poor oral absorption. Therefore, Abouheif et al. [86] evaluated the in-vivo bioavailability of curcuminoids upon extraction from turmeric with different DESs. Jeliński et al. [87] have found that the solubility of curcumin (**126**) in simulated gastrointestinal fluids shows that there is a significant increase of bioavailability of **126** that takes place in the small intestinal fluid. Another aspect worth discussing is the better light stability of curcumin in NADES over other solvents [86].

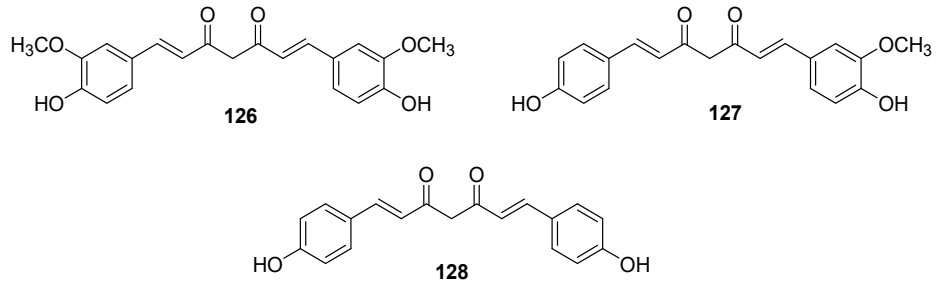


Figure 18. Curcuminoids found in turmeric (*C. longa*).

3.1.5. DES-Mediated Extraction of Natural Compounds from Olives

Frequently, DES systems have been used to extract phenols from olive products. Thus, García et al. [88] employed eutectic mixtures of ChCl in various ratios with sugars, alcohols, organic acids, and urea. Interesting results were obtained with the DES systems ChCl/xylitol (2:1) and ChCl/1,2-propane-diol (1:1) that could extract efficiently oleacein (**129**) and oleacanthal (**130**) (Figure 19), the most abundant secoiridiod derivatives found in virgin olive oil. Both compounds have anti-inflammatory, antioxidant, and anti-atherosclerotic properties [89]. They are held partially responsible for the relatively low occurrence of Alzheimer's [90] and heart disease [91] associated with a Mediterranean diet. Alañón et al. [18] could identify 48 phenolic compounds in the DES extract of olive leaves using high performance liquid chromatography-diode array detection-electrospray ionization-quadrupole time-of-flight-mass spectrometry (HPLC-DAD-ESI-TOF-MS). The authors found the combination of choline chloride (**1**) and ethylene glycol to be the most effective among the nine tested DESs, showing extraction yields similar to those exhibited by conventional solvents such as aqueous ethanol [92], when the extraction was performed under microwave irradiation at 79.6 °C and with a 43.3% water content in the solvent.

Oleuropein (**131**), a glycosylated seco-iridoid was identified as the most abundant phenolic compound in the examined olive leaves. Interestingly, oleuropein (**131**) is standardly removed to make olives edible as it has a bitter taste. Other compounds that were identified in the DES extract were elenolic acid glucoside (**132**), oleoside (**133**), hydroxyoleuropein (**134**), ligostroside (**135**), and luteolin glucoside (**136**).

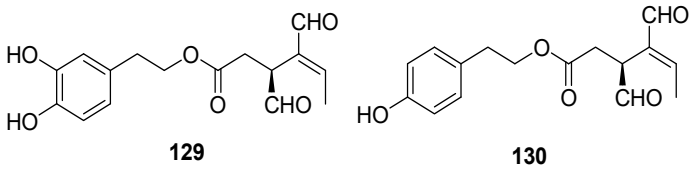


Figure 19. Oleacein (**129**) and oleacanthal (**130**), two phenols isolated from olive oil.

Rodriguez-Juan et al. [93] optimized the phenolic extraction from virgin olive oil utilizing a NADES made from ChCl and Xyl in the presence of water. The highest concentration of phenols (555.4 mg phenolic compounds/kg oil) was obtained from a 1h extraction at 40 °C. Apart from oleacein (**129**), oleacanthal (**130**), oleuropein (**131**), and ligotroside (**135**), hydroxytyrosol (**137**), tyrosol (**138**), 1-acetoxypinoresinol (**139**), pinoresinol (**140**), apigenin (**75**) and luteolin (**76**) could be identified in the extract (Figure 20).

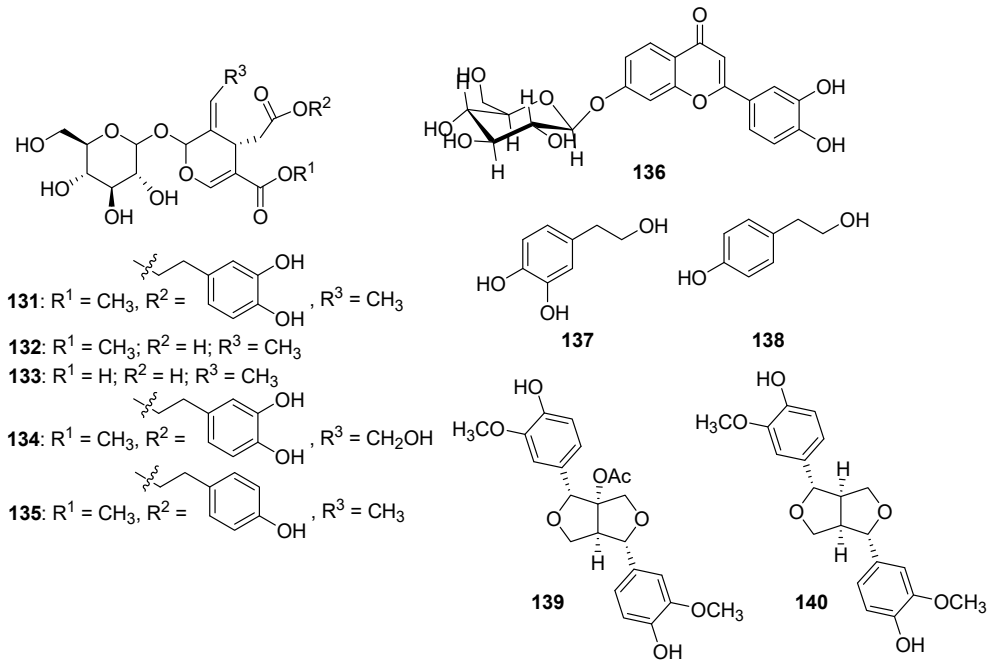


Figure 20. Phenolic compounds found in olive oil.

Morgana et al. [35] looked at the effect of three food-grade NADESs on the extraction of valuable biomolecules from olive pomace, utilizing LGH (lactic acid-glucose-water; molar ratio 5:1:9.3); Ch-CH (choline chloride-citric acid-water; molar ratio 1:1:2.7) and Ch-Le (choline chloride and levulinic acid, molar ratio 1:2). The extractions were carried under ultrasonication at 40 °C for 60 min. The authors noted that NADES LGH gave excellent recovery rates of phenols and anthocyanins from olive pomace. In addition, the used NADES enhanced the bioavailability of hydroxytyrosol (**137**) and luteolin (**76**).

3.1.6. DES-Mediated Extraction of Natural Compounds from Dates (*Phoenix dactylifera* L.)

The extraction of natural products from date palm using DESs is gaining attention. Djaoudene and Louaileche [94] studied the extraction of phenolic compounds from two date fruit cultivars in Algeria, locally known as Ourrous and Ouksaba. The extraction

of phenolics was based on the use of lactic acid (**21**) and sucrose (**141**) as DES components. The extraction was carried out under ultrasonication. The optimized conditions for the extraction were found to be the use of lactic acid (**21**) and sucrose (**141**) as NADES in a 3:1 molar ratio with a sample: solvent ratio of 100 mg: 15 mL, and with an extraction duration of 33–40 min. These conditions allowed an extraction of 1393.5 mg gallic acid equivalents (GAE)/100 g for the Ourrous cultivar and 528.4 mg (GAE)/100 g for the Ouksaba cultivar and produced DPPH radical scavenging activities of 948.1 mg and 170.4 mg ascorbic acid equivalents (AAE)/100 g fresh weight (FW) for Ourrous and Ouksaba cultivars, respectively. However, no attempt was made to separate or identify the phenolic compounds obtained.

In a later study, Djaoudene and coauthors [95] studied the extraction of phytochemical constituents from eight Algerian date fruit cultivars known locally as Ourous, Tazizaout, Tazarzeit, Tazoughart, Ouaouchet, Oukasaba, Delat, and Tamezwertn'telet, using a mixture of sucrose-lactic acid as NADES under ultrasonication. Their study showed that the Ourous cultivar has the highest total phenolic content with 1288.7 mg GAE/100 g dry matter (DM), a total flavonoid content of 53.8 mg QE (quercetin equivalent)/100 g DM, a total proanthocyanidin content of 179.5 mg CE (cyanidin equivalent)/100 g DM, and a total triterpenoid content of 12.88 mg OAE (oleanolic acid equivalents)/100 g DM among all tested cultivars.

The extracts were analyzed using HPLC-DAD-MS. Five distinct phenolic compounds could be identified, including three phenolic acids [ferulic acid (**142**), vanillic acid (**143**), and gallic acid (**144**)) and two flavonoids [isoquercetin (**145**), and rutin (**54**)] (Figure 21). Among the cultivars, the Ourous cultivar showed the highest content of vanillic acid (**143**) and rutin (**54**). The research group used six different assays to monitor the antioxidant capacity of the individual date palm cultivars: the ferric reducing antioxidant potential (FRAP), the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay, the 2-azinobis-3-ethylbenzothiazoline-6-sulphonic acid (ABTS) radical scavenging assay, the phosphomolybdenum (PhMo) method, the nitric oxide radical scavenging assay, and the linoleic acid lipid peroxidation inhibition assay (LALP). Among the cultivars, the Ourous cultivar showed the highest FRAP value (704.2 mg AAE/100 g DM), the highest DPPH scavenging activity (594.8 mg AAE/100 DM), and the largest ABTS scavenging activity (838.7 mg TE [Trolox equivalents]/100 g DM). However, the Oukasaba cultivar showed the highest value in the PhMo test (1229 mg GAE/100 DM) and the highest NO radical inhibition capacity (69.1%). In respect to LALP inhibition, the Ouaouchet cultivar showed the highest value (30.5%).

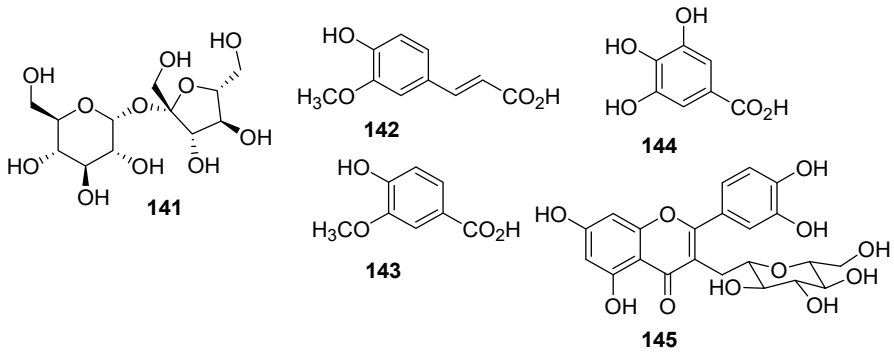


Figure 21. Phenolic acid and flavonoid glucosoid constituents found in dates. Dates also possess a high sugar content, including sucrose (**141**) which can be used as a NADES component to extract phenolic acids and flavonoids from dates.

The group also tested the enzyme inhibition activities of the obtained NADES date extracts. Specifically, the acetylcholinesterase inhibition activity and the α-amylase inhibi-

tion activity were studied. Galantamine (**146**) and acarbose (**147**) (Figure 22), commercially available enzyme inhibitors of acetylcholinesterase and α-amylase, were used as reference. The highest acetylcholinesterase inhibition activity was recorded for the Ourous cultivar extract (37.10%) along with the highest α-amylase inhibition (45.24%) while the reference compounds galantamine (**146**) showed 76% inhibition and acarbose (**147**) showed 79% inhibition. These results suggest that the date NADES extracts can serve as neuroprotective and anti-hyperglycemic agents [95].

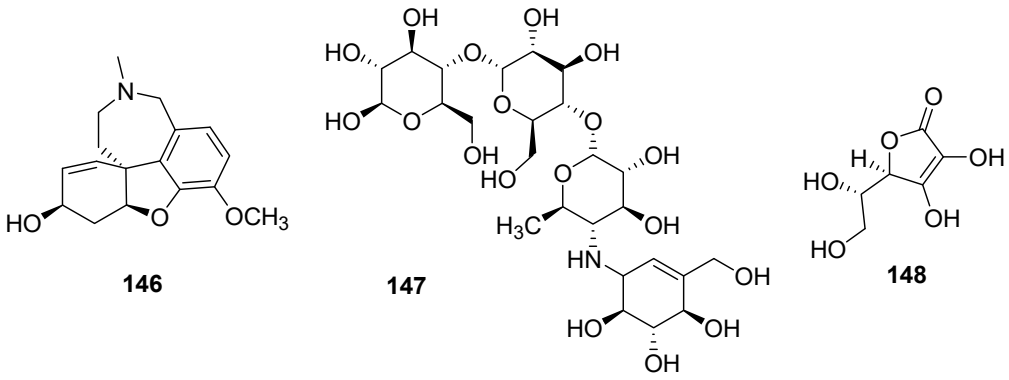


Figure 22. Galantamine (**146**) and acarbose (**147**) used as references for acetylcholinesterase and α-amylase inhibition tests. Ascorbic acid (vitamin C, **148**) is found as a food additive (E-300). Antioxidant activity of materials often are given in ascorbic acid equivalent antioxidant capacity (AEAC). Incidentally, ascorbic acid is also used as HBD in NADES formulations.

It has been noted that dates have between 50 and 80 g carbohydrate/100 g date fruit, mostly in the form of glucose (**29**), fructose (**30**) and sucrose (**141**). Thus, dates are a source for refined sugar, although in this regard they have not been exploited fully, yet [96]. Currently, the extraction process of liquid date sugar (date syrup) suffers from low sugar yield and extraction efficiency. 40–50% of the sugar content is lost during the pressing and mixing process [97]. In this regard, AlYammahi et al. [98] developed an extraction process of date fruit powder utilizing the NADES system ChCl-CA-H_2O (1:1:1) under ultrasonication to yield 87.8 g TSC (total sugar content)/100 g fruit. This is 43.1% higher as compared to using a conventional hot water extraction.

The utilization of date waste material has also been the topic of articles. Thus, Airouyuwa and coworkers [99,100] studied the use of different NADES in the extraction of phenolics from date pit powder. Their method relies on the use of microwave irradiation to enhance the extraction performance. The two most efficient NADES were found to be choline chloride-lactic acid (ChCl-LA) and choline chloride-xylose (ChCl-Xylo). The optimal extraction conditions using the ChCl-LA NADES were 80 °C with a 5 min. irradiation time, using a 63% concentration of the NADES, which was diluted with water. For ChCl-Xylo NADES an extraction temperature of 80 °C, 20 min. irradiation time, and a NADES concentration of 50% were found to give the best results. Under these conditions the total phenolic content obtained was 147.92 mg GAE/g date pit powder for ChCl-LA and 234.65 mg GAE/g date pit powder for ChCl-Xylo. The phenolic compounds were analyzed by UHPLC, with the main phenolics detected being catechin (**32**), 3,4-dihydroxybenzoic acid (**151**), and caffeic acid (**17**) [99]. The same group [100] used four different NADES prepared from combinations of choline chloride (**1**) with the carboxylic acids lactic acid (LA, **21**), malic acid (MA, **64**), acetic acid (AC) and citric acid (Cit, **24**) to extract phenolics, including phenolic acids and carboxylic acids from date seed powder. From 100 g date seed powder, gallic acid (**144**, 57.9 mg), 4-hydroxybenzoic acid (**16**, 50.7 mg), vanillic acid (**143**, 52.0 mg), syringic acid (**149**, 41.3 mg), *p*-coumaric acid (**150**, 30.4 mg), ferulic acid (**142**,

107.9 mg), quercetin (**59**, 148.0 mg), chlorogenic acid (**116**, 413.2 mg) and protocatechuic acid (**151**, 144.9 mg) could be extracted with ChCl-Cit (Figure 23). While no benzoic acid could be detected in the ChCl-Cit extract, interestingly benzoic acid (at 535.9 mg and 811.2 mg, respectively) could be found in the ChCl-AC and ChCl-MA extracts [100].

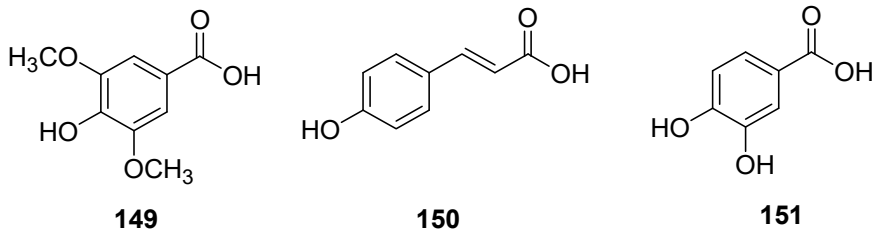


Figure 23. Phenolic carboxylic acids extracted from date seed powder [100].

3.1.7. Release of the Extracted Phenolic Compounds from DES

The previous sections notwithstanding, often the extracted components are needed in pure form. In those cases, once extracted from the bio-source with DES/NADES, the extracted compounds need to be released from the eutectic solvent. The recovery of phenolic compounds extracted from virgin olive oil with a mixture of Chl-Xyl-H_2O (2:1:3) has been achieved with an amberlite XAD-16 sorbent, pretreated with ethanol and MQ water before loading with the extract. The extracts once loaded onto the sorbent in the column were washed down with MQ water before the extracted phenols were eluted from the column with ethanol [93].

3.2. Applications of DESs for Biopolymer Extraction

Deep eutectic solvents have been utilized to extract biopolymers, including polysaccharides (Figure 24) cellulose (**152**), hemicelluloses (**153**), starch (**154**), carrageenans such as **155**, chitin (**156**), xylans such as **157** and pectins (**158**) [101,102]. Polysaccharides constitute one of the most abundant fractions of biomass originating from natural lignocellulosic material as well as from food waste [103]. Cellulose in form of dietary fibers is part of our daily food intake and is also added to processed food [104,105]. Additionally, it is used in food packaging (Liu et al. [106], see below). Chitin (**156**), the second most abundant natural polysaccharide after cellulose, chitosan (**159**) and their derivatives are used in the food industry as food preservatives [107–109]. Both chitin (**156**) and chitosan (**159**) have anti-oxidative as well as antimicrobial properties [110]. They are main constituents of seasonings, sauces, ketchups and mayonnaise. Pectins **158** are used in food as thickeners, gelling agents, and emulsifiers [111,112]. They are also used in food packaging [113,114]. Many of the oligo- and polysaccharides can be depolymerized to give monomeric sugars such as glucose (**29**), fructose (**30**) and xylose (**160**) or other small organic molecules such as succinic (**161**), malic (**64**), and fumaric (**162**) acids, 2,5-furandicarboxylic acid (**163**) as well as sorbitol (**115**) and xylitol (**114**) (Figure 25), all of which can be used as building blocks for more complex organic materials [101]. Hemicelluloses can be converted to furfural derivatives such as **164** and **165** [115,116]. Nevertheless, there is great merit to extract the sugar polymers themselves as they present great value as food additives, as shown above, but can also be used as materials for a large number of applications including textiles and filters. Classical extraction methods include the extraction of cellulose with dimethyl acetamide–lithium chloride (**166**) [117], the extraction of starch with dimethylsulfoxide (**167**) [118], and the extraction of chitin with dichloroacetic acid (**168**) and trichloroacetic acid (**169**) as well as with dimethyl acetamide–lithium chloride (**166**) [119] (Figure 26). Oftentimes, an initial separation of the sugar polymers from lignin is essential. With an annual production of 1.1×10^{11} tons per year lignocellulose is the most important natural renewable resource

we have [101,120]. It is here that the classical extraction procedures suffer from low selectivity [121,122]. Additionally, they require high temperatures [123,124] and extensive biomass pre-treatment [125]. For these reasons new solvent systems on the basis of ionic liquids as well as deep eutectic solvents have been attempted for the dissolution of cellulose and other polysaccharides [101].

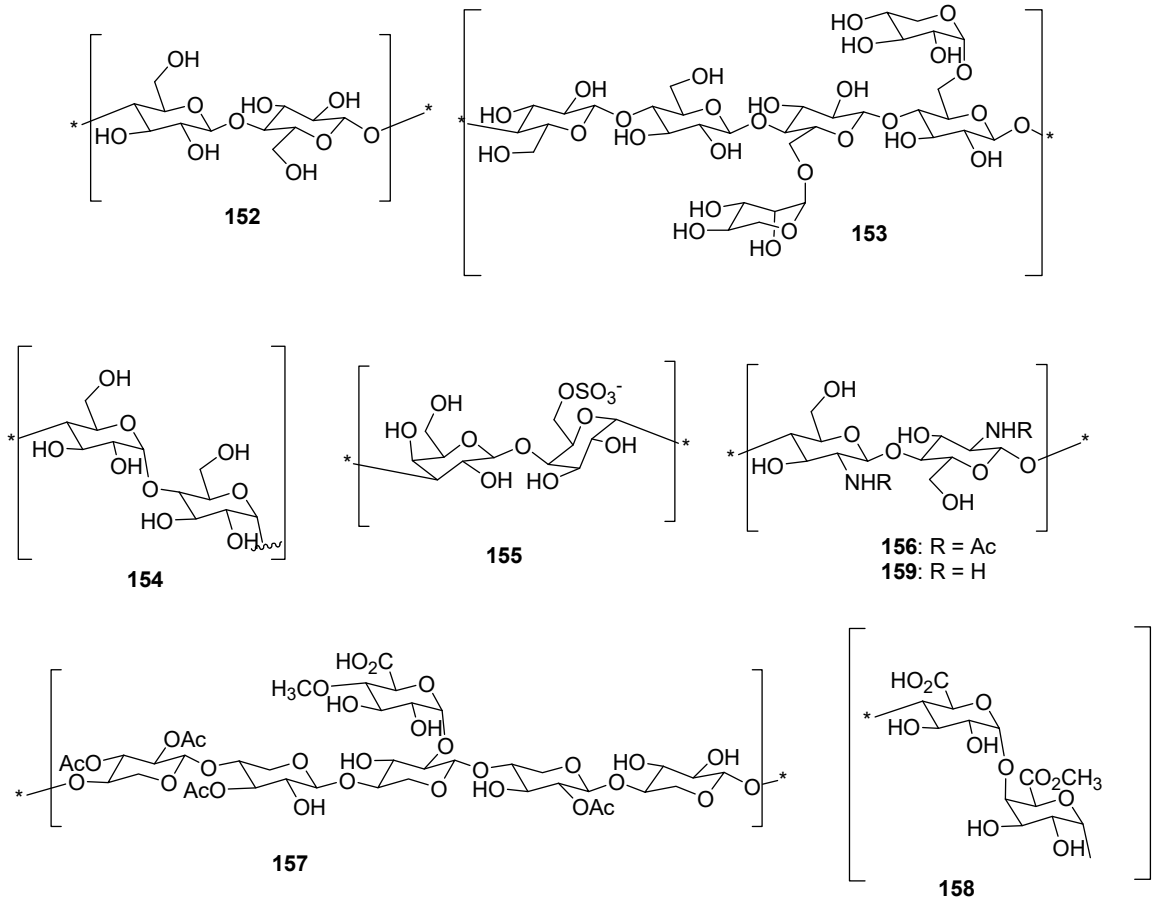


Figure 24. Structural representation of the most important classes of natural sugar polymers. Representing starch, only the amylose **154** is shown.

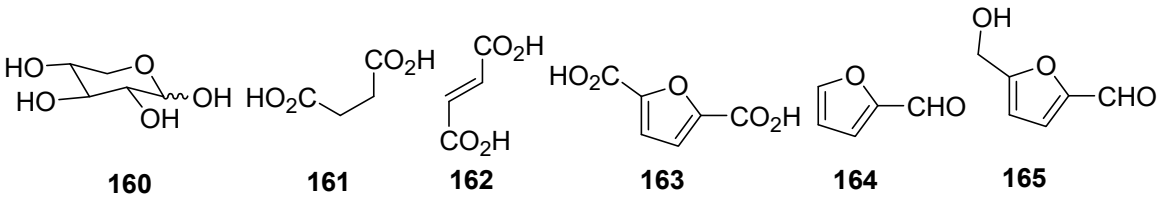


Figure 25. Typical small organic molecules obtained by the deconstruction of polysaccharides.

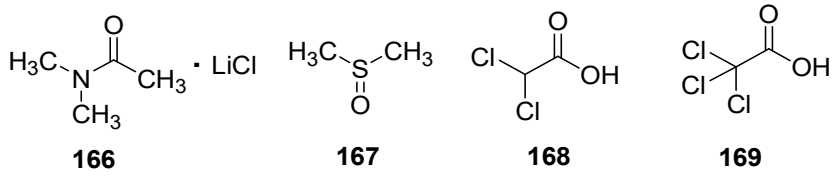


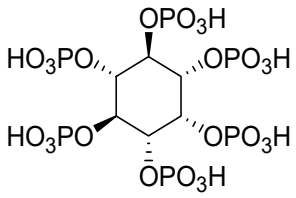
Figure 26. Typical classical solvent systems for the dissolution of polysaccharides including cellulose.

With the current focus on biomass valorization it has also been found that some agricultural wastes have the thus far non-utilized potential to be a source of plant proteins with nutritional characteristics similar to those of animal proteins [126,127]. For the extraction of

proteins from biomass, the extraction efficiency as well as the degree of protein degradation are two important factors to consider. For the extraction process, organic solvents can for the most part not be used as solvent remnants would make the extracts unusable in food production. In aqueous solvents, at elevated pH values, that is under basic conditions, there is significant degradation, including denaturation of the proteins, while in acidic medium there is reduced cell wall degradation [128]. The use of enzymatic processes and the use of reverse micelles in protein extraction from biomass have led to advances but are still too costly to be economical processes [126,127]. This is one of the reasons that DESs have found entry as solvents for the extraction of proteins, also with the idea that DESs could stabilize protein structures in the extracts.

3.2.1. Applications of DESs for Protein Extraction

Deep eutectic solvents can be used to obtain protein isolates from various plant-based samples. Thus, Karimi et al. [129] extracted protein from cold-pressed Canola rapeseed (*Brassica napus*) meal using ChCl-based DESs. The samples were first defatted with *n*-hexane. Thereafter, the samples were tested with four different DESs-ChCl (**1**) with D-sorbitol (**115**), glycerol (**18**), D-glucose (**29**), and urea (**14**). Also, the group compared the tested DESs with conventional alkaline treatment methods that are normally used to isolate proteins at pH 12 and pH 9. All tested DES formulations contained water during their preparation. A molar ratio HBA ChCl: HBD (sugars, glycerol, or urea): water of 1:2:1 was used. All tested DESs showed a higher protein extraction efficiency (44.2% to 52.9%) than the conventional alkaline method at pH 9 (39.2%). A better color characteristic was found when using DESs as compared to the conventional alkaline method at pH 12. Among all the tested DESs, ChCl-urea-water at a ratio of 1:2:1 led to the largest amounts of protein extracted (52.9%), gave the best color, and exhibited the lowest phytic acid (inositol hexaphosphate, **170**, Figure 27) content (25.4 mg/g). It must be noted that phytic acid is known to complex certain dietary trace elements such as calcium, iron and zinc, forming precipitates and inhibiting the resorption of these elements in the small intestine [130]. To separate the protein isolates from the DESs, the group used a dialysis bag with a molecular cutoff of 3.5 KDa. The dialysis bag separation technique seemed the best option, as many other "back extraction" techniques are still not effective. The starting material utilized here is not costly as it is a waste from rapeseed pressing, and the filtration membrane techniques currently are scalable and affordable [129,131].



170

Figure 27. Structure of phytic acid (**170**).

In this respect, another research group also used a dialysis bag with a molecular cutoff of 3.5 KDa to separate fava bean (*Vicia faba* L.) protein utilizing a DES made of ChCl- glycerol-water [132]. The fava beans used were dehulled and tannin free. The optimized conditions were found to be a ChCl:glycerol ratio of 1:2 with 40% water (*w*/*w*) for the DES, and a DES to sample ratio of 28:1 (*w*/*w*). The best extraction results were obtained at 50 °C and after 1 h extraction. Applying these conditions, the DES used showed a similar protein content (92.3%) as compared to the alkaline method at pH 9.5

(92.5%). However, experiments carried out under optimized DES conditions showed a higher protein yield (65.4%) and recovery rate (23.2%) than were obtained with the alkaline method (60.8% protein yield) and (21.8% recovery rate), respectively [132].

3.2.2. Biomass Utilization from Lignocellulosic Agricultural Waste Using DES for the Extraction of Keratin, Cellulose, Lignins, and Others

As stated above, lignocellulose represents one of the most abundant renewable material resources on earth. It is composed of cellulose (40–45%), hemicellulose (15–30%) and lignin (16–33%), where frequently lignin is covalently bound to hemicellulose. Often, hemicellulose encapsulates cellulose and hinders enzymatic hydrolysis of cellulose to defined smaller organic molecules. Therefore, in order to acquire defined products from lignocellulose effectively, it is important to separate lignin from cellulose/hemicellulose first. Then, cellulose can be used as a material in its own right, or cellulose and hemicellulose can be transformed enzymatically to pentoses and hexoses and then further to furfural (**164**) and 5-hydroxymethylfurfural (**165**). Vanillin (**171**, Figure 28) and dimethyl sulfoxide (**167**) among other small chemicals such as phenols can be obtained from lignin. A number of methods have been developed for the separation of lignin from cellulose/hemicellulose such as the alkaline-assisted pre-treatment [133], the organosolv process [134], and the oxygen delignification [135]. However, in recent times, more and more processes involving DESs for the separation and/or removal of lignin have been published. Thus, Ji et al. [136] removed lignin from garlic skin and green onion roots as vegetable wastes. Here, the group used a ternary DES (TDES) consisting of choline chloride (ChCl, **1**) as HBA, and glycerin, oxalic acid, or urea and a metal chloride as HBD, where the treatment of the wastes happened under ultrasonication and microwave irradiation. The best TDS proved to be ChCl-Gly-$AlCl_3 \cdot 6\ H_2O$ (1:2:0.2) for which a lignin removal rate of 90.14% and 92.34% was achieved for garlic skin and green onion skin, respectively. The group saw this as a high-performance pretreatment method for effective lignocellulose deconstruction.

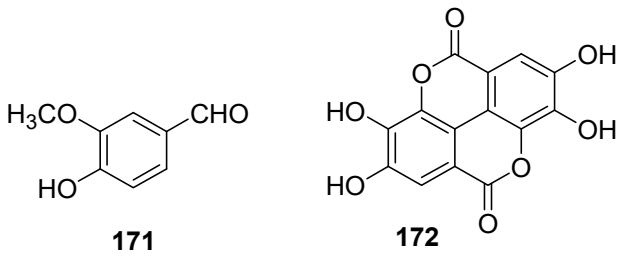


Figure 28. Structures of vanillin (**171**) and ellagic acid (**172**).

In 2022, Moccia and coworkers [137], developed a multistep protocol using DESs for the extraction of ellagic acid (**172**) and lignin rich material from chestnut wood fibers. First, the chestnut wood fiber was treated mildly with a DES made of ChCl (**1**) and tartaric acid (**65**) in a 1:2 molar ratio with 20w% H_2O to obtain the ellagic acid (**172**) rich fraction. In this step, 100 g solid/kg solvent were stirred for 90 min at 50 °C. The solution was centrifuged. Then the obtained supernatant was poured into a 1% aq. KCl solution and kept for 4h at room temperature to allow for the precipitation of the target compound, ellagic acid (**172**). The precipitate obtained was centrifuged and then washed three times with 1% KCl. This procedure gave 75 mg ellagic acid (**172**, Figure 28) from 1 g chestnut wood fibers. The second step of the process involved the reuse of the extracted chestnut wood fibers by treating them with ChCl (**1**)—lactic acid (**21**) in a 1:2 molar ratio with 20w% H_2O, but now under much harsher conditions, to obtain a guaiacyl-syringyl lignin rich fraction. Here, 100 g solid/kg solvent were stirred for 8h at 120 °C. The solution obtained was centrifuged, and the resulting dark brown liquid was poured into either a 1w% aq.

KCl solution or into 0.01M HCl and kept overnight at 4 °C. The formed precipitate was recovered by centrifugation and washed three times with 1% KCl or 0.01 M HCl and lyophilized. This gave 50 mg yield for 1 g of chestnut wood fibers used as starting material in step 1. To recover the (1:2) ChCl-lactic acid DES from the second step, the water that remained after the lignin extraction was removed under vacuum rotary evaporation. The recovered DES was reused in another extraction cycle and gave 4% *w*/*w* yield with respect to the starting chestnut wood fibers [137]. Meanwhile, Li et al. [138] have looked at a new process of obtaining cellulose nanofibers from okara, a water-insoluble residue remaining when pureed soybeans are filtered in tofu and soybean milk production. The degreasing, deproteinization and cellulose extraction from okara were studied with the different DESs ChCl-Gly, ChCl-Ox and ChCl-urea. Thereafter, the treated products were subjected to high pressure homogenization. ChCl-Ox pretreatment with subsequent high pressure homogenization gave cellulose nanofibers with a diameter of 20–25 nm. It must be noted that nanocellulose is used as food stabilizer, dietary fiber, thickener, flavor carrier, and can also be used to diminish the caloric value of food [139].

3.3. The Use of DES in Food Preservation

Food preservation is seen to become an increasingly important issue, especially when food needs to be stored for longer periods of time because of delays in the supply chain or because of the unavailability of fresh food for long periods of time. Diverse gums, polysaccharide exudants from plants, have been used as food coating. Examples are Persian gum from almond [140], traganth gum from shrimps [141] and gellan gum from mushrooms [142]. In this regard, Fang et al. [143] found that NADES can form a eutectogel with durian (*Durio zibethinus*) gum. Eutectogels [144,145] are an emerging class of soft ionic materials that complement the more temperature-intolerant hydrogels and the more costly ionogels. Eutectogels have also been formed with xanthan gum as gelator and NADES, prepared from choline chloride–xylitol (ChCl–Xyl, 1:1), choline chloride–glycerol (ChCl–Gly, 1:2), choline chloride–sorbitol (m, 1:1), and choline chloride–citric acid (ChCl–Cit, 1:1) [146]. Water is necessary for the gelation to proceed with the possible exception of ChCl-Gly, where weak gel formation was noted even under anhydrous conditions. Proper annealing treatment is also necessary for the eutectogel formation, although mixing temperatures of 80 °C were found to be sufficient.

Deep Eutectic Solvents for Fruit Preservation Applications

Wan and coworkers [147] developed active packaging materials with moisture regulating properties for fruits and vegetables based on DESs. In this case the produce to be packaged were cherry tomatoes (*Solanum lycopersicum* L.). The developed active packaging materials were made by using gelatin plasticized with, separately, two different DESs. The tested DESs were (1:2) ChCl-glycerol (CG) and (1:2) betaine-glycerol (BG). The active packaging materials were made as films using the solution-casting method, and their effect on the quality of fresh cherry tomatoes was studied for 9 days. The films were tested in comparison to polythene wrapping (PE), gelatin films (Gel) and gelatin-glycerin cast films (Gel + Gly). After 9 days, the degree of spoilage was in the order PE > Gel > Gel + Gly > CG~BG.

The quality attributes of the samples were also tested at day 0 and after 9 days. The CG and BG boxes showed fruits with less bacterial count (5.54 and 5.29 log CFU g^{-1}) than the control group (C) and the other reference samples (7.51 for C, 7.70 for PE, 6.98 for Gel, and 6.33 for Gel + Gly log CFU g^{-1}). Also, CG and BG boxes showed fruits with higher firmness levels (7.57 and 7.50 N, respectively) than the control and the PE samples (6.93 and 4.53 N, respectively). The water content was 91.20% and 92.46% for the fruits placed in CG and BG

boxes, respectively. While it was 91.97% for the ones in the C and 94.43% for the fruits in the PE boxes, respectively. The total soluble solids (TSS) were 3.53 °Brix and 3.00 °Brix for the CG and BG samples, respectively, while it was 3.28 °Brix and 1.98 °Brix for the control and the PE samples. The pH was 4.38 and 4.42 for the CG and the BG fruit samples, respectively. On the other hand, it was 4.27 and 5.26 for the control and the PE fruit samples. Titratable acid was 0.03 g/L for the CG, BG, and control fruit samples, however it was 0.01 for the PE fruit sample [147]. Further studies by Wan et al. [148] were carried out using different concentrations of ChCl-glycerol in water to produce the DES-derived packaging films. The fruit preservation experiments with these films demonstrated that DES-based films have the ability to control the fruit spoilage effectively while at the same time maintaining a stable packaging relative humidity (RH).

Also, one can use DES solvents to coat fruits directly for post-harvest preservation applications. For instance, Gupta and coworkers [149] studied the effect of using starch-based coating modified with DESs on the quality of stored strawberries (*Fragaria* × *ananassa Duch. cv. Sweet Charlie*). The starch used had a high amylose content and was derived from Joymoti rice (*Oryza sativa* L.). It had an amylose starch content of 26.06%. The studied DES was prepared from (5:1) lactic acid-fructose, from which different coating solutions were made using different starch percentages. The studied coatings had starch contents ranging from 0% as the control sample (N0) to 10% (N10). They were simply prepared by mixing the appropriate amount of starch with the synthesized DES for 25 min while stirring at 70 °C. After sterilizing the strawberries with 200 mg/kg chlorinated water and drying them, they were dipped into the DES-starch solution and kept to dry at room temperature for 30 min. Then they were stored in polyethylene terephthalate clamshell boxes that have venting holes and kept stored for 18 days at 20 °C.

The quality attributes were monitored during the storage period. The firmness level was found to decrease in all samples during the storing period. However, it was reduced by only about 27% in N10 sample while in the control sample the reduction was up to 59% at the end of the storage period. In terms of fruit weight loss, all the coated samples showed a significant reduction in weight loss during the storage period compared to the control sample. The best reduction in weight loss at the end of the storing period was for the N6 sample where the weight was reduced by approximately 21%, while the weight of the control sample was reduced by more than 40%. For the TSS, all the coated samples showed less reduction percentages of TSS compared to the control sample. On day 18, N10 showed approximately 4.1% TSS while the control sample showed approximately 1% of TSS. The ascorbic acid content was reduced for all samples during the storing period however all the coated samples slowed down its reduction compared to the control sample. At the end of the storage period, the control sample showed an approximate value of 11 mg/100 g of ascorbic acid, however, the N10 sample showed an approximate value of 29 mg/100 of ascorbic acid. In terms of fruits appearance, all samples showed a decrease in the redness of the fruits skin. Nevertheless, the coated ones showed lower reduction percentages. The red color of the control samples showed a reduction of redness of around 83% while for N10 it was around 45% at the end of the storing period. For the microbial growth, the control sample on day 9 and day 12 showed a yeast and mold count of 1.4×10^2 and 2.9×10^2 cfu/mL, respectively, and the sample was spoiled by day 15. However, none of the coated samples showed any yeast and mold count until day 15. On day 18, they showed a yeast and mold count, where the lowest count was for N10 samples with a value of 10 cfu/mL [149].

3.4. In-Situ DES Formation for Food Analysis and the Purification of Food Additives

DESs/NADES can be utilized in solvent-based extraction techniques for food analysis [150]. Thus, Zhu and coworkers [151] developed a new method to isolate antioxidants that had migrated from food packaging materials into food products. Measuring migrated antioxidants from food packaging materials is of significance as high migration levels into food can pose health problems, and in extreme cases can contribute to cancer, the disruption of the endocrine system, and to the damage of the immune system [152,153]. There are regulations for the limit of antioxidant migration from food contact materials into food, known as the specific migration limits (SML) of antioxidants. In China, the national food safety standard (GB 9685-2016 [154]) states that the SML for BHA and BHT is 30 mg/kg. In Europe, the European Union Commission Regulation No 10/2011 gives a value of 3 mg/kg [151]. The method developed by Zhu et al. relies on the use of low toxicity medium chain fatty acid alcohol as an HBA, while the antioxidants that have migrated to the food product should act as an HBD [151]. Shi et al. [155] used parabens as HBDs for the in-situ formation of hydrophobic DES for the extraction of fluorescent brightener 52 (FWA52 [FWA140], **173**) from food and food-contacting materials [155]. In their method, four different HBDs were tested from the paraben family, namely, methyl 4-hydroxybenzoate (**174**), butyl 4-hydroxybenzoate (**175**), n-octyl 4-hydroxybenzoate (**176**), and 2-ethylhexyl 4-hydroxybenzoate (**177**). Among the four, 2-ethylhexyl 4-hydroxybenzoate (**177**, EE) showed the highest extraction efficiency (almost quantitative) and was the best for the in-situ formation of the DES with FWA52 (**173**) (Figure 29).

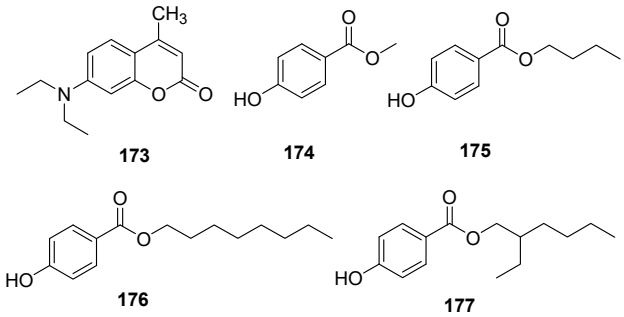


Figure 29. Fluorescent brightener FWA-52 (**173**) and parabens **174**–**177** to form DES in situ for the extraction and quantification of FWA-52 in foods [155].

Contents of natural oils can be quantified by DES extraction using the ultrasound-assisted liquid–liquid microextraction (UALLME) method with subsequent direct injection of the DES phase into a HPLC system. The work of Liu et al. [156] gives an example of this, where ChCl was mixed with cresol (**178**) to give a DES, which was used to extract sesame oil. Direct injection into reversed phase HPLC system led to the quantification of the lignans sesamol (**179**), sesamolin (**180**), and sesamin (**181**) (Figure 30).

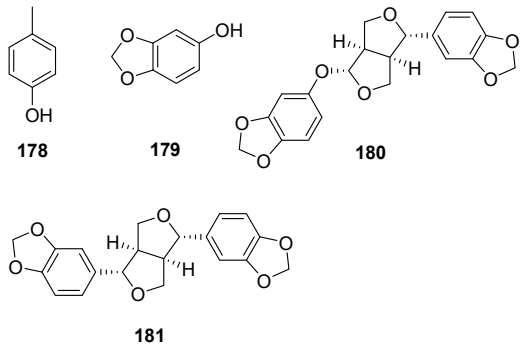


Figure 30. Sesamol (**179**), sesamolin (**180**), and sesamin (**181**) extracted from sesame oil with DES based on *p*-cresol (**178**) and ChCl (**1**) and quantified by HPLC by direct injection of the DES phase [156].

Also, the extraction of polar natural antioxidants with DES/NADES systems with subsequent electrochemical quantification with a screen-printed electrode has been advocated [157].

Oftentimes, natural food additives incorporate unwanted components that either shorten the shelf-life of the product or even present a health hazard to consumers. One such class of contaminants are the unsaturated terpenoids. He and coworkers [158] developed theoretically and experimentally an in-situ deep eutectic solvent-based strategy for the deterpenation of citrus essential oil. In their method, the conductor-like screening model for real solvents (COSMO-RS) and density functional theory (DFT) were used to model the interactions between a set of organic salt extractants and the target terpenes in the essential oil. The COSMO-RS method was used initially to find which of the components would act as a HBD and which would act as a HBA. This was based on the use of the charge density (σ) which was utilized to calculate the interaction energy between the tested organic salts and the terpenoids/terpenes formed by misfit, hydrogen bonding, and van der Waals interactions [158]. Experimentally, tetrabutylammonium chloride (**8**, TBAC) was used to extract the hydroxyl-terpenoids linalool (**182**), menthol (**10**) and α-terpineol (**183**), present in essential oils. Similarly, Li et al. [159] utilized associative extraction with TBAC to extract limonene (**184**) and linalool (**182**) from citrus essential oil. The two compounds could be obtained in pure form by re-extraction of the formed DES by the stepwise addition of "anti-extractants", first of hexane to re-extract limonene and then a mixture of water and hexane to extract linalool (**182**) (Figure 31).

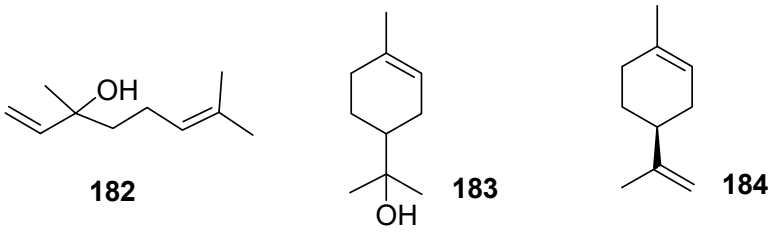


Figure 31. Linalool (**182**) and α-terpineol (**183**) as examples of hydroxyl-terpenoids that can be extracted with TBAC (**8**) from essential oils [158]. Limonene (**184**) and linalool (**182**) could be extracted with TBAC, with separate back extractions for the two compounds using hexane and subsequently water-hexane [159].

3.5. DESs for Flavor and Food Texture Enhancement

DES can be used to enhance the texture of food products. In this regard, Liu et al. [160] prepared a protein-based emulsion with the use of a ChCl and glycerol derived DES as the bulk solution that resulted in an enhanced freeze-thaw stability emulsion. The DES was prepared by mixing (1:2) ChCl-glycerol and then diluting it to 25 wt%, 50 wt%, and 75 wt% by adding water. Wheat gluten protein was used to form the emulsion under study while soy protein isolate was used as a control sample. The two proteins were dispersed separately in the DES solutions, and then sunflower oil was added to them. After that, the solutions were homogenized to yield suspensions. The DES shows a great advantage in such applications as it keeps water in the liquid state at low temperatures. It was found that the melting point of 75% DES, 50% DES and 25% DES was −31.70 °C, −28.93 °C, −23.80 °C, respectively which is much lower than the melting point of pure water (0 °C). This is a great trait of DES as the addition of the DES can change the nucleation and crystal growth in the water phases at low temperatures, resulting in the preparation of more stable freeze-thaw emulsions [14,160]. The surface protein load (Γ) of the emulsion increased with an increase of the concentration of the DES, where the highest protein content was 8.12 mg/m^2 for the 75% DES wheat gluten emulsion compared to 3.33 mg/m^2 for the 75% soy protein isolate emulsions. The freeze-thaw stability of the emulsion was studied with a confocal laser

scanning microscope (CLSM), by observing the change of the emulsion structures during successive freeze-thaw cycles (for one cycle: −40 °C, 24 h; 25 °C, 2 h). Interestingly, the 75% DES wheat gluten emulsion had no structural changes even after the third cycle. It was found that the type of the protein also affects the emulsion stability, as some structural changes were noted when the 75% DES soy protein emulsion was processed under the same conditions. These findings can help in the development of oil emulsions as ingredients that can be used in the preparation of frozen meat products like surimi or in new types of products such as those developed in molecular gastronomy and that necessitate flash freezing [160].

NADESs have been used as a reaction medium to synthesize different Maillard-type food enhancers. The increasing demand for healthier products with the use of fewer amounts of table salt, sugar, and mono sodium glutamate, and the growing dislike by certain consumers of the addition of non-natural components to food provide an incentive for the development of novel food enhancers that are isolated from nature or synthesized from food-grade kitchen-type chemical reactions such as the Maillard reaction [161]. Kranz and Hofmann studied the use of different NADESs as reaction media to synthesize the three food enhancers 1-deoxy-D-fructosyl-*N*-β-alanyl-L-histidine (**185**), N^2-(1-carboxyethyl)guanosine-5′-monophosphate (**186**), (N-(1-methyl-4-oxoimidazolidin-2-ylidene)aminopropionic acid (**187**) [161]. The NADES studied include (4:1:4) ChCl-sucrose-water, (1:2:1) ChCl-urea-water, (1:1:5) malic acid-sucrose-water, (1:1:9) glucose-sucrose-water, (2:1:9) betaine-sucrose-water, and (1:2:2) betaine-glycerol-water. The group was able to synthesize the three mentioned food enhancers in improved reaction yields, using NADESs as the reaction medium. Reaction temperatures were relatively low (80–100 °C) and the reactions were complete within 2h. The group was able to achieve a 49% yield for (1-deoxy-D-fructosyl-*N*-β-alanyl-L-histidine) (**185**), a 54% yield for *N*-(1-methyl-4-oxoimidazolidin-2-ylidene)aminopropionic acid (**187**), and a 22% yield for N^2-(1-carboxyethyl) guanosine-5′-monophosphate (**186**) (Figure 32) [161].

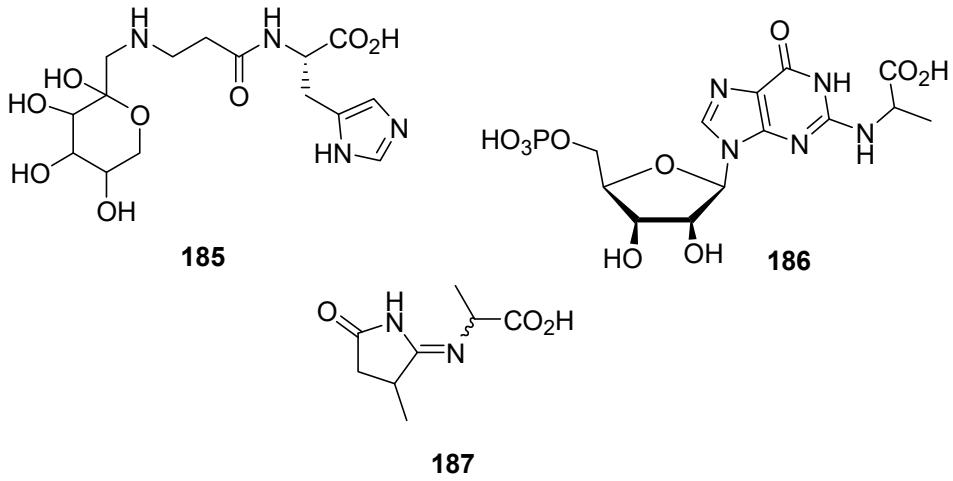


Figure 32. Food enhancers 1-deoxy-D-fructosyl-*N*-β-alanyl-L-histidine (**185**), N^2-(1-carboxyethyl)guanosine-5′-monophosphate (**186**), and (N-(1-methyl-4-oxoimidazolidin-2-ylidene)aminopropionic acid (**187**) prepared in an aq. NADES medium [161].

In general, thermal food processing using aqueous, low-moisture, lipid, or lipid emulsions and self-assembled lipid structures reaction systems to prepare such Maillard-type food enhancing compounds suffer from such limitations as low yield, typically in the range of 1–2%, low solubility of the educts in the reaction system, hydrolytic instability of the reaction products, and often the tendency of products or starting materials to polymerize

at high temperature [161–163]. This is where NADESs as reaction media can help as could be seen above.

Xu and coworkers [164] studied the effect of using different DESs derived from ginger extracts on the reduction of harmful compounds that are generated during the thermal processing of food by means of chemical reactions, including the Maillard reaction. Their results on roasted beef meat patties showed that many DESs can be applied to such food products to decrease the development of a number of unhealthy heterocyclic amines and advanced glycation end products. The addition of DESs has no significant effect on the texture of the meat patties [164].

4. Considerations on the Commercialization of NADES

Many studies involving NADES in food science and food processing are carried out in research laboratories at lab-scale. This is especially true for the use of NADES for the extraction of biomolecules from plants and biowastes. Industrial scale use of DES in the paper-making industry is taking form, where cellulose needs to be separated from lignin (see Section 3.2.2).

For commercialization of a process, cost is a key consideration. At time of writing this review, the cost of 1 ton of choline chloride was ca. US$ 1070 [165]. 1 ton of ethylene glycol went for US$ 550–650 [166], 1 ton of sugar for US$ 500–550 [167]. This compares with US$ 380–400 for methanol [168], ca. US$ 820 for ethanol per ton [169], US$ 450 for dichloromethane per ton [170], and US$ 1190 for hexane [171]. While prices of traditional solvent systems and deep eutectic solvent systems compare, it must be realized that in DES/NADES extractions often higher solvent to biomass ratios are used than in traditional extractions using aq. ethanol. DES/NADES extractions usually take less time and run at lower temperatures than comparable extractions with aq. ethanol. This saves on energy costs and needed reactor space. The significant difference between DES/NADES extractions and traditional extractions with polar low weight molecules is the isolation of the extracted compounds from the solvent system and the subsequent recycling of the solvent. In the case of ethanol or a similar solvent, the solvent can be stripped off relatively easily and can then be re-used. This saves on costs. As discussed above, the isolation of the extracted components from DES/NADES in most cases turns out to be difficult, giving those processes an advantage in which no separation of NADES and extract is necessary as NADES remains a part of the product.

Commercialization of NADES utilization in food preservation and for flavor and food texture enhancement is most likely more straightforward [172]. Here, NADES is not separated from the product.

Especially in those cases where DES/NADES constituents are not separated from the final food product, it is of utmost importance to have a good understanding of any potential toxicity linked to DES/NADES. It has been noted that DES/NADES toxicity is a complicated subject as one needs to look at potential hazards linked to each constituent component as well as the entire DES structure [42]. Although initial findings suggest that specific DES formulations may be more biodegradable and less harmful than typical organic solvents, more study on this topic needs to be carried out.

Regulatory constraints must also be taken into account. For instance, regulations on solvents used as extractants in the food industry in the European Community (EC) are governed by Directive 2009/32/EC and its amendments [173]. It must be noted, however, that due to environmental concerns also traditional solvents such as dichloromethane, which has been used in hop and coffee extractions [174], are seeing regulatory changes. Thus, the use of dichloromethane will be restricted significantly over the next few years [175]. In many cases, NADES may offer themselves as alternative, more friendly solvent systems.

5. Shifting from Petroleum-Based Solvents to Green DES Solvents: Will Start-Up Companies Accelerate This Movement?

Innovation in the chemical industry is not a new concept. It has just changed from a traditional R & D that is held religiously within companies' labs to a more open form where established companies are working with external partners and startup companies. This shift was accelerated by several factors: (a.) the increased use of business models that are closer to end applications. This means more interaction between a chemical company with downstream manufactures and with customers; (b.) the growing power of digital technology, which helps companies to interact more easily, where new digital technology tasks are often outsourced; (c.) an increase of sustainability requirements from the side of regulators, investors, and customers. This requires manufacturers of materials and additives to collaborate to produce environmentally oriented products; (d.) advancing commoditization, which pushes the use of novel technologies and capabilities such as advanced analytics to enhance production efficiency and lower costs. Start-up companies play an important role in shaping the future of the chemical industry, as they are involved in the collaborative innovation strategies of many chemical companies. There are several strategies that chemical companies follow to increase their collaborative innovations. Competitions and crowd-sourcing is one strategy that chemical companies follow to have access to early-stage ideas and offerings. In some cases, interactions within such activities can lead to a contentious relationship between the chemical companies and the startup companies [176].

New start-up companies are emerging worldwide for the development of DESs. These companies could help in the development of more sustainable chemical processes and research environments, should they succeed in the production and commercialization of their products and find sufficient support from chemical industrial partners and other investors. Thus, startups alone cannot change the chemical industry. Established chemical companies also have an important role to play. They have many options to foster collaborative innovations, from offering their own venture capital investment, working on fast and efficient partnership models, to partnering with academia and innovation hubs [176,177].

Examples of such companies focusing on the development of DES/NADES and their applications include bioeutectics, Des Solutio, and Nades Design. Bioeutectics is working on the development of more than 200 products related to DESs. Des Solutio is a spin-off company that has a database of more than 600 NADES formulations that are fully characterized and tested. They provide tailor-made solutions for customers in addition to consultancy and research and development services. Nades Design offers the service of producing custom-made NADESs according to the problems and requirements of the customer. The world is waiting for a change from the chemical industry both to meet the demands of rapidly changing global communities and to take advantage of the unprecedented speed of technological development. However, for such a change, significant innovation is needed. This can be achieved by proper collaboration between incumbents, investors, and startups [177].

6. Conclusions

Natural Deep Eutectic Solvents (NADES), a class of solvents composed of natural, non-toxic components, often including a mixture of a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA), such as sugars, amino acids, organic acids, and choline chloride, have gained increasing attention for their potential in extracting valuable biomolecules from biomass, including fruit pomace and food waste. Their ability to disrupt cell walls and cell membranes in plant tissues enhances the release of these biomolecules. As many NADES components are naturally occurring and generally recognized as safe (GRAS),

meaning they can be safely consumed or used in food without significant risk, NADES can often remain in the extract and still be safe for use in food products. On the other hand, when trying to extract or purify biomolecules from NADES, processes like phase separation or the addition of solvents may sometimes be inefficient, leading to low yields or to contamination of the final products. Also, recycling NADES is not always straightforward because of their tendency to degrade or lose their solvent properties over time, especially under industrial processing conditions (e.g., high temperatures, repeated exposure to air, or the presence of moisture). Here, there is certainly room for additional research. Also, more work needs to be devoted to the scale-up of operations.

In this review, different applications for the use of NADES in food and agricultural applications were discussed. Those solvents have become "attractive" solvents compared to petroleum-based solvents because of their "greener" nature. R&D in the field of chemistry is becoming more open due to a shift of the chemical industry to more sustainable processes, of which NADES can be part. Innovation in this area is certainly needed to find easier ways of separation of NADES from the extracted components, to scale up operations and to recycle NADES with a minimum of waste and a minimum of energy input.

Author Contributions: Conceptualization, R.A. and T.T.; methodology, R.A. and T.T.; investigation, R.A. and T.T.; resources, T.T.; writing—original draft preparation, R.A. and T.T.; writing—review and editing, T.T.; visualization, R.A.; supervision, T.T.; project administration, T.T. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

AAE	ascorbic acid equivalent(s)
ABTS	2-azino-bis-3-ethylbenzothiazoline-6-sulphonic acid
AC	acetic acid
CE	cyanidin equivalent(s)
CGE	cyanidin-3-glucoside equivalent
ChCl	choline chloride
Cit	citric acid
CLSM	confocal laser scanning microscope
DES	deep eutectic solvent
DPPH	2,2-diphenyl-1-picrylhydrazyl
ECE	epicatechin equivalent
ESI-QAD-TOF	Electrospray ionization-quadrupole time-of-flight-mass spectrometry
GAE	gallic acid equivalent(s)
Gel	Gelatine
Gly	glycerine/glycerol
HBA	hydrogen bond acceptor
HBD	hydrogen bond donor
HPLC-DAD-MS	high performance liquid chromatography–diode array detection–mass spectrometry
LA	lactic acid
LALP	lipid peroxidation inhibition assay
MA	malic acid
NADES	natural deep eutectic solvent
OAE	oleanolic acid equivalent(s)
Ox	oxalic acid
PCM	polarizable continuum model
PE	Polythene

PhMo	Phosphomolybdenum
Pro	Proline
QE	quercetin equivalent(s)
SML	specific migration limits
Sor	Sorbitol
TBAC	tetrabutylammonium chloride
TDES	ternary deep eutectic solvent
TE	Trolox equivalent(s)
TSS	total soluble solids
UHPLC	Ultra-high-performance liquid chromatography
Xyl	Xylitol
Xylo	Xylose

References

1. Abbott, A.P.; Capper, G.; Davies, D.L.; Rasheed, R.K.; Tambyrajah, V. Novel solvent properties of choline chloride urea mixtures. *Chem. Commun.* **2003**, 70–71. [CrossRef]
2. Wilkes, J.S.; Levisky, J.A.; Wilson, R.A.; Hussey, C.L. Dialkylimidazolium chloroaluminate melts: A new class of room-temperature ionic liquids for electrochemistry, spectroscopy and synthesis. *Inorg. Chem.* **1982**, *21*, 1263–1264. [CrossRef]
3. Liu, X.; Zhai, Y.; Xu, Z.; Zhu, Y.; Zhou, Y.; Wang, Z.; Liu, L.; Ren, W.; Xie, Y.; Li, C.; et al. The novel application of type II deep eutectic solvents (DES) for sludge dewatering. *Sep. Purif. Technol.* **2023**, *306B*, 122714. [CrossRef]
4. Smith, E.L.; Abbott, A.P.; Ryder, K.S. Deep Eutectic Solvents (DESs) and their applications. *Chem. Rev.* **2014**, *114*, 11060–11082. [CrossRef]
5. Li, X.; Row, K.H. Development of deep eutectic solvents applied in extraction and separation. *J. Sep. Sci.* **2016**, *39*, 3505–3520. [CrossRef] [PubMed]
6. Gontrani, L.; Donia, D.T.; Bauer, E.M.; Tagliatesta, P.; Carbone, M. Novel synthesis of zinc oxide nanoparticles from type IV deep eutectic solvents. *Inorganica Chim. Acta* **2023**, *545*, 121268. [CrossRef]
7. Yuan, Z.; Liu, H.; Yong, W.F.; She, Q.; Esteban, J. Status and advances of deep eutectic solvents for metal separation and recovery. *Green Chem.* **2022**, *24*, 1859–1929. [CrossRef]
8. Abranches, D.O.; Martins, M.A.R.; Silva, L.P.; Schaeffer, N.; Pinho, S.P.; Coutinho, J.A.P. Phenolic hydrogen bond donors in the formation of non-ionic deep eutectic solvents: The quest for type V DES. *Chem. Commun.* **2019**, *55*, 10253–10256. [CrossRef]
9. Liu, Y.; Friesen, J.B.; McAlpine, J.B.; Lankin, D.C.; Chen, S.N.; Pauli, G.F. Natural Deep Eutectic Solvents: Properties, applications, and perspectives. *J. Nat. Prod.* **2018**, *81*, 679–690. [CrossRef]
10. Choi, Y.H.; van Spronsen, J.; Dai, Y.; Verberne, M.; Hollmann, F.; Arends, I.W.C.E.; Witkamp, G.-J.; Verpoorte, R. Are natural deep eutectic solvents the missing link in understanding cellular metabolism and physiology? *Plant Physiol.* **2011**, *156*, 1701–1705. [CrossRef] [PubMed]
11. Dai, Y.; van Spronsen, J.; Witkamp, G.-J.; Verpoorte, R.; Choi, Y.H. Natural deep eutectic solvents as new potential media for green technology. *Anal. Chim. Acta* **2013**, *766*, 61–68. [CrossRef] [PubMed]
12. Florindo, C.; Oliveira, F.S.; Rebelo, L.P.N.; Fernandes, A.M.; Marrucho, I.M. Insights into the synthesis and properties of deep eutectic solvents based on cholinium chloride and carboxylic acids. *ACS Sustain. Chem. Eng.* **2014**, *2*, 2416–2425. [CrossRef]
13. Hammond, O.S.; Bowron, D.T.; Edler, K.J. The effect of water upon deep eutectic solvent nanostructure: An unusual transition from ionic mixture to aqueous solution. *Angew. Chem.* **2017**, *56*, 9782–9785. [CrossRef] [PubMed]
14. Dai, Y.; Witkamp, G.-J.; Verpoorte, R.; Choi, Y.H. Tailoring properties of natural deep eutectic solvents with water to facilitate their applications. *Food Chem.* **2015**, *187*, 14–19. [CrossRef]
15. Negi, T.; Kumar, A.; Sharma, S.K.; Rawat, N.; Saini, D.; Sirohi, R.; Prakash, O.; Dubey, A.; Dutta, A.; Shahi, N.C. Deep eutectic solvents: Preparation, properties, and food applications. *Heliyon* **2024**, *10*, e28784. [CrossRef]
16. Bajkacz, S.; Adamek, J. Development of a method based on natural deep eutectic solvents for extraction of flavonoids from food samples. *Food Anal. Methods* **2018**, *11*, 1330–1344. [CrossRef]
17. Chen, X.-Q.; Li, Z.-H.; Liu, L.-L.; Wang, H.; Yang, S.-H.; Zhang, J.-S.; Zhang, Y. Green extraction using deep eutectic solvents and antioxidant activities of flavonoids from two fruits of Rubia species. *LWT* **2021**, *148*, 111708. [CrossRef]
18. Alañón, M.E.; Ivanović, M.; Gómez-Caravaca, A.M.; Arráez-Román, D.; Segura-Carretero, A. Choline chloride derivative-based deep eutectic liquids as novel green alternative solvents for extraction of phenolic compounds from olive leaf. *Arab. J. Chem.* **2020**, *13*, 1685–1701. [CrossRef]
19. Zhuang, B.; Dou, L.L.; Li, P.; Liu, E.H. Deep eutectic solvents as green media for extraction of flavonoid glycosides and aglycones from *Platycladi cacumen*. *J. Pharm. Biomed. Anal.* **2017**, *134*, 214–219. [CrossRef]

20. Jeong, K.M.; Zhao, J.; Jin, Y.; Heo, S.R.; Han, S.Y.; Yoo, D.E.; Lee, J. Highly efficient extraction of anthocyanins from grape skin using deep eutectic solvents as green and tunable media. *Arch. Pharmacal Res.* **2015**, *38*, 2143–2152. [CrossRef]
21. Bosiljkov, T.; Dujmić, F.; Cvjetko Bubalo, M.; Hribar, J.; Vidrih, R.; Brnčić, M.; Zlatic, E.; Radojčić Redovniković, I.; Jokić, S. Natural deep eutectic solvents and ultrasound-assisted extraction: Green approaches for extraction of wine lees anthocyanins. *Food Bioprod. Process.* **2017**, *102*, 195–203. [CrossRef]
22. Dai, Y.; Rozema, E.; Verpoorte, R.; Choi, Y.H. Application of natural deep eutectic solvents to the extraction of anthocyanins from *Catharanthus roseus* with high extractability and stability replacing conventional organic solvents. *J. Chromatogr. A* **2016**, *1434*, 50–56. [CrossRef]
23. Benvenutti, L.; Sanchez-Camargo, A.d.P.; Zielinski, A.A.F.; Ferreira, S.R.S. NADES as potential solvents for anthocyanin and pectin extraction from *Myrciaria cauliflora* fruit by-product: In silico and experimental approaches for solvent selection. *J. Mol. Liq.* **2020**, *315*, 113761. [CrossRef]
24. Chen, S.; Xiao, L.; Li, S.; Meng, T.; Wang, L.; Zhang, W. The effect of sonication-synergistic natural deep eutectic solvents on extraction yield, structural and physicochemical properties of pectins extracted from mango peels. *Ultrason. Sonochemistry* **2022**, *86*, 106045. [CrossRef]
25. Chen, M.; Lahaye, M. Natural deep eutectic solvents pretreatment as an aid for pectin extraction from apple pomace. *Food Hydrocoll.* **2021**, *115*, 106601. [CrossRef]
26. Bakirtzi, C.; Triantafyllidou, K.; Makris, D.P. Novel lactic acid-based natural deep eutectic solvents: Efficiency in the ultrasound-assisted extraction of antioxidant polyphenols from common native Greek medicinal plants. *J. Appl. Res. Med. Aromat. Plants* **2016**, *3*, 120–127. [CrossRef]
27. Lanjekar, K.J.; Gokhale, S.; Rathod, V.K. Utilization of waste mango peels for extraction of polyphenolic antioxidants by ultrasound-assisted natural deep eutectic solvent. *Bioresour. Technol. Rep.* **2022**, *18*, 101074. [CrossRef]
28. Wang, T.; Jiao, J.; Gai, Q.-Y.; Wang, P.; Guo, N.; Niu, L.-L.; Fu, Y.-J. Enhanced and green extraction polyphenols and furanocoumarins from Fig (*Ficus carica* L.) leaves using deep eutectic solvents. *J. Pharm. Biomed. Anal.* **2017**, *145*, 339–345. [CrossRef] [PubMed]
29. Yue, J.; Zhu, Z.; Yi, J.; Lan, Y.; Chen, B.; Rao, J. Structure and functionality of oat protein extracted by choline chloride–dihydric alcohol deep eutectic solvent and its water binary mixtures. *Food Hydrocoll.* **2021**, *112*, 106330. [CrossRef]
30. Kumar, K.; Yadav, A.N.; Kumar, V.; Vyas, P.; Dhaliwal, H.S. Food waste: A potential bioresource for extraction of nutraceuticals and bioactive compounds. *Bioresour. Bioprocess.* **2017**, *4*, 18. [CrossRef]
31. Ng, H.S.; Kee, P.E.; Yim, H.S.; Chen, P.T.; Wei, Y.H.; Lan, J.C.W. Recent advances on the sustainable approaches for conversion and reutilization of food wastes to valuable bioproducts. *Bioresour. Technol.* **2020**, *302*, 122889. [CrossRef]
32. Baiano, A. Recovery of biomolecules from food wastes—A review. *Molecules* **2014**, *19*, 14821–14842. [CrossRef] [PubMed]
33. Schieber, A.; Hilt, P.; Streker, P.; Endreβ, H.-U.; Rentschler, C.; Carle, R. A new process of the combined recovery of pectin and phenolic compounds from apple waste. *Innov. Food Sci. Emerg. Technol.* **2003**, *4*, 99–107. [CrossRef]
34. Plazzotta, S.; Manzocco, L. Food waste valorization. In *Saving Food—Production, Supply Chain, Food Waste and Food Consumption*; Academic Press: Cambridge, MA, USA, 2019; pp. 279–313. [CrossRef]
35. Morgana, N.M.; Magdalena, E.; Fernandez, M.A.; Fernanda, S.M. NADES for food industry innovation: Novel bioadditives based on olive oil byproducts. *Food Bioprod. Process.* **2022**, *134*, 193–201. [CrossRef]
36. Ferrentino, G.; Morozova, K.; Mosibo, O.K.; Ramezani, M.; Scampicchio, M. Biorecovery of antioxidants from apple pomace by supercritical fluid extraction. *J. Clean. Prod.* **2018**, *186*, 253–261. [CrossRef]
37. Araújo, M.; Pimentel, F.B.; Alves, R.C.; Oliveira, M.B.P. Phenolic compounds from olive mill wastes: Health effects, analytical approach and application as food antioxidants. *Trends Food Sci. Technol.* **2015**, *45*, 200–211. [CrossRef]
38. Panić, M.; Stojković, M.R.; Kraljić, K.; Škevin, D.; Redovniković, I.R.; Srček, V.G.; Radošević, K. Ready-to-use green polyphenolic extracts from food by-products. *Food Chem.* **2019**, *283*, 628–636. [CrossRef]
39. Jeong, K.M.; Ko, J.; Zhao, J.; Jin, Y.; Yoo, D.E.; Han, S.Y.; Lee, J. Multi-functioning deep eutectic solvents as extraction and storage media for bioactive natural products that are readily applicable to cosmetic products. *J. Clean. Prod.* **2017**, *151*, 87–95. [CrossRef]
40. Radošević, K.; Ćurko, N.; Gaurina Srček, V.; Cvjetko Bubalo, M.; Tomašević, M.; Kovačević Ganić, K.; Radojčić Redovniković, I. Natural deep eutectic solvents as beneficial extractants for enhancement of plant extracts bioactivity. *LWT-Food Sci. Technol.* **2016**, *73*, 45–51. [CrossRef]
41. Radošević, K.; Cvjetko Bubalo, M.; Gaurina Srček, V.; Grgas, D.; Dragičević, T.L.; Radojčić Redovniković, I. Evaluation of toxicity and biodegradability of choline chloride based deep eutectic solvents. *Ecotoxicol. Environ. Saf.* **2015**, *112*, 46–53. [CrossRef]
42. Sharma, A.; Lee, B.-S. Toxicity test profile for deep eutectic solvents: A detailed review and future prospects. *Chemosphere* **2024**, *350*, 141097. [CrossRef] [PubMed]
43. Mišan, A.; Nađpal, J.; Stupar, A.; Pojić, M.; Mandić, A.; Verpoorte, R.; Choi, Y.H. The perspectives of natural deep eutectic solvents in agri-food sector. *Crit. Rev. Food Sci. Nutr.* **2020**, *60*, 2564–2592. [CrossRef]

44. Hikmawanti, N.P.E.; Ramadon, D.; Jantan, I.; Mun'im, A. Natural deep eutectic solvents (NADES): Phytochemical extraction performance enhancer for pharmaceutical and nutraceutical product development. *Plants* **2021**, *10*, 2091. [CrossRef]
45. Aktaş, H.; Kurek, M.A. Deep eutectic solvents for the extraction of polyphenols from food plants. *Food Chem.* **2024**, *444*, 138629. [CrossRef]
46. Skarpalezos, D.; Detsi, A. Deep eutectic solvents as extraction media for valuable flavonoids from natural sources. *Appl. Sci.* **2019**, *9*, 4169. [CrossRef]
47. Mouratoglou, E.; Malliou, V.; Makris, D.P. Novel glycerol-based natural eutectic mixtures and their efficiency in the ultrasound-assisted extraction of antioxidant polyphenols from Agri-food waste biomass. *Waste Biomass Valorization* **2016**, *7*, 1377–1387. [CrossRef]
48. Fernández, M.D.L.Á.; Espino, M.; Gomez, F.J.V.; Silva, M.F. Novel approaches mediated by tailor-made green solvents for the extraction of phenolic compounds from agro-food industrial by-products. *Food Chem.* **2018**, *239*, 671–678. [CrossRef] [PubMed]
49. Singla, R.K.; Dubey, A.K.; Garg, A.; Sharma, R.K.; Fiorino, M.; Ameen, S.M.; Haddad, M.A.; Al-Hiary, M. Natural polyphenols: Chemical classification, definition of classes, subcategories, and structures. *J. AOAC Int.* **2019**, *102*, 1397–1400. [CrossRef] [PubMed]
50. Yao, L.H.; Jiang, Y.M.; Shi, J.; Tomás-Barberán, F.A.; Datta, N.; Singanusong, R.; Chen, S.S. Flavonoids in food and their health benefits. *Plant Foods Hum. Nutr.* **2004**, *59*, 113–122. [CrossRef]
51. Ali, M.C.; Chen, J.; Zhang, H.; Li, Z.; Zhao, L.; Qiu, H. Effective extraction of flavonoids from *Lycium barbarum* L. fruits by deep eutectic solvents-based ultrasound-assisted extraction. *Talanta* **2019**, *203*, 16–22. [CrossRef]
52. Bi, W.; Tian, M.; Row, K.H. Evaluation of alcohol-based deep eutectic solvent in extraction and determination of flavonoids with response surface methodology optimization. *J. Chromatogr. A* **2013**, *1285*, 22–30. [CrossRef]
53. Teo, Y.L.; Ho, H.K.; Chan, A. Metabolism-related pharmacokinetic drug-drug interactions with tyrosine kinase inhibitors: Current understanding, challenges and recommendations. *Br. J. Clin. Pharmacol.* **2015**, *79*, 241–253. [CrossRef] [PubMed]
54. Sloane, B.F. Cathepsin B and cystatins: Evidence for a role in cancer progression. *Semin. Cancer Biol.* **1990**, *1*, 137–152. [PubMed]
55. Zhao, B.Y.; Xu, P.; Yang, F.X.; Wu, H.; Zong, M.H.; Lou, W.Y. Biocompatible deep eutectic solvents based on choline chloride: Characterization and application to the extraction of rutin from *Sophora japonica*. *ACS Sustain. Chem. Eng.* **2015**, *3*, 2746–2755. [CrossRef]
56. Sharma, K.; Mahato, N.; Cho, M.H.; Lee, Y.R. Converting citrus wastes into value-added products: Economic and environmentally friendly approaches. *Nutrition* **2017**, *34*, 29–46. [CrossRef]
57. Xu, M.; Ran, L.; Chen, N.; Fan, X.; Ren, D.; Yi, L. Polarity-dependent extraction of flavonoids from citrus peel waste using a tailor-made deep eutectic solvent. *Food Chem.* **2019**, *297*, 124970. [CrossRef]
58. Oomen, W.W.; Begines, P.; Mustafa, N.R.; Wilson, E.G.; Verpoorte, R.; Choi, Y.H. Natural deep eutectic solvent extraction of flavonoids of *Scutellaria baicalensis* as a replacement for conventional organic solvents. *Molecules* **2020**, *25*, 617. [CrossRef]
59. Vo, T.P.; Ho, M.T.; Nguyen, P.U.N.; Pham, N.D.; Truong, K.V.; Nguyen, T.H.Y.; Nguyen, D.Q.; Vo, T.T.H. Extracting phenolics, flavonoids, and terpenoids from *Codonopsis pilosula* using green solvents. *Sustain. Chem. Pharm.* **2024**, *37*, 101395. [CrossRef]
60. Wang, Z.; Wang, D.; Fang, J.; Song, Z.; Geng, J.; Zhao, J.; Fang, Y.; Wang, C.; Li, M. Green and efficient extraction of flavonoids from *Perilla frutescens* (L.) Britt. leaves based on natural deep eutectic solvents: Process optimization, component identification, and biological activity. *Food Chem.* **2024**, *452*, 139508. [CrossRef]
61. Williams, R.J.; Spencer, J.P.; Rice-Evans, C. Flavonoids: Antioxidants or signaling molecules? *Free Radic. Biol. Med.* **2004**, *36*, 838–849. [CrossRef]
62. Garg, M.; Kaur, S.; Sharma, A.; Kumari, A.; Tiwari, V.; Sharma, S.; Kapoor, P.; Sheoran, B.; Goyal, A.; Krishania, M. Rising demand for healthy foods-anthocyanin biofortified colored wheat is a new research trend. Frontiers in Nutrition, Sec. *Nutr. Food Sci. Technol.* **2022**, *9*, 878221. [CrossRef]
63. EFSA Panel on Food Additives and Nutrient Sources. Scientific opinion on the re-evaluation of anthocyanins (E 163) as a food additive. *EFSA J.* **2013**, *11*, 3145. [CrossRef]
64. Meenu, M.; Bansal, V.; Rana, S.; Sharma, N.; Kumar, V.; Arora, V.; Garg, M. Deep eutectic solvents (DESs) and natural deep eutectic solvents (NADESs): Designer solvents for green extraction of anthocyanin. *Sustain. Chem. Pharm.* **2023**, *4*, 101168. [CrossRef]
65. Guo, N.; Ping-Kou Jiang, Y.W.; Wang, L.T.; Niu, L.J.; Liu, Z.M.; Fu, Y.J. Natural deep eutectic solvents couple with integrative extraction technique as an effective approach for mulberry anthocyanin extraction. *Food Chem.* **2019**, *296*, 78–85. [CrossRef] [PubMed]
66. Silva, D.T.; Pauletto, R.; Cavalheiro, S.S.; Bochi, V.C.; Rodrigues, E.; Weber, J.; Silva, C.B.; Morisso, F.D.P.; Barcia, M.T.; Emanuelli, T. Natural deep eutectic solvents as a biocompatible tool for the extraction of blueberry anthocyanins. *J. Food Compos. Anal.* **2020**, *89*, 103470. [CrossRef]
67. Zannou, O.; Koca, I. Greener extraction of anthocyanins and antioxidant activity from blackberry (*Rubus* spp.) using natural deep eutectic solvents. *LWT* **2022**, *158*, 113184. [CrossRef]

68. Fu, X.; Wang, D.; Belwal, T.; Xie, J.; Xu, Y.; Li, L.; Zou, L.; Zhang, L.; Luo, Z. Natural deep eutectic solvent enhanced pulse-ultrasonication assisted extraction as a multi-stability protective and efficient green strategy to extract anthocyanin from blueberry pomace. *LWT* **2021**, *144*, 111220. [CrossRef]
69. Bochi, V.C.; Godoy, H.T.; Giusti, M.M. Anthocyanin and other phenolic compounds in Ceylon gooseberry (*Dovyalis hebecarpa*) fruits. *Food Chem.* **2015**, *176*, 234–243. [CrossRef]
70. Ruesgas-Ramón, M.; Figueroa-Espinoza, M.C.; Durand, E. Application of deep eutectic solvents (DES) for phenolic compounds extraction: Overview, challenges, and opportunities. *J. Agric. Food Chem.* **2017**, *65*, 3591–3601. [CrossRef]
71. Ling, J.K.U.; Chan, Y.S.; Nandong, J. Degradation kinetics modeling of antioxidant compounds from the wastes of *Mangifera pajang* fruit in aqueous and choline chloride/ascorbic acid natural deep eutectic solvent. *J. Food Eng.* **2021**, *294*, 110401. [CrossRef]
72. Heitmann, E.; Ingram, D.K. Cognitive and neuroprotective effects of chlorogenic acid. *Nutr. Neurosci.* **2016**, *20*, 32–39. [CrossRef] [PubMed]
73. Park, H.E.; Tang, B.; Row, K.H. Application of deep eutectic solvents as additives in ultrasonic extraction of two phenolic Acids from *Herba Artemisiae Scopariae*. *Anal. Lett.* **2014**, *47*, 1476–1484. [CrossRef]
74. Miertuš, S.; Scrocco, E.; Tomasi, J. Electrostatic interaction of a solute with a continuum. A direct utilization of ab initio molecular potentials for the prevision of solvent effects. *Chem. Phys.* **1981**, *55*, 117–129. [CrossRef]
75. Cossi, M.; Rega, N.; Scalmani, G.; Barone, V. Energies, structures, and electronic properties of molecules in solution with the C-PCM solvation model. *J. Comput. Chem.* **2003**, *24*, 669–681. [CrossRef] [PubMed]
76. Yue, Y.; Huang, Q.; Fu, Y.; Chang, J. A quick selection of natural deep eutectic solvents for the extraction of chlorogenic acid from *herba artemisiae scopariae*. *RSC Adv.* **2020**, *10*, 22403–22409. [CrossRef]
77. Yuniarti, E.; Saputri, F.C.; Mun'im, A. Natural deep eutectic solvent extraction and evaluation of caffeine and chlorogenic acid from green coffee beans of *Coffea canephora*. *Indian J. Pharm. Sci.* **2019**, *81*, 1062–1069. [CrossRef]
78. Maimulyanti, A.; Nurhidayati, I.; Mellisani, B.; Rachmawati Putri, F.A.; Puspita, F.; Prihadi, A.R. Development of natural deep eutectic solvent (NADES) based on choline chloride as a green solvent to extract phenolic compound from coffee husk waste. *Arab. J. Chem.* **2023**, *16*, 104634. [CrossRef]
79. Fanali, C.; Posta, S.D.; Dugo, L.; Gentili, A.; Mondello, L.; de Gara, L. Choline-chloride and betaine-based deep eutectic solvents for green extraction of nutraceutical compounds from spent coffee ground. *J. Pharm. Biomed. Anal.* **2020**, *189*, 113421. [CrossRef]
80. Bezerra, F.S.; Ramos, G.S.M.; Carvalho, M.G.O.; Koblitz, M.G.B. Natural deep eutectic solvents characteristics determine their extracting and protective power on chlorogenic acids from sunflower meal. *Sustain. Chem. Pharm.* **2024**, *37*, 101430. [CrossRef]
81. Yu, Y.; Zhang, Z.; Chang, C. Chlorogenic acid intake guidance: Sources, health benefits, and safety. *Asian Pac. J. Clin. Nutr.* **2022**, *31*, 602–610. [CrossRef]
82. Silva, C.N.d.; Silva, R.M.d.; Lemes, A.C.; Ribeiro, B.D. Recovery of phenolic compounds by deep eutectic solvents in orange by-products and spent coffee grounds. *Sustainability* **2024**, *16*, 7403. [CrossRef]
83. Le, N.T.; Hoang, N.T.; Van, V.T.T.; Nguyen, T.P.D.; Chau, N.H.T.; Le, N.T.N.; Le, H.B.T.; Phung, H.T.; Nguyen, H.T.; Nguyen, H.M. Extraction of curcumin from turmeric residue (*Curcuma longa* L.) using deep eutectic solvents and surfactant solvents. *Analytical Methods* **2022**, *14*, 850–858. [CrossRef]
84. Liu, Y.; Li, J.; Fu, R.; Zhang, L.; Wang, D.; Wang, S. Enhanced extraction of natural pigments from *Curcuma longa* L. using natural deep eutectic solvents. *Ind. Crops Prod.* **2019**, *140*, 111620. [CrossRef]
85. Patil, S.S.; Pathak, A.; Rathod, V.K. Optimization and kinetic study of ultrasound assisted deep eutectic solvent based extraction: A greener route for extraction of curcuminoids from *Curcuma longa*. *Ultrason. Sonochemistry* **2021**, *70*, 105267. [CrossRef] [PubMed]
86. Abouheif, S.A.; Sallam, S.M.; El Sohafy, S.M.; Kassem, F.F.; Shawky, E. A green extraction approach using natural deep eutectic solvents enhances the in-vivo bioavailability of curcuminoids from turmeric extracts. *Ind. Crops Prod.* **2022**, *189*, 115790. [CrossRef]
87. Jeliński, T.; Przybyłek, M.; Cysewski, P. Natural deep eutectic solvents as agents for improving solubility, stability and delivery of curcumin. *Pharm. Res.* **2019**, *36*, 119. [CrossRef]
88. García, A.; Rodríguez-Juan, E.; Rodríguez-Gutiérrez, G.; Rios, J.J.; Fernández-Bolaños, J. Extraction of phenolic compounds from virgin olive oil by deep eutectic solvents (DESs). *Food Chem.* **2016**, *197*, 554–561. [CrossRef]
89. Tsolis, T.; Kyriakou, D.; Sifnaiou, E.; Thomos, D.; Glykos, D.; Tsiafoulis, C.G.; Garoufis, A. NMR Analysis of extra virgin olive oil of the Epirus region of Greece with emphasis on selected phenolic compounds. *Molecules* **2024**, *29*, 1111. [CrossRef]
90. Abuznait, A.H.; Qosa, H.; Busnena, B.A.; El Sayed, K.A.; Kaddoumi, A. Olive-oil-derived oleocanthal enhances β-amyloid clearance as a potential neuroprotective mechanism against Alzheimer's disease: In vitro and in vivo studies. *ACS Chem. Neurosci.* **2013**, *4*, 973–982. [CrossRef]
91. Beauchamp, G.K.; Keast, R.S.; Morel, D.; Lin, J.; Pika, J.; Han, Q.; Lee, C.-H.; Smith, A.B.; Breslin, P.A.S. Phytochemistry: Ibuprofen-like activity in extra-virgin olive oil. *Nature* **2005**, *437*, 45–46. [CrossRef]
92. Lama-Muñoz, A.; Del Mar Contreras, M.; Espínola, F.; Moya, M.; de Torres, A.; Romero, I.; Castro, E. Extraction of oleuropein and luteolin-7-O-glucoside from olive leaves: Optimization of technique and operating conditions. *Food Chem.* **2019**, *293*, 161–168. [CrossRef]

93. Rodríguez-Juan, E.; Rodríguez-Romero, C.; Fernández-Bolaños, J.; Florido, M.C.; Garcia-Borrego, A. Phenolic compounds from virgin olive oil obtained by natural deep eutectic solvent (NADES): Effect of the extraction and recovery conditions. *J. Food Sci. Technol.* **2021**, *58*, 552–561. [CrossRef]
94. Djaoudene, O.; Louaileche, H. Optimization of a green ultrasound-assisted extraction of phenolics and in vitro antioxidant potential of date fruit (*Phoenix dactylifera* L.). The Annals of the University Dunarea De Jos of Galati. *Fascicle VI-Food Technol.* **2018**, *42*, 109–122.
95. Djaoudene, O.; Bachir-Bey, M.; Schisano, C.; Djebari, S.; Tenore, G.C.; Romano, A. A Sustainable extraction approach of phytochemicals from date (*Phoenix dactylifera* L.) fruit cultivars using ultrasound-assisted deep eutectic solvent: A comprehensive study on bioactivity and phenolic variability. *Antioxidants* **2024**, *13*, 181. [CrossRef] [PubMed]
96. Samarawira, I. Date palm, potential source for refined sugar. *Econ. Bot.* **1983**, *37*, 181–186. [CrossRef]
97. El Sharnouby, G.A.; Aleid, S.M.; Al-Otaibi, M.M. Liquid sugar extraction from date palm (*Phoenix dactylifera* L.) fruits. *J. Food Process. Technol.* **2014**, *5*, 1000402. [CrossRef]
98. AlYammahi, J.; Darwish, A.S.; Almustafa, G.; Lemaoui, T.; AlNashef, I.M.; Hasan, S.W.; Taher, H.; Banat, F. Natural deep eutectic solvents for ultrasonic-assisted extraction of nutritious date sugar: Molecular screening, experimental, and prediction. *Ultrason. Sonochemistry* **2023**, *98*, 106514. [CrossRef]
99. Airouyuwa, J.O.; Mostafa, H.; Riaz, A.; Stathopoulos, C.; Maqsood, S. Natural deep eutectic solvents and microwave-assisted green extraction for efficient recovery of bioactive compounds from by-products of date fruit (*Phoenix dactylifera* L.). Processing: Modeling, optimization, and phenolic characterization. *Food Bioprocess. Technol.* **2023**, *16*, 824–843. [CrossRef]
100. Airouyuwa, J.O.; Mostafa, H.; Ranasinghe, M.; Maqsood, S. Influence of physicochemical properties of carboxylic acid-based natural deep eutectic solvents (CA-NADES) on extraction and stability of bioactive compounds from date (*Phoenix dactylifera* L.) seeds: An innovative and sustainable extraction technique. *J. Mol. Liq.* **2023**, *388*, 122767. [CrossRef]
101. Morais, E.S.; Lopes, A.M.C.; Freire, M.G.; Freire, C.S.R.; Coutinho, J.A.P.; Silvestre, A.J.D. Use of ionic liquids and deep eutectic solvents in polysaccharide dissolution and extractyion processes towards sustainable biomass valorization. *Molecules* **2020**, *25*, 3652. [CrossRef]
102. Yahaya, N.; Mohamed, A.H.; Sajid, M.; Zain, N.N.M.; Liao, P.C.; Chew, K.W. Deep eutectic solvents as sustainable extraction media for extraction of polysaccharides from natural sources: Status, challenges and prospects. *Carbohydr. Polym.* **2024**, *338*, 122199. [CrossRef] [PubMed]
103. Pereira, B.S.; Schmatz, A.A.; de Freitas, C.; Masarin, F.; Brienzo, M. Fruit and restaurant waste polysaccharides recycling producing xylooligosaccharides. *Recycling* **2023**, *8*, 16. [CrossRef]
104. Al Varqani, N.; Bastian, F. Review: Utilization of cellulose in food products. *IOP Conf. Ser. Earth Environ. Sci.* **2023**, *1230*, 012039. [CrossRef]
105. Sabbaghi, H. *Perspective Chapter: Cellulose in Food Production—Principles and Innovations*; IntechOpen: London, UK, 2023; p. 109204. [CrossRef]
106. Liu, Y.; Ahmed, S.; Sameen, D.E.; Wang, Y.; Lu, R.; Dai, J.; Li, S.; Qin, W. A review of cellulose and its derivatives in biopolymer-based for food packaging application. *Trends Food Sci. Technol.* **2021**, *112*, 532–546. [CrossRef]
107. Sethulekshmi, C. Chitin and its benefits. *Int. J. Adv. Res. Biol. Sci.* **2014**, *1*, 171–175.
108. Barikani, M.; Oliaei, E.; Seddiqi, H.; Honarkar, H. Preparation and application of chitin and its derivatives: A review. *Iran. Polym. J.* **2014**, *23*, 307–326. [CrossRef]
109. Shahidi, F.; Arachchi, J.K.V.; Jeon, Y.-J. Food applications of chitin and chitosans. *Trends Food Sci. Technol.* **1999**, *10*, 37–51. [CrossRef]
110. Khoushab, F.; Yamabhai, M. Chitin research revisited. *Mar. Drugs* **2010**, *8*, 1988–2012. [CrossRef]
111. Roman-Benn, A.; Contador, C.A.; Li, M.-W.; Lam, H.-M.; Ah-Hen, K.; Ulloa, P.E.; Ravanal, M.C. Pectin: An overview of sources, extraction and applications in food products, biomedical, pharmaceutical and environmental issues. *Food Chem. Adv.* **2023**, *2*, 100192. [CrossRef]
112. Maxwell, E.G.; Belshaw, N.J.; Waldron, K.W.; Morris, V.J. Pectin—An emerging new bioactive food polysaccharide. *Trends Food Sci. Technol.* **2012**, *24*, 64–73. [CrossRef]
113. Espitia, P.J.P.; Du, W.-X.; Avena-Bustillos, R.J.; Soares, N.F.F.; McHugh, T.H. Edible films from pectin: Physical-mechanical and antimicrobial properties—A review. *Food Hydrocoll.* **2014**, *35*, 287–296. [CrossRef]
114. Huang, J.; Hu, Z.; Hu, L.; Li, G.; Yao, Q.; Hu, Y. Pectin-based active packaging: A critical review on preparation, physical properties and novel application in food preservation. *Trends Food Sci. Technol.* **2021**, *118A*, 167–178. [CrossRef]
115. Mika, L.; Cséfalvay, E.; Németh, A. Catalytic conversion of carbohydrates to initial platform chemicals: Chemistry and sustainability. *Chem. Rev.* **2018**, *118*, 505–613. [CrossRef] [PubMed]
116. Delbecq, F.; Wang, Y.; Muralidhara, A.; El Ouardi, K.; Marlair, G.; Len, C. Hydrolysis of hemicellulose and derivatives—A review of recent advances in the production of furfural. Frontiers in Chemistry. *Front. Chem.* **2018**, *6*, 146. [CrossRef]

117. Dawsey, T.R.; McCormick, C.L. The lithium chloride/dimethylacetamide solvent for cellulose: A literature review. *J. Macromol. Sci.—Rev. Macromol. Chem. Phys.* **1990**, *30*, 405–440. [CrossRef]
118. Radosta, S.; Haberer, M.; Vorwerg, W. Molecular characteristics of amylose and starch in dimethyl sulfoxide. *Biomacromolecules* **2001**, *2*, 970–978. [CrossRef]
119. Zargar, V.; Asghari, M.; Dashti, A. A review on chitin and chitosan polymers: Structure, chemistry, solubility, derivatives and applications. *ChemBioEng Rev.* **2015**, *2*, 204–226. [CrossRef]
120. Badgujar, K.C.; Bhanage, B.M. Factors governing dissolution process of lignocellulosic biomass in ionic liquid: Current status, overview and challenges. *Bioresour. Technol.* **2015**, *178*, 2–18. [CrossRef]
121. Brandt, A.; Gräsvik, J.; Hallett, J.P.; Welton, T. Deconstruction of lignocellulosic biomass with ionic liquids. *Green Chem.* **2013**, *15*, 550–583. [CrossRef]
122. Clarke, C.J.; Tu, W.-C.; Levers, O.; Bröhl, A.; Hallett, J.P. Green and sustainable solvents in chemical processes. *Chem. Rev.* **2018**, *118*, 747–800. [CrossRef] [PubMed]
123. Silva, A.A.; Laver, M.L. Molecular weight characterization of wood pulp cellulose: Dissolution and size exclusion chromatography analysis. *Tappi J.* **1997**, *80*, 173.
124. Mosier, N.; Wyman, C.; Dale, B.; Elander, R.; Lee, Y.Y.; Holtzapple, M.; Ladisch, M. Features of promosing technologies for pretreatment of lignocellulosic biomass. *Bioresour. Technol.* **2005**, *96*, 673–686. [CrossRef]
125. De Bhowmick, C.; Sarmah, A.K.; Sen, R. Lignocellulosic biorefinery as a model for sustainable development of biofuels and value added products. *Bioresour. Technol.* **2015**, *178*, 2–18. [CrossRef] [PubMed]
126. Patra, A.; Prasath, V.A.; Pandiselvam, R. Deep eutectic solvent: An emerging trend for extraction of plant proteins. *J. Mol. Liq.* **2023**, *389*, 122887. [CrossRef]
127. Contreras, M.M.; Lama-Muñoz, A.; Gutiérrez-Pérez, J.M.; Espínola, F.; Moya, M.; Castro, E. Protein extraction from agri-food residues for integration in biorefinery: Potential techniques and current status. *Bioresour. Technol.* **2019**, *280*, 459–477. [CrossRef]
128. Kumar, M.; Tomar, M.; Potkule, J.; Verman, R.; Punia, S.; Mahapatra, A.; Belwal, T.; Dahuja, A.; Joshi, S.; Berwal, M.K.; et al. Advances in the plant protein extraction: Mechanism and recommendations. *Food Hydrocoll.* **2021**, *115*, 106595. [CrossRef]
129. Karimi, A.; Bhowmik, P.; Yang, T.C.; Samaranayaka, A.; Chen, L. Extraction of canola protein via natural deep eutectic solvents compared to alkaline treatments: Isolate characteristics and protein structural and functional properties. *Food Hydrocoll.* **2024**, *152*, 109922. [CrossRef]
130. Gupta, R.K.; Gangoliya, S.S.; Singh, N.K. Reduction of phytic acid and enhancement of bioavailable micronutrients in food grains. *J. Food Sci. Technol.* **2013**, *52*, 676–684. [CrossRef]
131. Zhou, Y.; Wu, W.; Zhang, N.; Soladoye, O.P.; Zhang, Y.; Fu, Y. Deep eutectic solvents as new media for green extraction of food proteins: Opportunity and challenges. *Food Res. Int.* **2022**, *161*, 111842. [CrossRef]
132. Hewage, A.; Olatunde, O.O.; Nimalaratne, C.; House, J.D.; Aluko, R.E.; Bandara, N. Improved protein extraction technology using deep eutectic solvent system for producing high purity fava bean protein isolates at mild conditions. *Food Hydrocoll.* **2024**, *147*, 109283. [CrossRef]
133. Subhedar, P.B.; Gogate, P.R. Alkaline and ultrasound assisted alkaline pretreatment for intensification of delignification process from sustainable raw-material. *Ultrason. Sonochemistry* **2014**, *21*, 216–225. [CrossRef]
134. Liu, J.; Li, X.; Li, M.; Zheng, Y. Lignin biorefinery: Lignin source, isolation, characterization, and bioconversion. In *Advances in Bioenergy*; Li, Y., Zhou, Y., Eds.; Elsevier: Amsterdam, The Netherlands, 2022; Chapter 6, Volume 7, pp. 211–270. [CrossRef]
135. Pang, C.; Xie, T.; Lin, L.; Zhuang, J.; Liu, Y.; Shi, J.; Yang, Q. Changes of the surface structure of corn stalk in the cooking process with active oxygen and MgO-based solid alkali as a pretreatment of its biomass conversion. *Bioresour. Technol.* **2012**, *103*, 432–439. [CrossRef] [PubMed]
136. Ji, Q.; Yu, X.; Yagoub, A.E.-G.A.; Chen, L.; Zhou, C. Efficient removal of lignin from vegetable wastes by ultrasonic and microwave-assisted treatment with ternary deep eutectic solvent. *Ind. Crops Prod.* **2020**, *149*, 112357. [CrossRef]
137. Moccia, F.; Gallucci, N.; Giovando, S.; Zuorro, A.; Lavecchia, R.; D'Errico, G.; Panzella, L.; Napolitano, A. A tunable deep eutectic solvent-based processing for valorization of chestnut wood fiber as a source of ellagic acid and lignin. *J. Environ. Chem. Eng.* **2022**, *10*, 107773. [CrossRef]
138. Li, P.; Wang, Y.; Hou, Q.; Liu, H.; Lei, H.; Jian, B.; Li, X. Preparation of cellulose nanofibrils from okara by high pressure homogenization method using deep eutectic solvents. *Cellulose* **2020**, *27*, 2511–2520. [CrossRef]
139. Perumal, A.B.; Nambiar, R.B.; Moses, J.A.; Anandharamakrishnan, C. Nanocellulose: Recent trends and applications in the food industry. *Food Hydrocoll.* **2022**, *127*, 107484. [CrossRef]
140. Samani, E.S.; Jooyandeh, H.; Behbahani, B.A. Shelf-life extension of buffalo meat using Farsi gum edible coating containing Shirazi thyme essential oil. *Food Sci. Nutr.* **2022**, *11*, 1599. [CrossRef]
141. Khaledian, S.; Basiri, S.; Shekarforoush, S. Shelf-life extension of pacific white shrimp using tragacanth gum-based coatings containing Persian lime peel (*Citrus latifolia*) extract. *LWT* **2021**, *141*, 110937. [CrossRef]

142. Criado, P.; Fraschini, C.; Shankar, S.; Salmieri, S.; Lacroix, M. Influence of cellulose nanocrystals gellan gum-based coating on color and respiration rate of *Agaricus bisporus* mushrooms. *J. Food Sci.* **2021**, *86*, 420–425. [CrossRef]
143. Fang, X.; Li, Y.; Kua, Y.L.; Chew, Z.L.; Gan, S.; Tan, K.W.; Lee, T.Z.E.; Cheng, W.K.; Lau, H.L.N. Insights on the potential of natural deep eutectic solvents (NADES) to fine-tune durian seed gum for use as edible food coating. *Food Hydrocoll.* **2022**, *132*, 107861. [CrossRef]
144. Wang, J.; Zhang, S.; Ma, S.; Yan, L. Deep eutectic solvents eutectogels: Progress and challenges. *Green Chem. Eng.* **2021**, *2*, 359–371. [CrossRef]
145. Panzer, M.J. Holding it together: Noncovalent cross-linking strategies for ionogels and eutectogels. *Mater. Adv.* **2022**, *3*, 7709–7725. [CrossRef]
146. Zeng, C.; Zhao, H.; Wan, Z.; Xiao, Q.; Xia, H.; Guo, S. Highly biodegradable, thermostable eutectogels prepared by gelation of natural deep eutectic solvents using xanthan gum: Preparation and characterization. *RSC Adv.* **2020**, *10*, 28376. [CrossRef]
147. Wan, H.; Zhu, Z.; Sun, D.-W. Deep eutectic solvents (DESs) films based on gelatin as active packaging for moisture regulation in fruit preservation. *Food Chem.* **2024**, *439*, 138114. [CrossRef]
148. Wan, H.; Zhu, Z.; Sun, D.-W. Buffering moisture variation during cherry tomatoes preservation through deep eutectic solvent films. *Postharvest Biol. Technol.* **2024**, *218*, 113171. [CrossRef]
149. Gupta, V.; Thakur, R.; Barik, M.; Das, A.B. Effect of high amylose starch-natural deep eutectic solvent based edible coating on quality parameters of strawberry during storage. *J. Agric. Food Res.* **2023**, *11*, 100487. [CrossRef]
150. Ortega-Zamora, C.; González-Sálamo, J.; Hernández-Borges, J. Deep eutectic solvents application in food analysis. *Molecules* **2021**, *26*, 6846. [CrossRef]
151. Zhu, W.; Jin, P.; Yang, H.; Li, F.; Wang, C.; Li, T.; Fan, J. A green extraction strategy for the detection of antioxidants in food simulants and beverages migrated from plastic packaging materials. *Food Chem.* **2023**, *406*, 135060. [CrossRef]
152. Xu, Y.; Jiao, Y.; Luo, J.; He, Z.; Zeng, M.; Shen, Q.W.; Chen, J.; Quan, W. The influence of deep eutectic solvents extract from ginger on the formation of heterocyclic amines and advanced glycation end products in roast beef patties. *Foods* **2022**, *11*, 3161. [CrossRef]
153. Muncke, J. Tackling the toxics in plastics packaging. *PLoS Biol.* **2021**, *19*, e3000961. [CrossRef] [PubMed]
154. *GB 9685-2016*; National Food Safety Standard: Standard for Uses of Additives in Food Contact Materials and Their Products. ChemSafetyPro.com: Shrewsbury, UK, 2016. Available online: https://chemsafetypro.com/Topics/Food_Contact/GB_9685_2016_National_Food_Safety_Standard_Standard_for_the_Use_of_Additives_in_Food_Contact_Materials_and_Articles.html (accessed on 20 October 2024).
155. Shi, Y.; Li, X.; Shang, Y.; Li, T.; Zhang, K.; Fan, J. Effective extraction of fluorescent brightener 52 from foods by in situ formation of hydrophobic deep eutectic solvent. *Food Chem.* **2020**, *311*, 125870. [CrossRef] [PubMed]
156. Liu, W.; Zhang, K.; Yang, G.; Yu, J. A highly efficient microextraction technique based on deep eutectic solvent formed by choline chloride and p-cresol for simultaneous determination of lignans in sesame oils. *Food Chem.* **2019**, *281*, 140–146. [CrossRef]
157. Shabani, E.; Zappi, D.; Berisha, L.; Dini, D.; Antonelli, M.L.; Sadun, C. Deep eutectic solvents (DES) as green extraction media for antioxidants electrochemical quantification in extra-virgin olive oils. *Talanta* **2020**, *215*, 120880. [CrossRef] [PubMed]
158. He, S.; Ho Row, K.; Tang, W. Deep eutectic solvents based in situ isolation technique for extractive deterpenation of essential oils. *Food Chem.* **2024**, *431*, 137153. [CrossRef] [PubMed]
159. Li, J.; Wang, J.; Wu, M.; Cheng, H.; Chen, L.; Qi, Z. Deep deterpenation of citrus essential oils Intensified by in situ formation of a deep eutectic solvent in associative extraction. *Ind. Eng. Chem. Res.* **2020**, *59*, 9223–9232. [CrossRef]
160. Liu, X.; Deng, Z.-Y.; Huang, Y.-Q.; Yanfg, X.-Q. Preparation of high freeze-thaw wheat gluten-based emulsions by incorporated deep eutectic solvents. *Food Hydrocoll.* **2020**, *98*, 105280. [CrossRef]
161. Kranz, M.; Hofmann, T. Food-Grade Synthesis of Maillard-Type Taste Enhancers Using Natural Deep Eutectic Solvents (NADES). *Molecules* **2018**, *23*, 261. [CrossRef]
162. Troise, A.D.; Vitiello, D.; Tsang, C.; Fiore, A. Encapsulation of ascorbic acid promotes the reduction of Maillard reaction products in UHT milk. *Food Funct.* **2016**, *7*, 2591–2602. [CrossRef]
163. Sagalowicz, L.; Moccand, C.; Davidek, T.; Ghanbari, R.; Martiel, I.; Negrini, R.; Mezzenga, R.; Leser, M.E.; Blank, I.; Michel, M. Lipid self-assembled structures for reactivity control in food. *Philos. Trans. R. Soc. A Math. Phys. Eng. Sci.* **2016**, *374*, 20150136. [CrossRef]
164. Xu, X.; Liu, A.; Hu, S.; Ares, I.; Martínez-Larrañaga, M.-R.; Wang, X.; Martínez, M.; Anadón, A.; Martínez, M.-A. Synthetic phenolic antioxidants: Metabolism, hazards and mechanism of action. *Food Chem.* **2021**, *353*, 129488. [CrossRef] [PubMed]
165. Choline Chloride Prices—Historical Graph. Available online: https://procurementtactics.com/choline-chloride-prices/ (accessed on 2 March 2025).
166. Intratec. Ethylene Glycol Prices—Current and Forecast. 2025. Available online: https://www.intratec.us/chemical-markets/ethylene-glycol-price (accessed on 2 March 2025).

167. International Sugar Organization. Daily Sugar Prices. 2025. Available online: https://www.isosugar.org/prices.php (accessed on 2 March 2025).
168. Methanex. Pricing—Methanex. 2025. Available online: https://www.methanex.com/about-methanol/pricing/ (accessed on 2 March 2025).
169. Statista. Wholesale Price of U.S. Omaha Ethanol From 1990 to 2023. 2025. Available online: https://www.statista.com/statistics/1440733/global-fuel-ethanol-benchmark-price/#:~:text=The%20world%20benchmark%20for%20fuel%20ethanol%20-%20U.S.,a%20high%20of%20$70.75%20per%20hectoliter%20in%202022. (accessed on 2 March 2025).
170. Procurement Resource. Dichloromethane Price Trend and Forecast. 2025. Available online: https://www.procurementresource.com/resource-center/dichloromethane-price-trends (accessed on 3 March 2025).
171. IMARC Group. Hexane Prices Report Analysis. Available online: https://www.supermarketresearch.com/2025/03/03/hexane-prices-report/#:~:text=In%20December%202024,%20hexane%20prices%20in%20the%20United,of%20hexane,%20which%20helped%20avoid%20major%20price%20changes (accessed on 2 March 2025).
172. Mišan, A.; Pojić, M. Applications of NADES in stabilizing food and protecting food compounds against oxidation. *Adv. Bot. Res.* **2021**, *97*, 333–356. [CrossRef]
173. Directive 2009/32/EC of the European Parliament and of the Council of 23 April 2009 on the Approximation of the Laws of the Member States on Extraction Solvents Used in the Production of Foodstuffs and Food Ingredients (Recast) (Text with EEA Relevance)—Document 32009L0032. Available online: https://eur-lex.europa.eu/eli/dir/2009/32/oj/eng (accessed on 2 March 2025).
174. Source Reduction Research Partnership Metropolitan, Water District of Southern California Environmental Defense Fund, Source Reduction of Chlorinated Solvents, Food Products Manufacture. 1991. Available online: https://p2infohouse.org/ref/19/18697.pdf (accessed on 2 March 2025).
175. Trager, R. EPA Proposes ban on most uses of dichloromethane. *ChemistryWorld*. 2023, p. 4017332. Available online: https://www.chemistryworld.com/news/epa-proposes-ban-on-most-uses-of-dichloromethane/4017332.article (accessed on 2 March 2025).
176. Hoffmann, C.; Sturm, C.; Rothman, A. *The State of Change in Chemical Innovation*; Boston Consulting Group: Boston, MA, USA, 2022. Available online: https://www.bcg.com/publications/2022/state-of-change-in-chemical-innovation (accessed on 28 February 2025).
177. Cao, R.; Lueck, K.; Musso, C.; Sarathy, V. *The Chemicals Industry of Tomorrow: Collaborate to Innovate*; McKinsey & Company: New York, NY, USA, 2024. Available online: https://www.mckinsey.com/industries/chemicals/our-insights/the-chemicals-industry-of-tomorrow-collaborate-to-innovate#/ (accessed on 28 February 2025).

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.