Review

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Posted Date: 3 January 2024

doi: 10.20944/preprints202312.2293.v1

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Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 3 January 2024 doi:10.20944/preprints202312.2293.v1

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Potential of Deep Eutectic Solvents in the Extraction of Organic Compounds from Food Industry By-Products and Agro-Industrial Waste

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Abstract: Global food waste has a huge impact on the environment, as it is a source of greenhouse gas (GHG) emissions and wasted natural resources. Across the world, over 30% of food is lost or wasted each year. Aside from this, food industry, as well, is one of the biggest sources of agro-industrial waste and by-products, which can be valorized and used for different purposes. Such waste is a good source of bioactive organic compounds which can be extracted without altering their properties, where deep eutectic solvents (DESs) can serve as green solvents and excellent replacement for volatile organic solvents. Isolated compounds can be used in innovative food production, chemical production, cosmetics and other industries. DESs have attracted extraordinary attention due to their advantages such as environmental friendliness, availability and easy preparation, easy handling and utilization of non-toxic components for their formation. Due to those properties, they are a greener alternative to classic organic solvents for many processes, including extractions. In this paper, we review the utilization of deep eutectic solvents as potential green media for the extraction of organic compounds such as polyphenols, carbohydrates, proteins, alkaloids from by-products of the food industry and agro-industrial-waste.

Keywords: Deep eutectic solvents; Bioactive organic compounds; Food industry by-products; Greener solvents; Agro-industrial waste

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1. Introduction

According to research conducted within the FUSIONS4 project [1] of the European Commission, about 88 million tons of food are thrown away in the EU member states annually. In EU member states, the amount of discarded food (edible and inedible) amounts to 173 kilograms per inhabitant. The total amount of food produced in the EU in 2011 was approx 865 kg/inhabitant, which would mean that 20% of the total produced food is wasted. Furthermore, food industry generates huge amounts of waste and by-products, which is usually discarded, making a huge load to the environment. Those by-products are usually rich in different benefitial compounds that can be isolated and used for different purposes [2,3].

Waste management is a complex and expensive process and has a harmful impact on the environment. Therefore, there is a need to develop a method to utilize the potential of by-products for conversion into bioactive organic compounds. Valorization can reduce or eliminate environmental pollution and achieve sustainable growth by creating value-added outcomes from new bioresources. The aim of this paper is to present new trends in solving the problem of food industry waste and agro-waste obtained from the processing of mostly plant raw materials. This is an area of research of exceptional importance since by-products such as bark, seeds and pulp are good sources of various bioactive organic compounds that can be used as functional ingredients or nutraceuticals in food production, cosmetics or in the pharmaceutical industry. Bioactive substances that are most often isolated from by-products are polyphenols, proteins, organic acids, alkaloids, carotenoids, sugars, lipids, etc. Many of these compounds possess multiple health benefits such as

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antitumor [4,5], antioxidant [6–8], antihypertensive [9,10], antimicrobial [11], hypoglycemic [12], antiviral [13,14] and others.

Conventional organic solvents such methanol, acetone, ethyl acetate, benzene, chloroform, dichloromethane, toluene, petroleum ether, and hexane are commonly used in extraction of the above-mentioned compounds from different byproducts. These solvents often show high vapour pressure and are usually harmful, flammable, as well as not environmentally friendly. Capello et al. [15] proposed a substitution of such solvents with *green solvents*, describing the characteristics, which green solvents should possess. The first is to replace hazardous organic solvents with less hazardous ones that have less impact on the environment, human health and safety, possess greater biodegradability or reduced ozone depletion potential. Another is to use biosolvents as ethanol, produced from renewable sources. The third is the use of supercritical fluids, which are harmless to the environment, and the fourth is use of ionic liquids with low vapour pressure, and thus less emission to air. Ionic liquids, solvents formed from organic cations and anions, do possess some advantages to conventional VOSs (volatile organic solvents), such as high thermal stability, non-volatility, but many of them showed toxic effects towards different organisms [16]. Very similar, but yet structurally different solvents have arisen in the last decade, showing some advantages over ILs, along with great potential for different processes, called deep eutectic solvents (DESs). DESs have attracted extraordinary attention due to their advantages such as environmental friendliness, good electrical conductivity, stability, low cost and easy preparation. They were first mentioned by Abbott et al. in 2003 [17], and numerous scientific reports have been published to date [18–22]. The extraction of various value-added bioactive compounds is of utmost importance using DESs because of their efficient analytic potential and low toxicity unlike the organic solvents [23].

2. Deep eutectic solvents

Since their first introduction in literature in 2003 by Abbot et al. [17], deep eutectic solvents have become a subject of many researchers. Abbot et al. (2003) [17] were investigating choline chloride and urea mixtures when they noticed a large melting point depression of the mixtures compared to the melting points of the pure components. Due to large melting point depression, such solvents were designated as „deep" eutectic solvents. Later, some authors suggested that a different definition of deep eutectic solvents is needed, and that their melting point should not be compared to the pure components, but to one of their ideal liquid mixture [24]. Therefore, Martins et al. designated them as: „*a mixture of two or more pure compounds for which the eutectic point temperature is below that of an ideal liquid mixture, presenting significant negative deviations from ideality*" [24]. Due to their interesting properties, DESs have found their application in many scientific areas. They have been extensively used in extraction of bioactive components from different materials [25–31], many synthetic procedures [32–40], stabilization od bioactive compounds [41–45], enhancement of drug delivery [46–48], pretreatment of food industry waste [49–51].

Hansen et al. [18] classified DESs into 5 types: *type 1* is formed by the combination of quaternary ammonium salt (QAS) and metal chloride; *type 2* of QAS and metal chloride hydrate; *type III* of QAS and HBD (organic acids, amides or polyoles); *type IV* of metal salt and HBDs and *type 5* consists of a new class of nonionic HBAs and HBDs. Furthermore, some authors classify them according to the nature of their components as NADES, which are formed of purely natural components, THEDES, the ones formed of pharmaceutically active components, TDES, the ones formed from three components, etc. Either way, DESs can be prepared by heating the mixture of desired components until the formaton of clear liquid, evaporation of water from the solution of desired components, freeze-drying or simply by grinding the components [18]. Phisycal and chemical properties of DESs are tuneable and can be adjusted for specific use, since different components can be mixed and combined in different ratios [19]. Net of hydrogen bonding, van der Waals interactions or ionic bonding between components causes a charge delocalization thus lowering the lattice energy of the system, consequently decreasing the melting point [18,19,52]. Although DESs show many promising properties, their high viscosity and density are one of their major drawbacks, especially is one is to scale the process up. These are governed by the strenght of intermolecular bonding between DESs'

 doi:10.20944/preprints202312.2293.v1

components [53,54] and can be reduced to some extent by the temperature rise or addition of water. On the other hand, the addition of high amounts of water can weaken the hydrogen bonding between HBAs and HBDs, causing the loss of eutectic properties [55]. Many authors designate them as desirable, compared to volatile organic solvents, as they show low vapour pressure, can be made of natural, non-toxic and biodegradable compounds and are easy to handle [41,52,56]. They have found their wide application since are considered to adhere the green chemistry principles and are thus designated as green solvents.

3. Extractions of organic compounds from fruits by-products

3.1. *Bioactive Compounds in Fruit Waste*

During the production process as well as after the consumption of food, a large amount of waste biomass is created. Great part of this can be attributed to fruit waste. Fruit wastes are one of the main sources of municipal waste. Rapid economic growth causes greater consumption of different varieties of fruit produced throughout the world. Due to the large-scale industrial processing of fruit, fruit waste such as peel, seeds and other inedible parts of fruit, accumulates. Fruit injuries during food transport and storage are the main contributors to the fruit waste productions. Fruits can be damaged at all stages of handling, during collection, transport, receiving, packaging, storage, as well as during preparation for consumption [57]. For that reason, it should be protected from external factors such as shocks, which cause mechanical damage, as well as internal ones, which can cause water loss. Two fruit waste disposal techniques include landfills and incineration. Inappropriate procedures with disposed waste can result in the emission of methane and CO_2, while burning can cause the formation of carcinogenic and toxic organic compounds such as dioxins, furans and acid gases [58]. Many strategies have been developed in recent years for food waste management. For the most part, fruit waste is used as animal feed or fertilizers [59].

Fruit waste is a rich source of extremely valuable bioactive compounds. It provides a reliable source of secondary metabolites for the development of possible food additives, functional foods, preservatives, and nutraceuticals [60]. It contains bioactive phytonutrients that have potential pharmacological properties and show positive effects on human health. Among the pharmacological properties, antioxidant activity stands out. Antioxidants attenuate generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) in human, animal and *in vitro* studies. Antioxidants prevent adversely alterations of lipids, proteins, and DNA. Hence, application of external source of antioxidants can assist in coping this oxidative stress [61–64].

Citrus fruits, the most produced crops in the world, yield up to 15 million tons of by-products per year through processing in the food industry. All of the citrus fruits belong to the *Rutaceae* family, which comprises oranges, mandarins, lemons, limes, grapefruit, pomelo, citrons, etc. [65]. By-products of fruit processing are usually seeds, peel, pulp and leaves. It has been proven that they are a rich source of a wide range of bioactive organic compounds such as polyphenols, enzymes, sugars (glucose, fructose, sucrose), polysaccharides (cellulose, starch, pectin, dietary fibers), organic acids (citric, malic, oxalic acids), essential oils (limonene), pigments (carotene, lutein), lipids (linolenic, oleic, palmitic, stearic acids) vitamins (Vitamin C, Vitamin B complexes) and others [66]. Therefore, one of the main goals of the food industry is to reuse and recycle fruit by-products [67].

Apple is the basis of fruit production. Because of the natural apple juice production, usually performed by pressing and squeezing the fruit, apple pomace is generated as the major by-product. Pomace makes up 25-30% of the apple, depending on the variety and the efficiency of processing. Apple pomace itself consists of seeds, seedpods and skin. It is a high-quality source of carbohydrates, pectin, fiber and minerals. It contains polyphenols: phlorizin, catechin, epicatechin, procyanidin B2, hyperin, quercetin, and others. The most important apple minerals are Ca, Na, K, P, and Mg, which play a key role in processes important for human health. It makes it even more important to develop new methods for bioactive compounds extraction from apple by-products and convert it into value-added products with different functionalities. It has been proven that apple pomace extracts possess anticancer, cardioprotective, and antimicrobial biological activities [68–71].

The grapevine (*Vitis vinifera*) is another of the most cultivated crops in the world. It is estimated that 80% of the annual production of grapes is processed into wine, with 20-30% of the mass of used grapes (pulp, skin, stems, seeds) remaining as solid bio-waste. The major by-product of the grape wine industry is grape pomace. Grape pomace is mainly used as fertilizer in vineyards, it is burned or dumped unplanned in the fields, which can represent a major ecological problem. It is a good source of flavanols, phenolic acids, and flavonols, and its extracts usually show enhanced antioxidant capacity [72]. Except antioxidant capacity, they possess various health benefits such anticarcinogenic, anti-inflammatory, antimicrobial, cardioprotective and neuroprotective [73].

Berries include chokeberry, raspberries, blackberries, blueberries, currants, cranberries and other berries. Some of them are used to manufacture juice, wine and their processing often results in a significant amount of by-product - pomace. This by-product often represents a valuable nutritional source of bioactive compounds and dietary fibers that could enhance either technological or nutritional properties of foods [74].

3.2. *Phenolic compounds*

Polyphenols are one of the largest groups of secondary metabolites with antioxidant properties [75–77]. They belong to the most important natural antioxidants that have numerous health benefits related to chronic diseases, such as cardiovascular disease, various cancers type [78–80]. The application of DESs for extraction of bioactive compounds from different food industry and agro-industrial waste in the past decade has been prominent. Newer techniques can improve the existing extraction mechanism and shorten the extraction time, reduce solvent consumption and reduce process costs. Therefore, techniques such as microwave [81], ultrasound [82,83], pulsed electric field (PEF) [84], and high-voltage electric discharge (HVED) [85] have already been combined with DESs to improve the extraction yield of polyphenols.

Mango peels, a by-product of mango processing, may be valorized as an efficient source of antioxidants. The extraction of polyphenols from ripe mango *Mangifera indica (L.)* peels was carried out using DES (lactic acid/sodium acetate/water, 3:1:4) using microwave-assisted extraction (MAE) technique. The extraction using MAE in combination with DESs showed a significant impact on the production proficiency of phenolic compounds (56.17 mg GAE/g dry weight (DW)) [86].

DESs and aqueous glycerol were used for solid-liquid extraction (SLE) of polyphenols from grapefruit peels. It was reported that DESs or aqueous glycerol is a good green alternative to replace the conventional solvents and enhance the yield of the flavonoid naringin from grapefruit peels [87].

Natural deep eutectic solvents (NADES) showed a satisfactory capacity to extract D-limonene, and excellent capacity to extract polyphenols and proteins from the orange peel [88]. The results of one study showed that DESs combined with ultrasound technology are excellent tools for extraction of anthocynanins and polyphenols from blueberry pomace. Better yields were obtained with DES ChCl:butane-1,4-diol (molar ratio 1:3) at a temperature of 63 °C compared to extraction with 70% ethanol [89].

3.3. *Carbohydrates*

NADESs were proved to be promising co-solvents and can be used for extracting a wide range of biomaterials, such as polysaccharides. Polysaccharides derived from agro- industrial waste include cellulose, hemicellulose, starch, pectin, fucoidan, carrageenan, chitosan and alginate. These polymers are linked by chemical bonds, such as β-1,4-glycosidic bond, α-1,6- glycosidic bond, α-1,4-glycosidic bond, and intermolecular forces, such as hydrogen bonds and van der Waals forces [90]. Pectins are water-soluble carbohydrates found in cell walls and are built from main monomer D-galacturonic acid and each unit is linked to the other by α-(1,4)-glycosidic bond. Pectin rich extracts are traditionally used in the food industry as an additive for gelling, thickening, swelling and hydration capacity [57]. The richest source of pectins are citrus fruits such as lemon peel [91–93], apple pomace [93], mango peel [94], pomegranate peel [95], kiwifruit pomace [96], papaya peel [97], passion fruit peel [98], jackfruit peel [99], sour orange peel [100], and in gape pomace [101]. Cellulose is a linear polysaccharide polymer consisting of D-glucose monosaccharide units linked by β-1,4-glycosidic bonds. Chemical reactions on the hydroxyl groups of cellulose are difficult, and the reason for this is intramolecular and intermolecular hydrogen bonds, which make it impossible to dissolve cellulose in water and most organic solvents [57]. Corn husk and grape stalk [102], pomegranate peel, marc of strawberry-tree fruit [103], chestnut shell [104], banana [105], and orange peel [106] are sources of cellulose. Cellulose as natural, biodegradable, and versatile polymer can be used for variety of food and non-food applications, as well as in pharmaceutical, paper, textile, wood, and industrial chemistry. It is also useful in production of micro and nanocellulose, which are important for polymer composite materials [107].

These carbohydrate polymers have demonstrated anti-tumor, antioxidant, and hypoglycemic functions, making them widely used in medicine, substance growth, and the preparation of chemicals [108–111].

In various studies, ChCl based eutectic solvents were used for the extraction of pectin from food industry by-products. In one study pectin was extracted from pomelo (*Citrus grandis* (L.) peels using natural deep eutectic solvents in combination with sonication. The results showed that the best solvents for extraction were choline chloride:malonic acid (ChCl:Mal) and choline chloride:glucose:water (ChCl:Glc:W) NADESs. Pectin was obtained in both NADEs in 94% yield after optimization at 80 °C, with 60 min of sonication, pH < 3.0, and a NADES-to-water ratio of 1:4.5 (v/v) [112]. Another study showed that treatment of apple pomace with eutectic solvents, such as ChCl:lactic acid and ChCl:urea improved the efficiency of pectin extraction. However, some solvents, like ChCl:oxalic acid, were not suitable for pectin extraction, since carbohydrate degradation occurred a lower yield was obtained [113].

3.4. *Proteins*

The data on the presence and extraction of proteins and amino acids from food industry by-products is limited. The protein content in pomegranate peel was reported to be approximately 3% [114]. However, a higher content was found in pomegranate seeds, reaching about 14% [115]. Regarding amino acid levels, some authors indicated that citrus peel had a high content of proline, asparagine, aspartate, alanine, serine, and arginine [116]. A sustainable methodology based on the use of high voltage electrical discharges (HVED) and DESs for the simultaneous extraction of proteins and polyphenols from pomegranate seeds was developed by Hernandez et al. (2022). Pomegranate seeds were firstly pretreated with HVED and, next, exposed to a solid-liquid extraction (SLE) using DESs. All DESs promoted the extraction of proteins and polyphenols, although the extraction of proteins was further improved, especially with ChCl:Glc, which increased the relative protein content in a 94% which indicate how DESs improved the diffusivity of both proteins and polyphenols [85].

3.5. *Other compounds*

Fruit peel from food industry by-products are an excellent sources of terpenes. Depending on the number of the isoprene units, they are classified as hemiterpenes (one isoprene unit), monoterpenes (2 unit), sesquiterpenes (3 unit), diterpenes (4 unit), sesterterpenes (5 unit)), triterpenes (6 unit), and tetraterpenes (8 unit). In orange peel were identified D-limonen, linalool, and myrcene, in tomato peel lycopene, in melon peel carotenoids such as *β*-carotene, zeaxantin, violaxantin and lutein.

Thymol, *p*-cymene, carvacrol are identified in by-products derived from essential oils distillation of aromatic plants. These compounds are active ingredients in flavoring, perfumery, and aromatherapy [57].

Due to their hydrophobic nature and harmless and renewable character, terpenes and terpenoids have been used in the design of eutectic solvents. Due to their eco-friendly properties, they are proposed as possible substitutes for conventional organic solvents in the separation of organic compounds from aqueous streams [117].

The extraction of vitamin E from red palm biodiesel has been also addressed using eutectic solvents. Manurung et al. (2018) used solvents formed by potassium carbonate and glycerol at salt:glycerol molar ratios of 1:5, 1:6 and 1:7. The highest extraction yields were achieved in the extraction of γ-tocotrienol, δ-tocotrienol and α-tocotrienol from biodiesel using the potassium carbonate + glycerol eutectic solvent with a molar ratio of 1:6 [118].

Deep eutectic solvents in combination with the ultrasonic method were used for delignification of watermelon rind, whereby a maximum lignin removal of 44% was achieved in a sonication time of 40 min at a temperature of 120 °C [119].

Table 1. Extraction of bioactive compounds from fruit waste using various DESs.

Fruits	Waste	Extraction technique/conditions	DESs	Bioactive compounds	Reference
Polyphenols					
Orange	peel	Solid-liquid extraction (SLE)	LA:glucose (GLC) (5:1), L-proline:malic acid (1:1)	polyphenols and flavonoids	[120]
		SLE , 50 °C, 30 min	ChCl:citric acid (CA) (1:1)	hesperidin	[121]
		SLE, 45 ±5 °C, 20 min	ChCl:malic acid ChCl:glycerol	flavonoids	[120]
Lemon	peel	RP-LC–QTOF-MS/MS	ChCl:glycerol (1:3)	quercetin, *p*-coumaric acid)	[122]
Tangerine	peel	USE (20 W, 35 kHz)	ChCl:levulinic acid:*N*-methyl urea (1:1.2:0.8)	polymethoxylated flavonoids and their glycosides	[123]
Grapefruit	peel	HVED SLE, 50 °C, 60 min Solid/liquid ratio (1:10)	LA:Glc (5:1)	polyphenols naringin	[124]
Mango	peel	MAE	Sodium acetate:LA (1:3)	mangiferin	[86]
Apple	pomace	USE, 83.2 W	ChCl:glycerol (1:2)	quercerin, chlorogenic acid, gallic acid, phloretin, phloridazin and rutin	[125]
		SLE, 60 °C, 6 h	ChCl:ethylene glycol (1:4)	procyanidin, chlorogenic acid, epicatehin hydrate, vanillin, phloridzin	[126]
Grape	pomace	MWE 300W + USE 50 W	ChCl:CA (1:2)	anthocyanins, gallic acid, catehin and quercetin 3-*O*-glucoside	[127]
				anthocyanins (malvidin-3-*O*-monoglucosid	[128]
		SLE, rt, 24 h.	betain:CA (1:1)	malvidin	[129]
		USE, 100 W	betain:Glc (1:1)	flavan-3-ols	[130]
		SLE, HPLE	ChCl:ethylene glycol:water, ChCl:glycerol:levulinic	phenolic acids, flavanols, flavonols	[131]

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			acid: water, Ethylene glycol:water, glycerol:water		
	skin	USE, 59 kHz	ChCl:CA (1:2)	flavan-3-ols, catechin, epicatechin, protocatechuic acid	[132]
Mangosteen	peel	USE	ChCl:LA (1:2)	anthocyanins	[133]
		SLE, 50 °C USE, 50 °C, 50 W	LA:ChCl 3:1, Malic acid Sucrose 1:1, Glycerol Glycine 3:1, ChCl:fructose 1.9:1, Glc:Tartaric acid 1:1, Glycerol Urea 1:1, Malic acid:Glc Glycerol 1:1:1, LA: Glycine 3:1	caffeic acid, kaempferol, luteolin, protocatechuic acid, ellagic acid, chlorogenic acid, hydroxybenzoic acid, gallic acid, quercetin	[134]
		SLE	ChCl :glycerol (1:11)	polyphenols and flavonoids	[135]
Pomegranate	peel	USE TPC (water content, 29.30%; liquid-to-solid ratio, 53.50 mL/g; ultrasonic power, 238.20 W; extraction time, 29.50 min¸ PC (water content, 25.65%; liquid-to-solid ratio, 44.20 mL/g; ultrasonic power, 120 W; extraction time, 20 min), and EC (water content, 33.13%; liquid-to-solid ratio, 60 mL/g; ultrasonic power, 300 W; extraction time, 20 min)		Total polyphenol content (TPC) punicalagin content (PC), an ellagic acid content (EC)	[136]
		pretreatment with HVED or US, SLE	ChCl:CA, ChCl:acetic acid, ChCl:LA, ChCl : glycerol, and ChCl :Glc	polyphenols	[85]
Jabuticaba	pomace	USE	ChCl:Propyleneglycol 1:2, ChCl:CA 1:1, ChCl:Malic acid 1:1, CA:Glc:Water 1:1:3 CA:Propylene glycol 1:1 Betaine:CA 3:1	anthocyanins	[137]
Blueberry	pomace	USE	ChCl: LA (1:1)	anthocyanins	[138]

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		USE	ChCl:oxalic acid (1:1)	anthocyanins	[139]
		USE	ChCl:butane-1,4-diol	cyanidin-3-O-rutinoside	[140]
Cranberry	pomace	USE	ChCl:betaine hydrochloride:levulinic acid (1:1:2)	procyanidins and anthocyanins	[141]
Strawberry and raspberry waste	extrudate	SLE	ChCl:glycolic acid:Oxalic acid (1:1.7:0.3)	anthocyanins	[142]
Black chokeberry	pulp	(UMAE-EtOH) solid–liquid ratio of 1:15, 230 W, 367 s, 52 °C	ChCl: CA (1:1), ChCl: malic acid (1:1), ChCl:LA (1:1), ChCl: Glc (1:1), ChCl: sucrose (1:1), ChCl: glycerol (1:2), ChCl:CA:Glc (1:1:1), ChCl:CA:glycerol (1:1:1)	cyanidin-3-*O*-galactoside, cyanidin-3-*O*-glucoside, cyanidin-3-*O*-arabinoside, cyanidin-3-*O*-xyloside, cyanidin-3,5-*O*-dihexoside, dimer of cyanidin-hexoside	[143]
Sour cherry	pomace	USE, 40 ◦C, 30 min MWE, 90 W three successive cycles of 5 s (15 s of total time)	ChCl:Mallic acid	cyanidin-3-*O*-sophoroside cyanidin 3-*O*-glucosylrutinoside cyanidin-3-*O*-rutinoside quercetin-3-*O*-glucoside quercetin-3-*O*-rutinoside quercetin-*O*-glycoside Isorhamnetin-3-*O*-rutinoside	[144]
Carbohydrates					
Pomelo	peel	USE, 80 °C, 60 min, liquid:solid ratio (40:1)	ChCl:Mal acid ChCl:Glc:Water	pectin	[112]
Apple	pomace		ChCl: LA, ChCl: oxalic acid, ChCl: urea, 1:2	pectin	[113]
Banana	puree	MWE, 25 ◦C, 30 min, water content: 30%,	Malic Acid:*β*-alanine:water (1:1:3)	soluble sugars	[145]
Grape	seed	USE, 30°C, 10 min,	Dodecanoic Acid: Octanoic Acid (1:1)	Gsps	[146]
Proteins					
Pomegranate	seed	Pressurized liquid extraction (PLE) and DES extraction	ChCl:CA, ChCl:AA, ChCl:LA, ChCl:glycerol, ChCl:glc	protein	[85]

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Orange	peel	4 °C, 15 min	ChCl -based NADES with ethylene glycol	protein	[88]
Other compounds					
Watermelon	rind	USE	ChCl:LA	lignin	[119]

4. Extraction from vegetables byproduct

Polyphenols

Onion, as one of the most grown cultures around the world, is a source of huge amounts of by-products, especially in the form of onion peel. It can be used as a source of valuable polypehnols, like quercetin, kaempferol, myricetin, as well as other polyphenols [147]. In order to apply a green extraction of such compounds, Pal and Jadeja (2019) used DESs for polyphenol extraction and comapred it to conventional methods, such as Soxhlet (with methanol) and microwave extraction (with distilled water). They found that choline chloride:urea:water DES can be effectively applied for the above mentioned extraction as a green solvent [147]. Use of NADESs in combination with ultrasound technology also proved the efficacy of these green type of solvents in extraction of quercetin from onion peels [148]. The same research proved the efficacy of NADESs in extraction of bioactive polyphenols from broccoli [148], while Cao et al. (2023) also effectively combined the use of NADESs and ultrasound technology to extract neochlorogenic, ferulic, erucic, quinic, chlorogenic and caffeic acid by combiningfrom broccoli leaves. Their extracts also showed greater TPC, antioxidant and antimicrobial activity than the ones obtained by other extraction methods [149].

Curcumionoides, *Curcuma longa* yellow pigments, as biologically active compounds with various pharmacological proerties, have a high potential for pharmaceutical, food or cosmetic applications. They can be extracted from *C. longa* rhizomes using NADESs, in higher yields compared to conventional solvents [150]. Another group of colorants, betalains, were extracted from beetroot waste, using NADES both as extracting and stabilizing solvent as well. Results for NADES extraction were comparable to those of conventional water extraction, while stabilization of betalaines was much higher than in water extracts [151]. Carotenoides are an important group of pigments, with significant biological activity. Tomatoes most significant carotenoid is lycopene, while tomato waste generated during production of tomato sauce, juice or paste, is rich in this health-promoting compound. Menthol:hexanoic acid (2:1) DES was found to be very effective in lycopene extraction compared to conventional solvents [152].

Potato peel is another example of the usual waste containing high amounts of bioactive compounds, like quercetin, chlorogenic acid, caffeic acid, α-solanine and α-chaconine [153]. Polyphenol and bioctive components content varies depending on variety and location, but it can go up to 20 mg/g of the peel [154]. An excellent source of polyphenols is black carrot waste as well. This vegetable is very popular in Turkey, where large amounts of waste are generated due to the production of beverage called Shalgam juice. This waste, in form of fermented black carrot, is rich in polyphenols, which can be effectively extracted using NADESs. According to Toprak and Unlu, ChCl:glycerol was very efficient in TPC extraction, while ChCl:fructose:water and ChCl:sucrose:water were very efficient in total flavonoids and total monomeric antocyanins extraction [155].

Farajzadeh et al. (2018) found a new application of DESs, when they investigated the extraction of pesticides from different friut juice and vegetables, finding that this approach is effective for fast and green analysis of these analytes [156].

Many authors also investigated the removal of lignin from different agro-industrial wastes to facilitate cellulose hydrolysis using green methodologies. Ternary DES (TDES) were succesfully utilized in this manner, both for pretreatment of onion roots and garlic skin, which increased the cellulose content in both cases [157].

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Table 2. Extraction of bioactive compounds from vegetable waste using various DESs.

Vegetable	Waste	Extraction technique	DESs	bioactive compounds	Reference
Polyphenols					
onion	peel	60 °C, 120 min, 20:1 (liquid:solid)	ChCl:U:H_2O (1:2:4)	TPC, quercetin, kaempferol, myricetin	[147]
Black carrot	waste	Ultrasonic bath, 50 °C, 30 min, 37 kHz, 140 W	ChCl:glycerol (1:2)	Polyphenols	[155]
Onion		20 °C, 35 min, 400 μL of DES	Methanol solution of betaine:D -mannitol	Quercetin, isorhamnetin, kaempferol	[148]
Curcuma longa	rhizomes	50 °C, 0.1:10 g/mL (solid:liquid), 30 min	1:1 citric acid:glucose (1:1), 15 % water	Pigments: curcuminoides	[150]
Broccoli		20 °C, 35 min, 400 μL of DES	Methanol solution of betaine:D -mannitol	Quercetin, isorhamnetin, kaempferol	[148]
Broccoli	leaves	Solvent:solid 36.35 mL/g, 49.5 °C, 31.4 min, ultrasonic power 383 W	ChCl:1,2-propylene glycol (1:2)	neochlorogenic acid, ferulic acid, erucic acid, quinic acid, chlorogenic acid, caffeic acid	[149]
Tomato	By-products	Solvent:solid 25:1, 90 min, 50 °C	Menthol:hexanoic acid (2:1)	carotenoides	[152]
Other					
Beet, cucumber, potato, and tomato		70 °C, 5 min, 142 μL DES, 1610 x*g* 5min centrifugation	ChCl:*p*-chlorophenol	Pesticides: diazinon, metalaxyl, bromopropylate, oxadiazon, fenazaquin	[156]
Garlic	skin	ultrasound 20+28+40 kHz, 30 min, r.t., followed by microwave 20 min, 80 °C	ChCl:Glycerin:$AlCl_3{\cdot}6H_2O$ (1:2:0.2)	Removal of lignin	[157]
Beetroot	Peel and pulp	1:30 g/mL (solid:liquid), 25 °C, ultrasonic bath, 3h, agitation 900 s	$MgCl_2$x6H_2O:urea (2:1)	Betalains	[151]
Onion	root	ultrasound 20+28+40 kHz, 30 min, r.t., followed by microwave 20 min, 80 °C	ChCl:Glycerin:$AlCl_3{\cdot}6H_2O$ (1:2:0.2)	Removal of lignin	[157]

5. Extraction from oilseed agro waste

Oilseeds crops are one of the major high-value agricultural commodities. Oils are organic compounds with a major role in the construction of living beings. According to their chemical composition, they are esters of glycerol and higher fatty acids, so they are classified as triglycerides, and they also belong in a wider group of compounds called lipids. For their production, the oilseeds have to be cleaned before refining processes and there should be effective refining steps including cleaning of seeds, mechanical expression, solvent extraction, degumming, neutralization, bleaching, and deodorization. These processes give good quality oil, but a huge quantity of by-products. Disposal of these by-products leads to environmental pollution and causes many other problems. Therefore, it is necessary to develop methods that will enable reuse and exploitation the by-products like husk, hull, cake, pomace or meal, gum, soap stock, spent bleach earth/clay, and distillate [158]. By-products obtained from olive wood and olive oil extraction are known as "olive by-products". A large number of by-products and residues obtained from olive (*Olea europaea*) harvesting industries have been preserved over the years, and had no practical application for a long time. More recently, it has been confirmed that residual mass is a favorable source of energy and chemicals. Olive pomace is one of the two byproducts of olive oil production. It consists of pits, skins and pulp of olives and contains 35–40 % of the total weight of olives. The most important ingredients of olive pomace are oil, water, proteins and polyphenols. Composition of olive pomace, apart from the variety of olive, it also depends on the method of production of virgin olive oil. If oil is obtained by pressing on hydraulic presses, olive pomace has a low oil content and vegetable water. Recently, olives, virgin olive oil and pomace have attracted a great interest among scientists due to their valuable compounds with health promoting benefits [159,160]. Their benefits mainly arise from the positive bioactive properties of their phenolic compounds (phenolic acids and alcohols, secoiridoid derivatives, lignans and flavones) which have been proved antiviral, antimicrobial, antioxidant, anti-inflammatory and anti-carcinogenic activities [161,162]. As bioactive phenolic compounds are important due to their potential applications in the pharmaceutical, food and nutraceutical industries, they have attracted much attention. Conventional procedures that were used in the past, require a long extraction time and usually a large amount of solvent [163,164]. Today green solvents, with alternative innovative extraction assisted methods using homogenization (HAE), microwaves (MAE), ultrasounds (UAE) and high hydrostatic pressure (HHPAE) has proven to be an efficient media for the extraction of phenolic compounds from olive pomace. The organic acid-based NADESs, ChCl:citric acid and choline chloride:lactic acid, were selected as most promising solvents and proved to be more effective in the extraction of olive pomace phenolic compounds compared to conventional solvent. ChCl:citric acid possessed the highest total phenolic content and antioxidant activity of all the extracts obtained by HAE at 60 °C /12000 rpm and by UAE at 60 °C. Additionally, the choline chloride:lactic acid was found to be the best NADES for the MAE at 60 °C and for HHPAE at 600 MPa/10 min in terms of TPC and antioxidant activity of the obtained extracts. Moreover, HAE was the best method with a better extraction efficiency than that of the MAE, HHPAE and UAE. HPLC phenolic profiles of extracts revealed that NADESs were superior extraction solvents for a wide range of compounds compared to aqueous ethanol or water. If NADES is combined with novel extraction assisted methods (HAE, MAE, UAE, HHPAE), high extraction efficiencies can be achieved in significantly reduced time. The results confirmed that the proposed combined methods could provide an excellent alternative for sustainable and green extraction of phenolic compounds from plant sources leading to novel industrial applications [165].

The term "olive leaf" describes a mixture of leaves and twigs preserved during the pruning of the olive trees and the cleaning and picking of the olives and contains for up to 10% of the total weight of the olives at olive-oil mills. The olive leaf has been postulated as a good source of natural bioactive compounds such as polyphenols, secoiridoids, phenylethanoids and other with many positive effects as antihypertensive, anticarcinogenic, anti-inflammatory, hypoglycemic, antimicrobial, antiviral, anti-tumor, antithrombotic and hypocholesterolemic [166–171]. A new methodology was developed for the extraction of phenolic compounds from olive leaves, which includes microwave assisted extraction techniques MAE in DESs. Of the nine tested DESs for the extraction of phenolic

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compounds, choline chloride ethylene glycol (1:2) proved to be the most effective. The optimal extraction conditions were: temperature 79.6 °C, 43.3% water and 16.7 min of irradiation time. The results of this research indicate the possibility of recovering value compounds for olive leaves, which means that MAE is a green extraction technique in accordance with the principles of green chemistry due to minimal amount of reagents, lower waste generation and the eco-friendly properties of DESs, their low flammability and negligible vapor pressure [172].

6. Extractions from animal byproducts

The largest part of animal waste originates from the meat industry during slaughtering like bones, tendons, skin, contents of the gastro-intestinal tract, blood, and internal organs. Most animal by-products are bioactive peptides that have been intensively researched recently [173]. Blood and collagen are an abundant source of protein and are present up to 4% of total animal weight [174]. Collagen is the main constituent of skin, hide, bones, and cartilage, and its nutritional value is very low, because it lacks essential amino acids. The cheapest way to generate bioactive peptides from collagen is through hydrolysis by microorganisms. Research has shown that peptides exhibit different biological properties such as AChE-inhibition [175], antimicrobial [176,177] or antioxidant [178].

NADES showed potential for application in industry, use in extraction, biocatalysis and electrochemistry [179]. NADES were used in a simple and green analytical method for the extraction of free selenium amino acids in lyophilized milk samples. The optimized extraction of free seleno-amino acids with NADES showed quantitative recoveries with good precision and sensitivity compatible with the SeCys, SeMet and Se-Met-SeCys concentrations in the samples. The method is applicable on real samples such as cow's milk powder samples, freeze-dried selenium-biofortified sheep's milk, and other. Extraction with eutectic solvents is a green method and at the same time a one-step alternative to the traditional solubilization of powdered milk samples [180]. Immunoglobulins (Ig) or antibodies are glycoproteins produced by plasma cells. High selective purification of Ig from quail egg was performed by ultrasound-assisted liquid-liquid microextraction (UA-LLME) in task-specific deep eutectic solvent (TDES). The ability of all glicerol-based eutectic solvents to form aqueous two-phase system (ATPS) with salts of various anionic (K_2HPO_4, Na_2SO_4 and Na_2CO_3) and cationic combinations were explored. Optimization of important parameters with response surface methodology was cultivated and highest yield was achieved for 85% (v/v) of NADES for feed of 18 μg/ml of egg yolk isolate with ultrasound temperature of 35 °C and 12 min contact time respectively [181].

Waste from the fish and seafood industry is a source of many bioactive substances such as omega-3 fatty acids, amino acids, peptides, enzymes, gelatine, collagen, chitin, vitamins, polyphenolic constituents, carotenoids etc. It can also serve as a favorable material for the production of biodiesel. Depending on the structural and functional characteristics, bioactive compounds from fish waste as well as from seafood waste have potential applications in the food industry, pharmaceutical industry, medicine and agriculture [182].

New studies have shown that NADESs based terpenes are an alternative extraction medium for the recovery of astaxanthin (AXT) from waste biomass from shrimp shells, mussels, *Heamatococcus pluvialis* shells and from other biomasses. The results show that the extraction in NADESs based terpenes at 60 °C in a time of 2 hours gives yields similar to the Soxhlet extraction of 6 hours with acetone as a solvent. With the application of NADES, AXT yields were increased up to 657 times. Research has shown that terpene-based NADES extracts have the potential to inhibit colon cancer cells and affect the negative growth of Gram-positive and Gram-negative bacteria. Of the tested NADES, menthol: myristic acid (8:1) proved to be the most effective solvent. The authors state that such extractscould be used as functional ingredients and natural preservatives in the pharmaceutical, food or cosmetic industries [183].

Fish scales (FS) are waste obtained in the fish processing industry. About 1 million tons of FS are produced every year [184]. FS are a rich source of biocompatible hydroxyapatite (HAp) and also contain proteins collagen and keratin, a small proportion of fat, and vitamins. HAp is increasingly

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used in the food industry for adsorption of heavy metals in food. Therefore, the use of waste from FS not only reduces the amount of produced waste but also uses it for the development of a new method for increasing the value of the waste. The research results showed that DES choline chloride:glycerol (1:2) is the optimal solvent for extraction. Under optimal conditions (extraction temperature 70 °C, solid:liquid ratio 1:15 g/g and extraction time 2.5 hours) a HAp yield of 47.67%±1.84% was obtained. The analysis of the chemical composition of HAp determined an irregular morphology and a high Ca/P ratio. However, research has shown that the authors have developed a new, environmentally friendly method of HAp recovery from FS [185].

In one study, a green and facile method based on NEDES choline chloride-malic acid, was developed for extracting chitin from shrimp shells. Chitin is linear polysaccharide composed of *β*-1,4-glycosidic linked *N*-acetyl-D-glucosamine units. The high extractability of chitin with the NADES can be attributed to the formation of the hydrogen bond interactions between the NADES and shrimp shell components. Competing hydrogen bond formation between the NADES and carbohydrates cause the breaking of the intramolecular hydrogen bond network, which causes weakening the hydrogen bond interactions in the shrimp shells. As a result, chitin is dissolved in the NADES and separated from the proteins. The research showed that this extraction method based on NADES is a suitable approach for the extraction of chitin from shrimp shells and reveals the potential of application in the extraction of biopolymers from natural sources [186].

7. Extractions from other Agri-Food byproducts

Eutectic solvents were used in protein extraction from bamboo shoots. Bamboo shoots or bamboo sprouts are the edible part of bamboo, of which the two most famous species are *Bambusa vulgaris* and *Phyllostachys edulis*. They are used in Asian cuisine in fresh, dried or canned form. Protein yield by extraction using the eutectic solvent choline chloride and levulinic acid under optimal conditions (80 °C, 50 min, HBD:HBA molar ratio of 6, solid:liquid ratio of 30 mg/mL, and water content of 40 % v/v) was 39 mg/g dry weight (DW) for the tender tip of the bamboo shoot (TBS), 15 mg/g dry weight (DW) for the basal bamboo shot (BBS), 9.54 mg/g DW for sheat. Compared to conventional extraction using sodium hydroxide, significantly higher protein yields were obtained with deep eutectic solvents [187].

Eucalyptus (*Eucalyptus globulus*) plantations provide a large amount of biomass residues such as leaves and branches. The leaves of *E. globulus* are rich in 1,8-cineole, sesquiterpene, phloroglucinol derivatives, flavonoids, tannins and related polyphenols [188]. Extracts and essential oils are used in pharmaceutical, health, agricultural, cosmetic and food industries and in medicine for the treatment of diseases such as tuberculosis, flu, fungal infections and diabetes. Results showed that intensification of extraction using ultrasounds and microwaves in DESs reduced the extraction time to 90 and 7 min, respectively, while maintaining the quality of the extract. The specific energy consumption is also reduced compared to that of the conventional extraction, and it was 2 and 13 times lower for ultrasound assisted extraction UAE and MAE, respectively. Eucalyptus leaves extracts are a rich source of biologically active polyphenolic compounds, such as sideroxylonal, quercetin 3-*O*-β-D-glucuronide, eucaglobulin or globulusin, ellagic acid and methylellagic acid pentoside and others [189].

The by-products of forestry, logging, and timber production (leaves, branches, cones, root, wood bark, etc.) are natural source of bioactive compounds. Ginkgo biloba is one of the oldest known trees on earth, whose fossil remains are around 200 million years old. It is a treasure of functional phytochemicals with multimedicinal applications. Several chemical compounds have been isolated from *G. biloba* with a wide range of therapeutic activities. About 38 different flavonoids have been isolated from Ginkgo biloba leaves [190]. Ginkgo flavonoids are strong antioxidants which act as free radical scavengers. They protect against capillary fragility, in reducing edema caused by tissue injury, have anti-inflammatory properties etc. In Ginko were identified and described new terpenoids, lignans, alkylphenols and alkylphenolic acids, carboxylic acids, proanthocyanidins, polyprenols, polysaccharides and others [191]. Plant extracts have exhibited a variety of pharmacological activities, including antibacterial, antioxidant, anti-inflammatory, antiallergic, and cytotoxic anticancer

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activities [192,193]. A new method of green extraction of flavonoids based on DESs was developed. Fifty DESs were prepared for the purpose in order to investigate the extraction of Ginkgo flavonoids. Compared to present most efficient extraction solvent (70% ethanol in water), in three DESs, choline chloride:1,3-butanediol (ChCl:B), choline chloride:levulinic acid (ChCl:LA1), and 1,2-propanediol:levulinic acid (P:LA1), higher extraction yields were obtained. The extraction process was optimized and the reaction conditions were: ChCl:LA1 containing 40 % (w/w) water was used as the solvent to extract Ginkgo flavonoids at a solvent:solid ratio of 10:1 (v/w), with stirring at 50 °C and 150 rpm for 15 min. under these optimal conditions, ginkgo flavonoids can be extracted from Ginkgo biloba leaf powder in a yield of 99.87%. Recovery of Ginkgo flavonoids in the DES extraction solution was achieved in 93.7% yield using macroporous resin [190].

5. Conclusions

Concern for the environment and the growing demand for various drugs and biologically active substances have led to an increase in finding new uses for food and agricultural by-products. Since waste is rich in bioactive compounds, it can be called "raw material" and not "waste". This review paper presents the overview of the DESs apllication for valorization of mainly food and agricultural industry waste, in order to obtain products with added value. The use of eutectic solvents as green solvents in the extraction of organic compounds from the by-products of the food industry and agro-waste is in accordance with green chemistry principles. The effectiveness of the eutectic solvent depends on the structure, polarity and other physical and chemical properties of the solvent and the extraction method used. Although the mechanisms underlying the extraction process are still understudied, DES have emerged as a promising green solvent due to their easy preparation, sustainability, low cost, and tunable properties. They are widely used in various extraction processes, especially in treatment of agricultural industrial waste, which is in line with the strategic goals of green sustainable development. Choosing the best solvent remains a challenge for further applications in the extraction of bioactive compounds. DES represent significant opportunities in various extraction processes and reaction systems. Valorization through biotechnological and green approaches helps in the development of bioproducts in a cost-effective and comprehensive way. Therefore, the continuation of such DES research and development could lead to breakthroughs in green sustainable technologies.

Author Contributions: Author Contributions: Conceptualization, M.M.; literature search, M.K. and M.J.K., M.M., D.G.S. and V.B. writing—original draft, preparation, M.M., D.G.S. and V.B.; writing—review and editing, and M.M. supervision. All authors have read and agreed to the published version of the manuscript.

Funding: The work was supported throuht the institutional project Faculty of Food Technology Osijek entitled"Synthesis and Characterization of Coumarin Semicarbazides", led by Maja Molnar, full professor.

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

Abbreviation

DES – deep eutectic solvent
QAS - quaternary ammonium salt
HIFU - high intensity ultrasound extraction
HBD – hydrogen bond donor
HBA – hydrogen bond acceptor
NADES – natural deep eutectic solvents
THEDES – therapeutic deep eutectic solvents
TDES – ternary deep eutectic solvents
SLE - solid-liquid extraction
ROS - reactive oxygen species
RNS - reactive nitrogen species
DNA - deoxyribonucleic acid
PEF - pulsed electric field
GAE - gallic acid equivalent
DW - dry weight
ChCl – choline chloride
Glc – glucose
LA – lactic acid
CA – citric acid
Mal – malonic acid
AA – acetic acid
TPC -total polyphenol content
PC - punicalagin content
EC - an ellagic acid content
RP-LC–QTOF-MS/MS - reversed phase ultra-pressure electrospray liquid chromatographic time-of-flight massspectrometric method
USE – ulrasound extraction
HVED - high voltage electrical discharges pre-treatment
MAE – microvawe assisted extraction
HPLE - hot pressurized liquid extraction
UMAE-EtOH - ultrasonic-microwave-assisted ethanol extraction methods solid–liquid
PLE - pressurized liquid extraction
Gsps - grape seed polysaccharides

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