

Review

A Review of the Use of Eutectic Solvents, Terpenes and Terpenoids in Liquid–liquid Extraction Processes

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Abstract: Diverse and abundant applications of the eutectic solvents have appeared in the last years. Their promising tunable properties, eco-friendly character and the possibility of being prepared from numerous compounds have led to the publication of numerous papers addressing their use in different areas. Terpenes and terpenoids have been employed in the formulation of eutectic solvents, though they also have been applied as solvents in extraction processes. For their hydrophobic nature, renewable character, low environmental impact, cost and being non-hazardous, they have also been proposed as possible substitutes of conventional solvents in the separation of organic compounds from aqueous streams, similarly to hydrophobic eutectic solvents. The present work reviews the application of eutectic solvents in liquid–liquid extraction and terpenes and terpenoids in extraction processes. It has been made a research in the current state-of-the-art in these fields, describing the proposed applications of the solvents. It has been highlighted the scale-up feasibility, solvent regeneration and reuse procedures and the comparison of the performance of eutectic solvents, terpenes and terpenoids in extraction with conventional organic solvents or ionic liquids. Ultimately, it has been also discussed the employ of predictive methods in extraction, the reliability of thermodynamic models in correlation of liquid–liquid equilibria and simulation of liquid–liquid extraction processes.

Keywords: liquid–liquid extraction; eutectic solvents; terpenes; terpenoids; separation

1. Introduction

In the past two decades, the number of research papers focused on the application of deep eutectic solvents as an alternative to conventional solvents and ionic liquids in various and numerous areas has increased. This rise is due to the search of processes environmentally friendly as eutectic solvent present promising and advantageous characteristics [1].

By the first time, Abbott et al. in 2003 [2] described a novel eutectic solvent formed by a mixture of quaternary ammonium salts with urea that presented a great depression in the melting point compared to the pure substances due to complexation between hydrogen bond acceptors and donors. Later, the term deep eutectic solvent (DES) was introduced to describe solvents composed of eutectic mixtures of Lewis or Brønsted acids and bases, which can include a variety of anionic and cationic compounds [1].

DES present similar tunable physicochemical properties to ionic liquids. Nevertheless, DES have notable advantages as starting materials could cost 10 times less than ionic liquids and can be prepared under mild conditions by simply mixing the components without further purification stages. For this reason, their potential scale-up is much bigger than the production of ionic liquids. Other

interesting properties of eutectic solvents are the low melting points, thermal and chemical stability, biodegradability, volatility and low toxicity, although these features depend on the constituents that compose them [3]. The possibility of starting from a great variety of compounds, such solid materials, has open the door for a great generation of DES and applications.

It should be noted that the term “deep” in DES has been subject to debate. Deep eutectic solvent, it must be applied to systems with eutectic point lower than the melting temperature of pure compounds but being a temperature much lower than that predicted by an ideal thermodynamic behavior [4]. Therefore, the presence of a eutectic point in a mixture cannot reflect whether a mixture is a deep eutectic solvent [5]. According to Martins et al. (2019), to properly characterize a DES, the solid–liquid phase diagram should be measured and compared with the ideal behavior to identify the real temperature depression [5]. Besides, some eutectic mixtures do not present a melting point, only a glass transition temperature. Because of this, they were also named as low-transition-temperature or low melting mixtures [6–8]. In many of the articles in this field, the solid–liquid phase diagram has not been studied, so hereinafter we will simply refer to “eutectic solvents” for the deep eutectic solvents found in the literature.

In the formulation of the eutectic solvents, natural compounds have been also employed, resulting in the term that can be found in literature as “natural deep eutectic solvents” or NADES [9,10]. The use of natural compounds presents certain advantages as biocompatibility and biodegradability, being able to be more environmentally friendly than conventional organic solvents and some ionic liquids [11]. Similarly to biocompatible ionic liquids, eutectic solvents can be based on natural products as sugars, organic acids or amino acids [12]. Furthermore, terpenes and terpenoids have been recently proposed as good candidates in the formation of eutectic solvents [13–16].

Terpenes and terpenoids are well-known natural compounds and the most numerous and various plant products. Terpenes generally relate to hydrocarbons derived from the basic unit of isoprene, while terpenoids are modified terpenes, with the addition of oxygen for example, although the term terpene can encompass both types of compounds [17].

They can be obtained from natural sources or produced from feedstocks as turpentine or petrochemical sources [18]. Terpenes and terpenoids are extensively used in perfumery and cosmetics and can be found in applications in medicine [18]. In this field, promising properties of terpenes and terpenoids have been reported, as biocidal effects on microorganisms *in vitro*, capacity for the reduction of tumor size and inhibition of cancer cell growth or lowering cholesterol levels [16].

Due to the increasing environmental regulations, in the search of greener solvents terpenes and terpenoids have been also investigated as possible substitutes of petroleum-based solvents. From their biomass origin could be considered renewable solvents, with low hazard risk and environmental impact [19]. The most commonly used terpene is limonene, a by-product of the citrus fruits industry. Limonene has been proposed for the substitution of *n*-hexane in some extraction processes, as well as other terpenes and terpenoids [20,21]. Nevertheless, the presence of other possible applications is still scarce and their future as solvents still unknown.

On the other hand, since the apparition of the eutectic solvents with their novel characteristics, numerous applications have appeared and it has been published reviews of the use of eutectic solvents as organic reaction media [6], employment in analytical chemistry [22], production and application in new materials [23] and separation and extraction processes [24,25]. Otherwise, it has been noted by the authors the lack of diverse reviews of the usage of terpenes and terpenoids in extraction processes.

Owing to the presence of numerous, various and increasing utilization of the eutectic solvents, the aim of this work is the establishment of the up-to-date state-of-the-art of the applications of eutectic solvents in liquid–liquid extraction processes, specifically. Besides, it will be reviewed the employment of terpenes and terpenoids in extraction processes as the presence of published works is notably lower than the eutectic solvents. Due to the hydrophobic nature of terpenes and terpenoids, these natural solvents have recently been used in the extraction of organic compounds from aqueous solutions, showing extractive properties comparable or higher than those of hydrophobic eutectic solvents [26,27].

A review of the current situation of the use of both types of solvents in liquid–liquid extraction is presented in this work since hydrophobic eutectic solvents and terpenes or terpenoids are currently being proposed for the separation of solutes or pollutants from aqueous streams.

Specifically, this review has been focused on discussing the technological feasibility of these applications, highlighting the industrial scalability by reviewing the extraction and reusability solvent methods and the comparison with conventional solvents and ionic liquids. Additionally, it has been addressed the use of predictive methodologies, correlation to thermodynamic models and simulation of industrial processes employed eutectic solvents, terpenes and terpenoids in liquid–liquid extraction.

2. Application of Eutectic Solvents in Liquid–liquid Extraction

To analyze the evolution of the use of eutectic solvents in recent years, a search was made in the Scopus database with the keywords: “eutectic solvents.” A total of 3766 publications on eutectic solvents were found in the cited database, until June 2020. In Figure 1, the evolution of the number of publications on eutectic solvents from 2004 to 2020 is plotted. As can be observed, the first paper with the term “deep eutectic solvent” was published in 2004, although in 2003 Abbott et al. [2] had previously published an article on a liquid solvent formed by mixing urea and several solid quaternary ammonium salts. Until 2010, the number of articles on eutectic solvents grew slowly but since 2012 an almost exponential growth has been observed. In 2019, more than 900 articles on eutectic solvents have been published and from January to June 2020, more than 630 works have already been published. Thus, it is expected that 2020 will be the year with the largest number of articles published in this field.

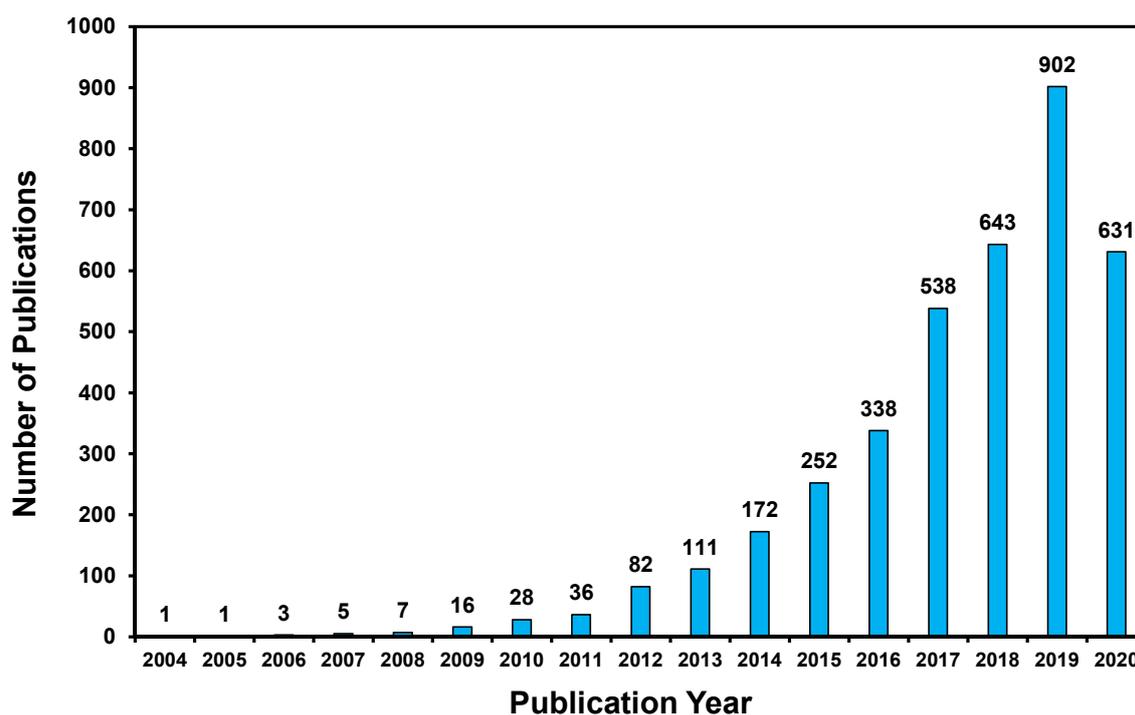


Figure 1. Number of papers in the field of eutectic solvents from 2004 to 2020 (internet search on Scopus, 15 June 2020). Keywords: “eutectic solvents.”

Among the more than 3700 articles found on the use of eutectic solvents, 217 of them have been focused on the application of these solvents in liquid–liquid extraction. In Figure 2, the evolution of the number of articles related to the use of eutectic solvents in liquid–liquid extraction processes is showed from 2007 to 2020. As can be seen, the growth of the publications in this specific application has been later than the growth previously commented for the general field of eutectic solvents, beginning to

increase substantially from the year 2017. In 2019, 54 publications were focused on the use of eutectic solvents in liquid–liquid extraction and 40 works have been already published in the first half of 2020.

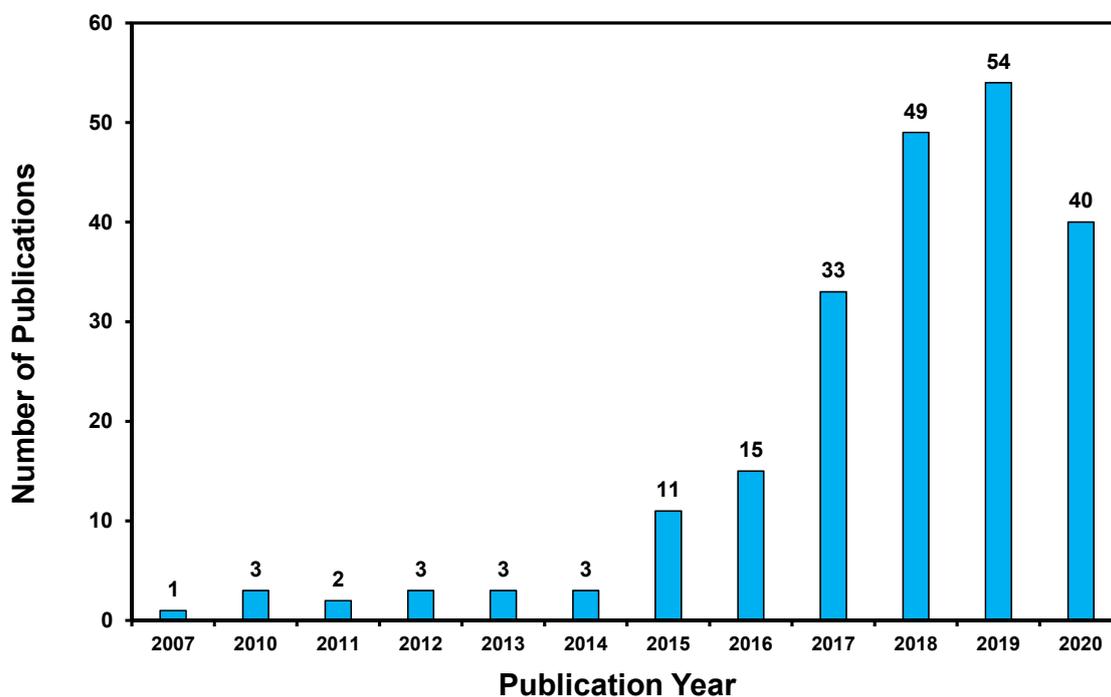


Figure 2. Number of papers on eutectic solvents in liquid–liquid extraction processes from 2007 to 2020 (internet search on Scopus, 15 June 2020). Keywords: “eutectic solvents” and “liquid–liquid extraction.”

To analyze in more detail the 217 publications found on liquid–liquid extraction with eutectic solvents, these works have been grouped into a total of 8 categories according to the type of application. These categories are listed below ordered from earliest to newest applications. Later, the articles published in each of these categories are analyzed:

1. Separation of solutes from oils and biodiesel.
2. Separation of hydrocarbons.
3. Separation of alcohols from hydrocarbons.
4. Separation of value-added compounds.
5. Formation of Aqueous Biphasic Systems (ABS) using eutectic solvents.
6. Separation of organic compounds using hydrophobic eutectic solvents (HES).
7. Separation of metals using hydrophobic eutectic solvents (HES).
8. Development of analytical methods using eutectic solvents.

Considering the categories described above, Figure 3 represents the percentage distribution of the 217 articles published on liquid–liquid extraction using eutectic solvents. As seen, eutectic solvents are being widely studied in the development of new analytical methodologies, being the category with the largest number of published articles.

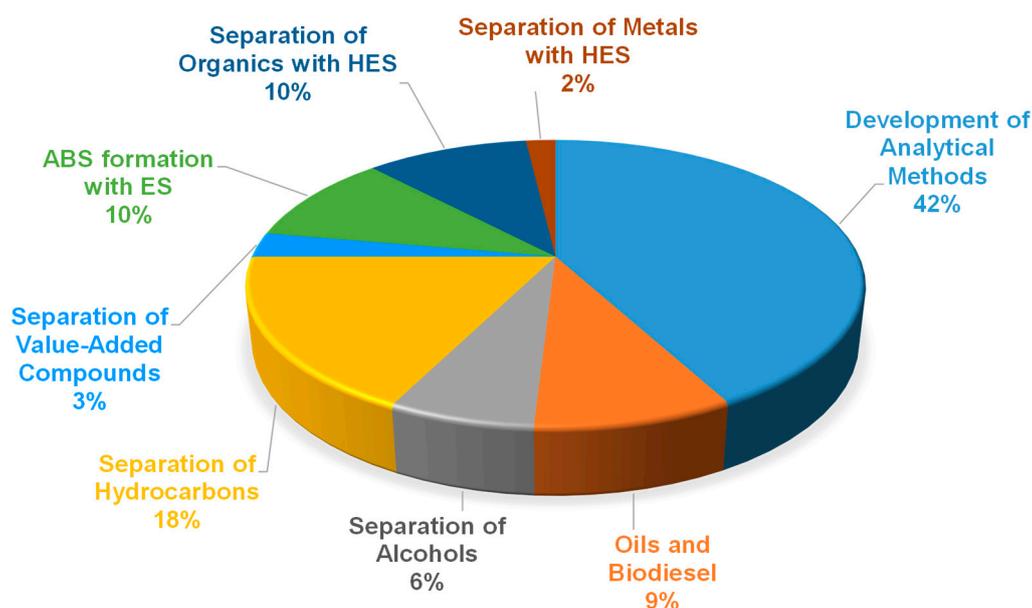


Figure 3. Percentage distribution of the 217 published papers (2007–2020) on eutectic solvents (ES) in liquid–liquid extraction as a function of the application.

This review is focused on the application of eutectic solvents in liquid–liquid extraction separation processes, so the development of analytical methods is out of the main objective of this work. Despite this, a global review of the analytical methods developed with these solvents will be carried out at the end of the section dedicated to eutectic solvents to describe the application of these alternative solvents in liquid–liquid microextraction. Recently, three reviews have been published focused on the analytical application of eutectic solvents [28–30]. In these works, the variables of analytical methods are analyzed in greater depth.

Among the 217 works found, 126 are focused on the development of separation and purification processes of solutes by liquid–liquid extraction. As seen in Figure 3, the application of eutectic solvents in hydrocarbon separation has been the most studied to date, followed by two other more recent applications, which are the formation of aqueous biphasic systems and the extraction of organic compounds using hydrophobic eutectic solvents. Two of the earliest proposed applications of eutectic solvents in liquid–liquid extraction, the separation of solutes from oils and biodiesel and the separation of alcohols from hydrocarbons are found below with 9% and 6% of the published papers, respectively.

2.1. Eutectic Solvents in Liquid–Liquid Extraction Processes

In this subsection, a critical review of the articles published to date on the application of eutectic solvents in liquid–liquid extraction processes is done. In each of the eight categories, a description of the evolution of the use of these solvents is made, highlighting the main results obtained. Special emphasis has been placed on comparing the results obtained using eutectic solvents with those using conventional organic solvents or other alternative solvents, such as ionic liquids. Besides, the extraction of solutes from real streams and the use of large scales have been also analyzed in the reviewed papers. Thus, the potential use of eutectic solvents at the industrial scale will be assessed in each of the applications.

Another important aspect that has been highlighted in the different articles is the regeneration and reuse of eutectic solvents to ensure the economic viability of the extraction process. At the end of this subsection, a review of the different predictive methods used in the selection of eutectic solvents, the thermodynamic models used for the correlation of the liquid–liquid equilibria and the simulation methodologies of the separation processes are also described.

2.1.1. Separation of Organic Compounds from Oils and Biodiesel

In 2007, Abbott et al. [31] proposed the use of the (quaternary ammonium salts + glycerol) eutectic solvent to extract glycerol from biodiesel. This was the first application of eutectic solvents in liquid–liquid extraction processes. From 2007 to 2020, the extraction of organic compounds from biodiesels and oils has been widely studied, as can be observed in the papers listed in Table 1.

Table 1. Eutectic Solvents (ES) in the Liquid–liquid Extraction from Vegetable Oils and Biodiesel.

Solute	Raffinate	Eutectic Solvent	Year	Ref.
Glycerol	Biodiesel	Quaternary ammonium salts + glycerol	2007	[31]
Glycerol	Palm Oil-Biodiesel	Choline chloride (ChCl) + ethylene glycol	2010	[32]
Glycerol	Palm Oil-Biodiesel	ChCl + 2,2,2-trifluoroacetamide		
Glycerol	Palm Oil-Biodiesel	ChCl + glycerol	2010	[33]
Glycerol	Palm Oil-Biodiesel	Methyl triphenyl phosphonium bromide + (glycerol, ethylene glycol or triethylene glycol)	2011	[34]
Glycerol	Palm Oil-Biodiesel	Ternary ES: ChCl + glycerol + ethylene glycol	2015	[35]
KOH	Palm Oil-Biodiesel	9 ES based on ChCl and 9 ES based on methyltriphenylphosphonium bromide (MTPB)	2011	[36]
Palmitic Acid	Palm Oil	Betaine monohydrate + propionic acid	2017	[37]
Palmitic acid, β -Carotene, α -tocopherol	Palm Oil	Binary ES: Betaine monohydrate + (glycerol or propylene glycol)		
Palmitic Acid	Palm Oil	Ternary ES: Betaine monohydrate + (propylene glycol + glycerol) or (propylene glycol + propionic acid) or (glycerol + propionic acid)	2018	[38]
Palmitic Acid	Palm Oil	Betaine monohydrate + propionic acid	2020	[39]
Tocols	Palm Oil	Betaine monohydrate + acetic acid		
Phenol, <i>p</i> -Cresol, β -naphthol	Model Oil	ChCl + acetic acid		
Hydroxybenzoic acid, Protocatechuic acid, Vanillic acid, Tyrosol, <i>p</i> -Coumaric acid, Caffeic acid, Apigenin, Pinoresinol	Virgin Olive Oil	ChCl + malonic acid	2015	[40]
Hydroxytyrosol and Tyrosol derivatives	Olive Oil	ChCl + citric acid		
Free Fatty Acids	Crude Rice Bran Oil	ChCl + ethylene glycol		
Terpenes	Citrus Essential Oils	ChCl + glycerol	2014	[41]
		ChCl + urea		
		MTPB + ethylene glycol		
		Lactic acid + glucose + water (mole ratio 6:1:6)	2016	[42]
		Lactic acid + glucose + water (mole ratio 3:1:3)	2019	[43]
		ChCl + ethylene glycol, ChCl + glycerol, ChCl + Urea, ChCl + Oxalic acid, and Betaine Monohydrate + Glycerol	2019	[44]
		ChCl + glycerol		
		ChCl + (1,3-butanediol, 2,3-butanediol, 1,2-propanediol or 1,3-propanediol)	2018–2019	[45,46]

The separation of glycerol from biodiesel has been studied in several published articles by extraction with eutectic solvents. Abbott et al. [31] tested various combinations of quaternary ammonium salts in the extraction of glycerol from biodiesel produced using KOH, ethanol and vegetable oils. A batch procedure was also used with both rapeseed and soybean oil (500 g) and 150 g of KOH, confirming the applicability of eutectic solvents in the extraction of glycerol from biodiesel at larger scales. The reuse of the eutectic solvent was also studied. To recycle the salt, the separation of choline chloride from glycerol was successfully done using 1-butanol as anti-solvent. The most outstanding results were obtained using the eutectic solvent formed by choline chloride and glycerol with a 1:1 glycerol:salt molar ratio.

Research on the separation of glycerol from biodiesel has been continued in several articles published by Shahbaz et al. [32,34], Hayyan et al. [33] and Ho et al. [35]. In all these works, the liquid–liquid extraction of glycerol from palm oil-based biodiesel has been studied using different eutectic solvents. Shahbaz et al. (2010) [32] used eutectic solvents formed by choline chloride and

(ethylene glycol or 2,2,2-trifluoroacetamide) in several mole ratios. According to the results, the optimal molar compositions of the eutectic solvents to maximize the removal of glycerol from palm oil-based biodiesel were (1:2.5) for the (choline chloride + ethylene glycol) eutectic solvent and (1:1.75) for the (choline chloride + 2,2,2-trifluoroacetamide) solvent.

Hayyan et al. (2010) [33] used the eutectic solvent formed by choline chloride and glycerol at 1:1, 1:1.5 and 1:2 molar ratios to separate glycerol from palm oil-based biodiesel. The optimal mole ratio in the solvent was 1:1, being this result in agreement with the optimization done by Abbott et al. [31]. In this work, the used solvent was recovered after the extraction by crystallizing the ammonium salt with 1-butanol and an industrial process for the recovery is fully described. The purified biodiesel was compared with the international standards EN 14214 and ASTM D6751, fulfilling both standards regarding glycerol content in biodiesel.

Shahbaz et al. (2011) [34] studied the application of methyl triphenyl phosphonium bromide-based eutectic solvents in the recovery of glycerol from palm oil-based biodiesel. Solvents formed by methyl triphenyl phosphonium bromide as hydrogen bond acceptor and three different hydrogen bond donors: glycerol, ethylene glycol and triethylene glycol were tested. The obtained biodiesel after the extraction was compared with the ASTM D6751 international biodiesel standard. The ethylene glycol and triethylene glycol were found to be successful to remove all of the free glycerol from palm-oil-based biodiesel fulfilling the cited standard. The optimum molar ratio for the ethylene glycol and triethylene glycol eutectic solvents was found to be 0.75:1 (DES:biodiesel) based on the high removal of total glycerol and minimum usage of solvent.

Shahbaz et al. (2011) [36] also used eutectic solvents to remove the residual catalyst (KOH) from palm oil-based biodiesel. Nine eutectic solvents based on choline chloride (ChCl) and another nine solvents based on methyltriphenylphosphonium bromide (MTPB) were studied. The highest values of KOH removal were obtained for the ChCl:glycerol and MTPB:glycerol eutectic solvents, with yields of 98.59% and 97.57%, respectively. In this work, the reusability of the solvents to remove KOH from biodiesel was also studied in five successive extractions using fresh biodiesel batches.

More recently, Ho et al. (2015) [35] studied the separation of glycerol from palm oil-based biodiesel using ternary eutectic solvents. These ternary mixtures were formed by choline chloride, glycerol and ethylene glycol in several proportions. The average total glycerol removal efficiency for the studied ternary eutectic solvents was 81.43%, which was higher than both ammonium and phosphonium-based solvents reported in the previously described works of Hayyan et al. (2010) and Shahbaz et al. (2011) [33,34]. Therefore, the use of ternary eutectic solvents seems to be justified as it has shown better yields than binary eutectic solvents.

Analyzing all the works that have studied the separation of glycerol from biodiesel, it should be noted that real biodiesel streams have been used and eutectic solvents have reached the requirements set by international standards. In addition, solvent recovery has been studied and relatively large-scale tests have been carried out. To confirm the real application of these solvents, successive extraction and regeneration cycles at larger scales should be done.

As seen in Table 1, the extraction of palmitic acid from palm oil using eutectic solvents has been studied in several works. In the papers published by Israyandi et al. (2017), Zahrina et al. (2018) and Mulia et al. (2020) [37–39], betaine monohydrate-based eutectic solvents were used for this application. The highest extraction yields of palmitic acids were obtained using the mixture of betaine monohydrate and glycerol in a molar ratio of 1:8, achieving an extraction efficiency of 49.4% [38]. The selective extraction of palmitic acid was studied, also analyzing the extraction efficiency of antioxidants (β -Carotene and α -tocopherol) present in the palm oil. According to the obtained results, most of the antioxidants were preserved in the refined palm oil, so the eutectic solvents for could be used in the deacidification of palm oil for food purposes [38]. The solvent recovery was also evaluated by simple cooling of the extract phase. The extracted palmitic acid solid was recovered using a vacuum filter [39]. In this application, real samples of palm oil have been used to study the selective separation of palmitic acid and the recovery of the extracted solute has been achieved. Larger

scale and successive cycle studies should be performed to demonstrate the technical feasibility of using eutectic solvents in the extraction of palmitic acid.

The separation of phenolic and value-added compounds from oils using eutectic solvents has also been studied in different works. In 2014, Gu et al. [41] proposed the use of solvents formed by choline chloride and (ethylene glycol, glycerol or urea) and the mixture (methyltriphenylphosphonium bromide + ethylene glycol) to extract phenol, *p*-cresol and β -naphthol from a model oil. The obtained extraction efficiencies using the eutectic solvents were comparable to those using the 1-ethyl-3-methylimidazolium tetrafluoroborate ([bmim][BF₄]) ionic liquid and were substantially higher than the efficiencies using water, ethylene glycol or the aqueous solution of choline chloride.

In 2015, the extraction of tocots from palm oil was studied by Abdul Hadi et al. [40] using eutectic solvents formed by choline chloride and (acetic, malonic or citric acid). The highest extraction yields were obtained for the choline chloride + malonic acid eutectic solvents. The regeneration and reuse of the solvents was studied using a mixture of water and hexane (4:1, *v/v*) to separate the extracted tocots. The eutectic solvent was regenerated in a rotary evaporator to remove volatiles at 60 °C for 15 h. The regenerated solvent showed a slightly yellow color, possibly due to traces of oil and tocots entrapped but it was successfully used in another set of extraction.

The application of eutectic solvents in the production of biodiesel from non-vegetable oils has been also studied. Pan et al. (2017) [47] used eutectic solvents formed by choline chloride and formic, acetic, oxalic and propandioic acids in the obtaining of biodiesel from wet and unbroken microalgae biomass. The highest yields were obtained using the eutectic solvent composed of choline chloride and acetic acid in one step of lipid extraction from microalgae and biodiesel production using H₂SO₄ as the catalyst.

The use of eutectic solvents in the production of biodiesel from animal fats has been also reported in the literature. Sander et al. (2018) [48] applied the eutectic solvent formed by choline-chloride and ethylene glycol in a molar ratio of 1:2.5 in the extraction of glycerol from biodiesel obtained from veal and beef tallow, lard, chicken and goose fats. The effect of temperature in the extraction of glycerol was studied obtaining extraction yields of glycerol close to 100% at 50 °C using the previously cited eutectic solvents in the extraction of glycerol from all tested biodiesels from animal fats.

Recently, Sander et al. (2020) [49] have also applied the eutectic solvents in the synthesis of biodiesel from waste coffee grounds. The eutectic solvent composed of potassium carbonate and ethylene glycol with a 1:10 molar ratio was used in the extractive deacidification of waste coffee grounds oil, obtaining extraction yields of 86–94%, being these values higher than those achieved using the conventional method based on esterification with H₂SO₄. In this work, the eutectic solvent composed of choline chloride and ethylene glycol with a 1.0:2.5 molar ratio was also used in the extraction of glycerol and glycerides from the obtained biodiesel. This extraction was performed in batch experiments and a continuous column extractor, achieving glycerol and glyceride contents in the purified biodiesel below the EN 14214 limit using the continuous method. Therefore, the eutectic solvents were successfully used in the deacidification of waste coffee grounds and the purification of the obtained biodiesel from the same waste.

Eutectic solvents have been also used to recover value-added compounds from olive oil. Paradiso et al. (2016 and 2019) [42,43] have reported the separation of hydroxybenzoic acid, protocatechuic acid, vanillic acid, *p*-coumaric acid, caffeic acid, apigenin, pinosresinol, tyrosol, hydroxytyrosol and tyrosol derivatives. In these works, ternary eutectic solvents formed by (lactic acid + glucose + water) have been employed. According to the authors, this separation technique based on eutectic solvents could be applied in olive mills to determine the amount of phenolic compounds in oils.

In 2019, Zullaikah et al. [44] applied several eutectic solvents to extract free fatty acids and a bioactive compound (γ -oryzanol) from crude rice bran oil. In this work, four eutectic solvents formed by choline chloride + (ethylene glycol, glycerol, urea or oxalic acid) were studied and a natural eutectic

solvent (NADES) formed by betaine monohydrate and glycerol in a mole ratio of 1:8 was also used. The highest value of recovery of γ -oryzanol was obtained using the NADES.

Finally, the eutectics solvents have been also proposed to be used in the deterpenation of citrus essential oils [45,46]. To this purpose, choline chloride + (glycerol, 1,3-butanediol, 2,3-butanediol, 1,2-propanediol or 1,3-propanediol) eutectic solvents have been tested in the separation of limonene from linalool and in the deterpenation of a crude orange essential oil. The eutectic solvents showed selectivities higher than those achieved using an ethanol aqueous solution and comparable to the values employing the 1-ethyl-3-methylimidazolium ethylsulfate ionic liquid. In addition, the distribution ratios of linalool were higher than those using ethylene glycol or the 1-ethyl-3-methylimidazolium methanesulfonate ionic liquid. Therefore, the tested eutectic solvents exhibited competitive extractive properties to be used in the deterpenation of essential oils.

2.1.2. Separation of Aromatic, Sulfur or Nitrogen Hydrocarbons from Alkanes

The separation of hydrocarbons with eutectic solvents is the most studied application until the date in liquid–liquid extraction, fundamentally seeking three objectives: to reduce the aromatic, sulfur or nitrogen contents in fuels. To analyze the evolution of the use of eutectic solvents in these applications, the published articles have been grouped according to the type of solutes extracted.

In Table 2, the articles that have studied the extraction of aromatic hydrocarbons (benzene, toluene, ethylbenzene and xylene) from *n*-alkanes using eutectic solvents are collected. As can be seen, the vast majority of works have studied the extraction of a single aromatic hydrocarbon from an *n*-alkane, despite the fact that liquid fuels are much more complex mixtures.

The first articles that studied the separation of aromatic hydrocarbons using eutectic solvents were published by Kareem et al. in 2012 and 2013 [50–52]. These authors studied the separation of benzene from *n*-hexane and the separation of toluene from *n*-heptane using mixtures of phosphonium salts with ethylene glycol or sulfolane as solvents. They studied the influence of the molar relationship between salt and hydrogen bond donor on the extractive capacity of the solvent, without working exactly at the eutectic point. The obtained benzene or toluene distribution ratios and the aromatic/aliphatic selectivities using eutectic solvents were lower than the reported using pyridinium-based ionic liquids in the same separation. A comparison with the extractive properties of sulfolane and *N*-formylmorpholine was also done, showing the eutectic solvents values close to those using the conventional solvents.

In 2013, the separation of aromatic hydrocarbons from *n*-alkanes using quaternary ammonium salts-based eutectic solvents was firstly studied [53]. Gonzalez et al. [53] tested the eutectic solvents formed by choline chloride + (lactic acid or glycerol) in the separation of benzene from *n*-hexane. The choline chloride-based eutectic solvents showed benzene distribution ratios lower than sulfolane and the obtained by Kareem et al. (2012) using the eutectic solvent formed by methyltriphenylphosphonium bromide and ethylene glycol in the molar ratio of 1:4 [50]. By contrast, the benzene/*n*-hexane selectivities were substantially higher using the choline chloride + (lactic acid or glycerol) eutectic solvents than those for the sulfolane and the phosphonium-based eutectic solvent.

Therefore, choline chloride-based eutectic solvents could be applied to obtain aromatic hydrocarbons with high purity but a higher solvent-to-feed ratio than that using sulfolane should be needed.

Table 2. Eutectic Solvents in the Liquid–liquid Extraction of Aromatic Hydrocarbons.

Solute	Raffinate	Eutectic Solvent	Year	Ref.
Benzene	<i>n</i> -Hexane	Methyltriphenylphosphonium bromide + ethylene glycol	2012	[50]
Benzene and Ethylacetate	<i>n</i> -Hexane	Choline chloride + lactic acid Choline chloride + glycerol	2013	[53]
Benzene, Toluene, Ethylbenzene and <i>m</i> -Xylene	<i>n</i> -Octane	Tetrabutylammonium bromide + sulfolane	2014	[54]
Benzene, Toluene or Pyridine	<i>n</i> -Hexane	Choline chloride + glucose (Tetramethylammonium chloride, tetraethylammonium chloride, tetrabutylammonium chloride, or tetrahexylammonium chloride) + (ethylene glycol or glycerol)	2016	[55]
Benzene	<i>n</i> -Hexane	Tetrabutylammonium bromide + (sulfolane or triethylene glycol)	2017	[56]
Benzene	Cyclohexane	Methyltriphenylphosphonium bromide + (triethylene glycol or 1,2 propanediol) Choline chloride + triethylene glycol	2017	[57]
Benzene, Toluene	Cyclohexane, <i>n</i> -Heptane	N-ethylpyridinium bromide + (N-formyl morpholine or levulinic acid)	2019	[58]
Benzene, Cyclohexane	Thiophene, Hexadecane	Choline chloride + (monoethylene glycol, diethylene glycol, triethylene glycol, monoethanolamine, diethanolamine; or triethanolamine)	2019	[59]
Toluene	<i>n</i> -Heptane	Tetrabutylphosphonium bromide + (ethylene glycol or sulfolane)	2012	[51]
Toluene	<i>n</i> -Heptane	Ethyltriphenylphosphonium iodide + (ethylene glycol or sulfolane)	2013	[52]
Toluene	<i>n</i> -Heptane	(Choline chloride, benzylcholinium chloride or tetrabutylammonium chloride) + levulinic acid	2016	[60]
Toluene, Quinoline	<i>n</i> -Heptane	Methyltriphenyl phosphonium bromide + (ethyleneglycol or glycerol)	2016	[61]
Toluene	<i>n</i> -Octane	Choline chloride + malonic acid	2018	[62]
Toluene	<i>n</i> -Hexane, <i>n</i> -Heptane	Choline chloride + Phenol	2019	[63]
Ethylbenzene	<i>n</i> -Octane	Tetrabutylammonium bromide + (pyridine and/or ethylene glycol)	2015	[64]
Ethylbenzene	Styrene	Tetrabutyl ammonium bromide + (ethylene glycol diethylene glycol or triethylene glycol)	2019	[65]
Benzene, Toluene, Ethylbenzene, Xylene	Reformer and Pyrolysis Gasolines	Choline chloride + (ethylene glycol, glycerol, levulinic acid, phenylacetic acid, malonic acid or urea)	2018	[66]

Mulyono et al. (2014) [54] studied the performance of the eutectic solvent formed by tetrabutylammonium bromide and sulfolane in the separation of benzene, toluene, ethylbenzene and *m*-xylene from *n*-octane. In this paper, a complete comparison between the distribution ratios and selectivities obtained with the eutectic solvent and those using sulfolane, propylene carbonate or ionic liquids was done. In the four separations of aromatics from *n*-octane, the eutectic solvent exhibited slightly lower distribution ratios than those for sulfolane or imidazolium and pyridinium-based ionic liquids and comparable selectivities.

Kurnia et al. (2016) [55] compared the performance of the choline chloride + glucose eutectic solvent in the separation of benzene and toluene from *n*-hexane with the sulfolane values, concluding that the distribution ratios for the conventional solvent were higher than those for the eutectic solvent, whereas the opposite trend was observed in the aromatic/aliphatic selectivity.

Naik et al. (2016) [61] also compared the extractive properties of the ethyltriphenyl phosphonium bromide + (ethyleneglycol or glycerol) eutectic solvents with those of sulfolane, obtaining lower toluene distribution ratios using the eutectic solvent. All these conclusions are in agreement with the comparison performed by Hadj-Kali et al. (2017) [67] between the extractive properties of a wide number of eutectic solvents and those for conventional solvents. They concluded that the use of eutectic solvents in the separation of aromatics from alkanes will enhance the selectivity but reduce the distribution ratio. This fact would imply that a greater flow rate of solvent in the extraction column would be necessary to achieve similar yields to those obtained with sulfolane.

As mentioned, the majority of works have been focused on the extraction process but the process of regeneration and reuse of the eutectic solvent has hardly been addressed. Salleh et al. (2017) [57] studied the separation of the extracted benzene from the tetrabutylammonium bromide + sulfolane eutectic solvent. This separation was performed in a rotary evaporator under 100 mbar vacuum and 40 °C. Four consecutive cycles of extraction and regeneration were done without observing a decrease in the extraction efficiency.

A similar approach was used by Larriba et al. (2018) [66] to regenerate the choline chloride + levulinic acid eutectic solvent after the extraction of benzene, toluene, ethylbenzene and *p*-xylene from reformer and pyrolysis gasoline models. The vapor–liquid equilibrium between the hydrocarbons and the eutectic solvents at 343.2, 353.2 and 363.2 K was determined using headspace gas chromatography, to optimize the solvent regeneration by flash distillation process. The used temperatures were selected after analyzing the thermal stability of the eutectic solvents obtained by thermogravimetric analyses. According to the results obtained, the regenerated eutectic solvent with a purity greater than 99% could be recovered in a flash distillation operating at 363.2 K and 5 kPa. Therefore, the regeneration of eutectic solvents by distillation using vacuum in the separation of hydrocarbons seems to be technically viable.

As observed in Table 2, the simultaneous extraction of several aromatic hydrocarbons from complex mixtures has been little studied to date and the majority of works used binary mixtures formed by an aromatic and an alkane. Larriba et al. (2018) [66] used pyrolysis and reformer gasoline models formed by six and seven hydrocarbons, respectively. However, the extraction of aromatics from real gasoline has not been studied to date. This fact should be addressed to realistically assess the potential of eutectic solvents to be used at the industrial scale. Similarly, all the works have been carried out using single-stage extraction tests, so it would be necessary to use continuous extractors to evaluate the industrial applicability of these solvents in the separation of aromatics.

The application of eutectic solvents in the separation of sulfur-containing hydrocarbons has also been extensively studied, as shown in Table 3. Zhu et al. (2015) [68] proposed the use of eutectic solvents formed by choline chloride and several straight-chain monobasic acids in the removal of dibenzothiophene from cyclohexane and *p*-xylene. Combining the liquid–liquid extraction with photochemical oxidative desulfurization, the removal of dibenzothiophene reached 98.6%.

Table 3. Eutectic Solvents in the Extraction of Sulfur-Containing Aromatic Hydrocarbons.

Solute	Raffinate	Eutectic Solvent	Year	Ref.
Thiophene	<i>n</i> -Heptane	Choline chloride + phenol + FeCl ₄ Choline chloride + ethylene glycol + FeCl ₄	2017	[69]
Thiophene	<i>n</i> -Hexane <i>n</i> -Octane	Tetrahexylammonium bromide + (ethylene glycol or glycerol)	2017	[70]
Thiophene	<i>n</i> -Hexane	(Tetraethylammonium chloride or methyltriphenylphosphonium bromide) + (ethylene glycol or glycerol)	2018	[71]
Thiophene	<i>n</i> -Hexane <i>n</i> -Octane	(Tetraethylammonium chloride, tetrahexylammonium bromide or methyltriphenylphosphonium bromide) + (ethylene glycol or glycerol)	2018	[72]
Thiophene Benzothiophene Dibenzothiophene	<i>n</i> -Octane	Choline chloride + glycerol	2016	[73]
4,6-dimethyl-dibenzothiophene	<i>n</i> -Dodecane	Choline acetate + glycerol		
Thiophene Benzothiophene Dibenzothiophene	<i>n</i> -Decane	Choline chloride + 1,5-pentandiol Choline chloride + glycerol	2017	[74]
Thiophene Dibenzothiophene	Fuel	Tetrabutylammonium bromide + imidazole		[75]
Thiophene Benzothiazole	<i>n</i> -Heptane	Tetrahexylammonium bromide + (ethylene glycol or glycerol)	2018	[76]
Thiophene Dibenzothiophene	Model Oil	Tetrabutylammonium bromide + polyethylene glycol	2019	[77]
Dibenzothiophene	Cyclohexane	Choline chloride + 2C _n H _{2n+1} COOH, n = 0, 1, 2, 3, 4)	2015	[68]
Dibenzothiophene	<i>p</i> -Xylene			
Dibenzothiophene	Fuel	Tetrabutylammonium bromide + polyethylene glycol 200	2017	[78]
Dibenzothiophene	<i>n</i> -Octane	Screening with 49 eutectic solvents	2018	[79]
Dibenzothiophene Benzothiophene	Fuel (Molecular Simulation)	Choline chloride + urea Choline chloride + ethylene glycol	2018	[80]
2,3-Methylthiophene	<i>n</i> -Heptane	Tetrahexylammonium bromide + (ethylene glycol or glycerol)	2018	[81]

In 2016, Zhao et al. [73] studied the extraction of thiophene, benzothiophene, dibenzothiophene and 4,6-dimethyl-dibenzothiophene from *n*-octane and *n*-dodecane using choline chloride + glycerol and choline acetate + glycerol eutectic solvents. In this paper, a comparison between the performance of both eutectic solvents and those using 71 ionic liquids was done.

The sulfur-containing hydrocarbon partition coefficients using the eutectic solvent were substantially lower than the results obtained for the majority of used ionic liquids. Therefore, the tested eutectic solvents were considered as solvents with low potential to be applied in the desulfurization of fuels.

A comparison between the extractive properties of tetrahexylammonium bromide + (ethylene glycol or glycerol) eutectic solvents and those for ionic liquids in desulfurization was also performed by Warrag et al. (2017) [70]. According to these authors, the distribution coefficients and the selectivities for the eutectic solvent were somewhat lower than those of all the studied ionic liquids. Warrag et al. (2018) [71] also compared the performance of the eutectic solvents formed by (tetraethylammonium chloride or methyltriphenylphosphonium bromide) and (ethylene glycol or glycerol) in the extraction of thiophene with the results showed by ionic liquids. The thiophene distribution ratios for all the tested eutectic solvents were lower than those using ionic liquids except for the 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([emim][NTf₂]). By contrast, the selectivity of the eutectic solvent formed by tetraethylammonium chloride and glycerol was the highest. Hence, eutectic solvents in sulfur-containing aromatic hydrocarbons extraction have shown low distribution coefficients but some of them may show higher selectivities than other alternative solvents, such as ionic liquids. This conclusion is similar to that previously discussed for the extraction of aromatics from alkanes.

The desulfurization of complex model fuels using eutectic solvents was first studied by Gano et al. (2017) [75]. In this work, a model fuel formed by *n*-decane, cyclohexane, iso-octane and toluene was used to extract 500 mg/kg of sulfur compounds (thiophene and dibenzothiophene) using the tetrabutylammonium bromide + imidazole eutectic solvent. In addition, two commercial fuels were also used, obtaining lower sulfur extraction yields in commercial fuels than in the simulated. The regeneration of the eutectic solvent was also studied in this work using back-extraction with water followed by evaporation under vacuum. Five consecutive extraction and regeneration cycles were done without a significant decrease in the sulfur removal efficiency of the eutectic solvent.

Therefore, eutectic solvents have shown lower extraction capacities than those of conventional organic solvents or ionic liquids in desulfurization of fuels but they have been successfully used and regenerated in extraction from real fuels. In the near future, large-scale and continuous extraction tests should be carried out with the solvents that have shown the best extraction properties in simple stage experiments, to evaluate the potential of these solvents to be applied in refineries.

The eutectic solvents have been also tested in the extraction of nitro-containing aromatic hydrocarbons and polycyclic aromatic hydrocarbons, as can be observed in Table 4. The most studied solutes have been pyridine and quinoline. In 2016, Sander et al. [82] proposed the use of the eutectic solvents formed by choline chloride + (urea or glycerol) to separate pyridine from *n*-heptane. These authors compared the extractive properties of the eutectic solvents with literature values for ionic liquids. They found that the pyridine distribution ratios were higher using ionic liquids but the selectivity was higher for the tested eutectic solvents.

Warrag et al. (2019) [83] also compared the extractive properties of the ethyltriphenylphosphonium bromide + ethylene glycol eutectic solvent in the separation of pyridine from *n*-hexane and *n*-heptane with the literature value for ionic liquids. According to these authors, the eutectic solvent exhibited the highest values of pyridine distribution ratios and pyridine/*n*-alkane selectivities higher than the majority of ionic liquids tested. Similar conclusions were recently published by Warrag et al. (2020) [84] in the extraction of pyridine from *n*-hexane and *n*-heptane using the methyltriphenylphosphonium bromide + glycerol eutectic solvent. This solvent showed selectivities substantially higher than those for ionic liquids and comparable pyridine distribution ratios. Therefore, the phosphonium-based eutectic solvents seem to be good candidates to be applied in the denitrogenation of fuels.

However, analyzing the articles collected in Table 4, the denitrogenation of fuels using eutectic solvents has been only focused on the separation of nitro-containing aromatic hydrocarbons from model mixtures with alkanes. Real fuels should be also tested to confirm the applicability of these solvents at the industrial scale and the regeneration and reuse of the solvents should be also studied.

The eutectic solvents have been also proposed in the separation of polycyclic aromatic hydrocarbons from *n*-alkanes. Specifically, the separation of tetralin from *n*-dodecane has been recently studied using the eutectic solvents formed by tetrabutylphosphonium bromide (propionic acid, formic acid or levulinic acid) [85]. In this work, the regeneration of the eutectic solvent after the extraction of tetralin was studied. Due to the high boiling points of solutes, the solvent regeneration was done using back-extraction instead of distillation. In the back-extraction, water was used as a solvent to dissolve the hydrophilic eutectic solvent and to separate the hydrophobic tetralin. The subsequent separation of water and the eutectic solvents was done using flash distillation. Four cycles of extraction and regeneration were performed without observing a significant decrease in the values of selectivity and tetralin distribution ratio.

Table 4. Eutectic Solvents in the Extraction of Nitro-Containing Aromatic Hydrocarbons and Polycyclic Aromatic Hydrocarbons.

Solute	Raffinate	Eutectic Solvent	Year	Ref.
Pyridine Toluene	<i>n</i> -Hexane	Choline chloride + urea Choline chloride + glycerol	2016	[82]
Pyridine Benzothiazole	<i>n</i> -Hexane <i>n</i> -Heptane	Methyltriphenylphosphonium bromide + ethylene glycol	2019	[83]
Pyridine	<i>n</i> -Hexane <i>n</i> -Heptane <i>n</i> -Octane	Binary: (Methyltriphenylphosphonium bromide + glycerol) Ternary: (Methyltriphenylphosphonium bromide + glycerol + ethylene glycol)	2020	[84]
Quinoline Indoline	<i>n</i> -Heptane Toluene	Methyltriphenylphosphonium bromide + ethylene glycol	2017	[86]
Quinoline	<i>n</i> -Heptane (Molecular Simulation)	Methyltriphenylphosphonium bromide + ethylene glycol	2018	[87]
Tetralin	<i>n</i> -Dodecane	Tetrabutylphosphonium bromide + (Propionic Acid, Formic acid, or Levulinic acid)	2020	[85]

2.1.3. Separation of Alcohols from Hydrocarbons

As seen in Table 5, the eutectic solvents formed by choline chloride as hydrogen bond acceptor has been widely used in the separation of linear alcohols (methanol, ethanol, *n*-propanol and *n*-butanol) from hydrocarbons due to the hydrophilic character of these solvents.

In 2013, Oliveira et al. [88] proposed the use of eutectic solvents to separate the azeotropic mixture of ethanol and *n*-heptane using the solvents formed by choline chloride with glycerol, levulinic acid or ethylene glycol. These authors compared the extractive properties of the eutectic solvents with those from literature for ionic liquids. The eutectic solvent formed by choline chloride and levulinic acid showed higher ethanol distribution ratios than ionic liquids, whereas the other two tested eutectic solvents exhibited distribution ratios comparable to the values for ionic liquids. In terms of ethanol/*n*-heptane selectivities, the eutectic solvents achieved higher values than the majority of ionic liquids. In this work, the recovery and reuse of the eutectic solvents were also addressed. The separation of the extracted ethanol and *n*-heptane from the solvent was also successfully achieved by evaporation. Using NMR, these authors confirmed that the structure of the regenerated eutectic solvent was coincident with that for the fresh solvent.

The separation of ethanol from *n*-hexane and *n*-heptane was also studied by Rodríguez et al. (2015) using the eutectic solvents formed by choline chloride and glycolic acid or lactic acid [89]. A comparison

with the extractive properties of ionic liquids was also done, concluding that the eutectic solvents exhibited ethanol/*n*-alkane selectivities higher than the ionic solvents and comparable distribution ratios. In this work, the regeneration of the solvent was also achieved by evaporation of the solutes in a vacuum line.

Table 5. Eutectic Solvents in the Liquid–liquid Extraction of Alcohols from Hydrocarbons.

Solute	Raffinate	Eutectic Solvent	Year	Ref.
Methanol	Toluene <i>n</i> -Heptane	Choline chloride + malic acid	2017	[90]
Methanol Ethanol	Benzene	Choline chloride + (ethylene glycol, levulinic acid or 1,2-propanediol)	2018	[91]
Ethanol	<i>n</i> -Heptane	Choline chloride + (glycerol, levulinic acid or ethylene glycol)	2013	[88]
Ethanol	<i>n</i> -Hexane <i>n</i> -Heptane	Choline chloride + (glycolic acid or lactic acid)	2015	[89]
Ethanol	Methyl ethyl ketone	(Choline chloride or tetramethylammonium chloride) + glycerol	2016	[92]
Ethanol	<i>n</i> -Hexane <i>n</i> -Heptane <i>n</i> -Octane	Choline chloride + (urea or 1,2-propanediol) Tetrabutylammonium bromide + levulinic acid	2017	[93]
Ethanol	<i>n</i> -Hexane	Choline chloride + (oxalic acid or malonic acid)	2017	[94]
Ethanol	<i>n</i> -Hexane <i>n</i> -Heptane	Binary: Choline chloride + 1,2-propanediol Ternary: Choline chloride + (1,2-propanediol + water)	2018	[95]
Ethanol	Dimethyl carbonate	Choline chloride + (glycerol, ethylene glycol, urea or malonic acid)	2019	[96]
Ethanol <i>n</i> -Propanol <i>n</i> -Butanol	Ethyl acetate <i>n</i> -Propylacetate <i>n</i> -Butylacetate	Choline chloride + malonic acid	2018	[97]
Ethanol <i>n</i> -Propanol <i>n</i> -Butanol	(Ethyl, propyl or butyl)acetate (Ethyl, propyl or butyl)propionate	Choline chloride + glutaric acid	2019	[98]
Phenol Cresol	<i>n</i> -Hexane, Toluene <i>p</i> -Xylene	Choline chloride, triethylamine hydrochloride or ethylamine hydrochloride to form eutectic solvents	2012	[99]
Phenol, <i>o,m,p</i> -Cresol Cresols	Coal tar <i>n</i> -Hexane	Imidazole to form eutectic solvents Imidazole to form eutectic solvents	2015 2016	[100] [101]
Phenol	Toluene	Choline chloride, triethylethanaminium chloride or trimethylmethanaminium chloride to form eutectic solvents	2016	[102]

Samarov et al. (2017) [97] studied the application of the eutectic solvents formed by choline chloride and oxalic acid or malonic acid in the extraction of ethanol from *n*-hexane. A comparison with the literature values of ionic liquids and water was done. These authors concluded that the eutectic solvents exhibited better ethanol/*n*-hexane selectivities than the ionic liquids. By contrast, water was revealed as a better agent to separate ethanol from *n*-hexane than the eutectic solvents considering distribution ratios and selectivities. This comparison shows the low real applicability of eutectic solvents in this application, as they showed worse extractive properties than water.

In addition to studying the separation of linear alcohols from linear or aromatic hydrocarbons, the extraction of ethanol from methyl ethyl ketone [92] and dimethyl carbonate [96] has been reported. In the separation from the ketone, the eutectic solvents composed of choline chloride or tetramethylammonium chloride and glycerol exhibited better extractive properties than those using pure glycerol [92]. In the separation of ethanol from dimethyl carbonate, selectivities higher than 400 were obtained using the (choline chloride + urea) [96]. Therefore, promising results have been obtained in both separations of ethanol. In the nearest future, solvent extraction and regeneration cycles should be also addressed and it is necessary a more complete comparison with other solvents.

The extraction of linear alcohols (ethanol, *n*-propanol and *n*-butanol) from acetates and propionates using eutectic solvents have also been studied by Samarov et al. [97,98]. These authors compared the selectivities obtained using the eutectic solvent formed by choline chloride and malonic acid with

those for ionic liquids from literature. They concluded that the 1-ethyl-3-methylimidazolium hydrogen sulfate ([emim][HSO₄]) and 1-hexyl-3-methylimidazolium hydrogen sulfate ([hmim][HSO₄]) ionic liquids exhibited higher values of selectivity than the experimental for the eutectic solvents in the separation of ethanol from ethyl acetate, in the separation of *n*-propanol from *n*-propyl acetate and in the extraction of *n*-butanol from *n*-butyl acetate.

Finally, the separation of phenols and cresols from hydrocarbons has been studied using salts or imidazole to form a eutectic solvent. In 2012, Pang et al. [99] proposed the use of three salts (choline chloride, triethylamine hydrochloride or ethylamine hydrochloride) to separate phenol and cresol from hydrocarbons by forming eutectic solvents. To recover and reuse the choline chloride, diethyl ether was found to be an efficient solvent to recover the ammonium salt. Three consecutive cycles of separation and salt regeneration were done without affecting the phenol removal. A similar approach was used by Jiao et al. in the separation of phenols and cresols from coal tar and *n*-hexane using imidazole to form a eutectic solvent with the solutes [100,101]. In this case, water was used as an efficient solvent to recover the imidazole and three separation-regeneration cycles were successfully performed. Lin et al. (2016) [102] also studied the separation of phenol from toluene using choline chloride, triethylethanaminium chloride or trimethylmethanaminium chloride as salts to form eutectic solvents with the extracted phenol. According to these authors, the highest extraction yields were obtained using the choline chloride.

2.1.4. Separation of Value-Added Compounds

From 2017, several papers have been focused on the separation of value-added compounds using liquid–liquid extraction with eutectic solvents. As seen in Table 6, a wide variety of compounds has been separated: vitamins, amino acids, monosaccharides, pyrethroid or antibiotics. In some of these works, in addition to the eutectic solvent, a second phase formed by organic solvents has been used for the extraction or partitioning of the solutes.

Bezold et al. (2017) [103] studied the separation of α -tocopherol from β -tocopherol using a biphasic system formed by the eutectic solvents of choline chloride + (levulinic acid or 1,4-butanediol) and other liquid phase composed of *n*-heptane and ethanol. The proportions of the solvents were optimized to maximize the separation yield of tocopherols. The system formed by *n*-heptane/ethanol/(choline chloride + 1,4-butanediol) in the proportions 30/40/30 (wt./wt./wt.), was revealed as the most promising in partition chromatography experiments. In 2019, Bezold et al. [104] used a similar system in the partition of coumarin, β -ionone, β -carotene and α -tocopherol. In this case, the eutectic solvents were formed by menthol and levulinic acid, whereas the other liquid phase was a mixture of *n*-heptane and methanol. The effect of modifying the proportions of solvents on the partition coefficient of solutes was studied, concluding that this system was a high potential to separate the studied solutes by centrifugal partition chromatography.

Table 6. Eutectic Solvents in the Separation of Value-added Compounds

Solute	Raffinate	Eutectic Solvent	Year	Ref.
α -Tocopherol	β -Tocopherol	Choline chloride + (levulinic acid or 1,4-butanediol) with other liquid phase formed by (<i>n</i> -heptane + ethanol)	2017	[103]
Chloromycetin Thiamphenicol Vitamin E	Milk Red Palm Biodiesel	Choline chloride + glycerol with other liquid phase formed by chloroform Potassium carbonate + glycerol	2017 2018	[105] [106]
Partition of: Coumarin, β -Ionone, β -Carotene and α -Tocopherol		Menthol + levulinic acid with other liquid phase formed by (<i>n</i> -heptane + methanol) Two phases using hydrophilic and hydrophobic eutectic solvents.	2019	[104]
Monosaccharides and Amino Acids	Kelp	Hydrophilic: Choline chloride + (caffeic acid and/or glycerol) Hydrophobic: Tetrabutylammonium chloride + (octanoic acid and/or decanoic acid)	2020	[107]

The extraction of vitamin E from red palm biodiesel has been also addressed using eutectic solvents. Manurung et al. (2018) [106] 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.

The extraction of the antibiotics, chloromycetin and thiamphenicol from milk was studied by Li et al. (2017) [105] using the eutectic solvent formed by choline chloride and glycerol and a second liquid phase composed of chloroform. Using the ratio of 2:1 in volume for (the eutectic solvent: chloroform) system, the recoveries of chloromycetin and thiamphenicol achieved values of 87.23% and 83.17%, respectively.

Finally, the use of systems formed by hydrophobic and hydrophilic eutectic solvents has recently been proposed for the recovery of monosaccharides and amino acids from kelp [107]. Li et al. (2020) have used air assisted dispersive liquid–liquid microextraction in a liquid–liquid system consisting of a hydrophilic eutectic solvent composed of choline chloride and (caffeic acid and/or glycerol) and a hydrophobic eutectic solvent formed by tetrabutylammonium chloride and (octanoic acid and/or decanoic acid). Using this innovative separation system, high values of recovery of galactose, fucose, tyrosine and valine from kelp were obtained.

As seen, the application of eutectic solvents in the separation of high added value compounds requires the addition of a second organic phase to achieve the partition of the solutes. This approach is similar to that used in the formation of aqueous biphasic systems that will be described below, in which the generation of two immiscible phases for the partition of solutes is sought.

2.1.5. Aqueous Biphasic Systems (ABS) with Eutectic Solvents to Separate Organic Compounds

Aqueous biphasic systems composed of polymers or salts have been widely used to selectively separate or purify bioactive compounds. From 2003, the application of ionic liquids in the formation of ABS has been increased, tending in recent years towards the use of biocompatible ionic liquids [108]. In 2014, Zeng et al. first proposed the use of eutectic solvents in the formation of ABS for protein partitioning [109]. In this work, extraction efficiencies of bovine serum albumin close to 100% were obtained using the eutectic solvent formed by choline chloride and urea and adding K_2HPO_4 . Since this first article, 21 articles have been published on the use of eutectic solvents in the formation of ABS, as can be seen in Table 7.

Table 7. Formation of Aqueous Biphasic Systems (ABS) with Eutectic Solvents

Solute	Eutectic Solvent	Salt or Polymer	Year	Ref.
Bovine serum albumin	Choline chloride + (urea or methylurea)	K ₂ HPO ₄	2014	[109]
Bovine serum albumin	(Tetramethylammonium chloride or tetrapropylammonium bromide) + urea			
Trypsin	Choline chloride + (ethylene glycol, glycerol, D-glucose, D-sorbitol)	K ₂ HPO ₄	2015	[110]
Bovine serum albumin				
Trypsin	Betaine + (urea, methylurea, D- glucose, D-sorbitol, ethylene glycol or glycerol)	K ₂ HPO ₄ K ₃ PO ₄	2016	[111]
Ovalbumin				
Textile dyes: Sudan III and PB 29	Choline chloride + (carboxylic acids or urea)	Poly(propylene) glycol 400	2016	[112]
Bovine serum albumin	Binary: Tetramethylammonium chloride (TMAC) + (urea, glycerol, ethylene glycol or D-(+)-glucose).	K ₂ HPO ₄	2016	[113]
	Ternary: TMAC + glycerol + (urea, ethylene glycol, D-(+)-glucose or D- sorbitol)			
Anthraquinones	(Choline chloride, decyltrimethylammonium bromide, dodecyltrimethylammonium bromide or tetradecyltrimethylammonium bromide) + hexafluoroisopropanol	Na ₂ SO ₄ K ₂ HPO ₄ Na ₂ HPO ₄ (NH ₄) ₂ SO ₄ KH ₂ PO ₄	2017	[114]
Gallic acid	Choline chloride + sugars: (D-glucose, D-fructose or saccharose)	K ₂ HPO ₄	2017	[115]
Phenolic compounds				
Amino-acids, Alkaloids	Choline chloride + glucose	Poly(propylene)glycol 400	2017	[116]
Bovine serum albumin				
Papain	Choline chloride + PEG (molar ratio of 20:1)	NaH ₂ PO ₄ Na ₂ CO ₃ Na ₃ C ₆ H ₅ O ₇ Na ₂ CO ₃	2017	[117]
RNA	(Tetrabutylammonium chloride, tetrabutylammonium bromide, tetraethylammonium chloride or tetraethylammonium bromide) + PEG polymers	NaH ₂ PO ₄ Na ₂ SO ₄ K ₂ HPO ₄ Sodium citrate	2017	[118]
Phenolic compounds	Choline chloride + (ethanol, <i>n</i> -propanol	K ₂ HPO ₄	2018	[119]
Amino-acids, Alkaloids	1,2-propanediol or ethylene glycol)			
Phenylalanine	Choline chloride + (urea, lactic acid or sorbitol)			
Enantiomers	Betaine + (urea, glucose or glycol)	11 salts, being the optimal: K ₃ PO ₄	2018	[120]
DNA from bovine blood	(Tetrabutylammonium bromide or betaine) + (PPG 400, D-(+)-glucose, sucrose, D-sorbitol or xylitol)	Na ₂ CO ₃ K ₂ HPO ₄ NaH ₂ PO ₄ Sodium citrate	2018	[121]
Pigments: Amaranth, Sunset yellow FCF, Sudan III.	Tetrabutylammonium bromide + polypropylene glycol 400	12 salts, including Na ₂ CO ₃ and Na ₂ SO ₄	2018	[122]
Gallic acid				
Caffeine	Tetrabutylammonium chloride + (ethanol or <i>n</i> -propanol)	K ₃ C ₆ H ₅ O ₇ or K ₃ C ₆ H ₅ O ₇ / C ₆ H ₈ O ₇ buffers	2018	[123]
L-tryptophan				
Proteins from porcine pancreas	(L-proline or lysine) + (glycerol, ethylene glycol, D-sorbitol or xylitol)	Tetrabutyl-ammonium chloride + PPG 400	2019	[124]
Phycobiliprotein from Spirulina	(Glucose, fructose, sucrose, maltose or xylose) + glycerol	Na ₂ SO ₄ Na ₂ CO ₃ K ₂ HPO ₄ PEG 6000	2019	[125]
Lysozime from chicken egg white	(Tetrabutylammonium bromide or benzyltributylammonium bromide) + carboxylic acids	Na ₂ SO ₄ Na ₂ CO ₃ K ₂ HPO ₄ NaH ₂ PO ₄	2019	[126]
Thyptophan	Choline chloride + polyethylene glycol 2000	Sodium citrate	2019	[127]
Dyazo Dyes	Choline chloride + urea	Triton X-100 surfactant	2020	[128]
Dyes: Tartrazine Methylene blue Sudan III	Hydrophilic: Choline chloride + (glycerol, glucose, malonic acid or urea)			
	Hydrophobic: (Decyl trimethyl ammonium chloride, dodecyl trimethyl ammonium chloride or tetradecyl trimethyl ammonium chloride) + hexafluoroisopropanol.	-	2020	[129]
	Tetrabutylammonium bromide + polypropylene glycol 400			

In 2015, the partitioning of bovine serum albumin and trypsin in ABS formed by choline chloride-based eutectic solvents was studied by Xu et al. [110]. In the optimal conditions, the extraction efficiencies for bovine serum albumin and trypsin achieved values of 98.16% and 94.36%, respectively, confirming the great potential of ABS formed by eutectic solvents in the purification of proteins and enzymes.

In 2016, Passos et al. published a very relevant article on the application of eutectic solvents in the formation of ABS [112]. In this work, these authors demonstrated that the eutectic solvent integrity is destroyed in the ABS, because of the disruption of the eutectic solvent hydrogen-bond complex and the preferential solvation of the isolated components by water. In addition, a nonstoichiometric partition of the hydrogen bond donor and acceptor were found in the coexisting phases. Therefore, the eutectic solvent-based ABS must be considered as quaternary instead of ternary systems. Passos et al. also proposed in this paper the use of systems formed by choline chloride, (carboxylic acids or urea) and poly(propylene) glycol 400 in the separation of two textile dyes: Sudan III and PB 29. The application of eutectic solvent-based ABS in the separation of dyes has been subsequently studied in various articles. Zhang et al. (2018) [122] have applied the eutectic solvents formed by tetrabutylammonium bromide and polypropylene glycol 400 in the separation of three dyes: Amaranth, Sunset yellow FCF and Sudan III. The highest extraction efficiencies were above 98% and Na_2CO_3 was revealed as the most adequate salt to split two phases. Dyazo dyes has been also separated by Fernandez et al. (2020) using the eutectic solvent composed of choline chloride and urea [128]. In this work, the selective separation of dye mixtures and their complete removal from a polluted aqueous stream was successfully achieved.

The separation of three dyes: Tartrazine, Methylene blue and Sudan III has been also studied by Xu et al. (2020) [129]. In this paper, a system formed by a hydrophilic eutectic solvent and a hydrophobic eutectic solvent was proposed. In this system, the recoveries of Tartrazine and Methylene blue in the hydrophilic phase were 88.64% and 92.63%, respectively, the recovery of Sudan III was close to 100% in the hydrophobic phase. Therefore, the ABS formed by immiscible eutectic solvents has been revealed as good systems to separate dyes with different hydrophobicity.

In addition to the separation of dyes, ABS formed with eutectic solvents have been widely used in the separation and purification of proteins and enzymes. As previously discussed, the first proteins and enzymes studied in ABS formed by eutectic solvents were the bovine serum albumin and trypsin [109,110]. In 2016, Li et al. [102] proposed the use of a betaine-based eutectic solvent to extract bovine serum albumin, trypsin and ovalbumin. At the optimal conditions, the protein extraction yields achieve a value of 99.82%. In addition, in this work the back-extraction of proteins from the eutectic solvents was studied mixing the extract phase with an equal volume of fresh K_3PO_4 aqueous phase, obtaining back-extraction yields of 32.66%.

Real biological samples have been recently used in the recovery of proteins using ABS formed by eutectic solvents. Meng et al. (2019) [124] studied the separation of proteins from porcine pancreas using eutectic solvents formed by L-proline or lysine as hydrogen bond acceptors and glycerol, ethylene glycol, D-sorbitol or xylitol as hydrogen bond donors. The highest yield was obtained for the extraction of chymotrypsin with a value of 97.30%. The separation of phycobiliprotein from *Spirulina* has been reported by Rathnasamy et al. (2019) [125] using eutectic solvents formed by glucose, fructose, sucrose, maltose or xylose as hydrogen bond acceptors and glycerol as hydrogen bond donor. In this system, 5.8 mg of phycocyanin was obtained for each gram of *Spirulina*. Finally, the extraction of lysozyme from chicken egg white has been also studied by Xu et al. (2019) [126] using eutectic solvents formed by tetrabutylammonium bromide or benzyltributylammonium bromide and carboxylic acids. The extraction yield of lysozyme was 98% and the activity of lysozyme after the process of extraction was 91.73% of initial activity.

The separation of amino acids has been also addressed using ABS formed by eutectic solvents. Farias et al. (2018) [119] studied the partition of L-tryptophan and L-phenylalanine, L-tyrosine and glycine using eutectic solvents formed by choline chloride as hydrogen bond acceptor and ethanol, *n*-propanol 1,2-propanediol or ethylene glycol as hydrogen bond donors. The highest values of partition

coefficients were obtained for the L-tryptophan: 180, followed by L-phenylalanine: 23, L-tyrosine: 7 and glycine: 0.35. The pH effect on the partition of L-tryptophan in ABS formed by choline chloride based-eutectic solvents was also studied by Farias et al., obtaining a higher partition coefficient at pH 9 than at pH 5 [123]. The separation of phenylalanine enantiomers have been also researched using ABS formed by choline chloride or betaine as hydrogen bond acceptors and urea, lactic acid, glucose or sorbitol as hydrogen bond donors [120]. Among the tested eutectic solvent-based ABS, the highest separation factor was obtained by the (choline chloride + lactic acid) with a value of 1.2.

The application of ABS formed with eutectic solvents in the extraction and purification of nucleic acids has recently been proposed. Zhang et al. (2017) [118] studied the extraction and back-extraction of RNA using ABS formed by eutectic solvents composed of quaternary ammonium salts and PEG polymers. Extraction efficiencies for RNA close to 100% were obtained, whereas the RNA back-extraction using Na_2SO_4 solution achieved yields higher than 90%. The extraction of DNA from bovine blood has also studied using ABS composed of ionic liquids and eutectic solvents [121]. The extracted DNA was analyzed by agarose gel electrophoresis and the results indicated that the proposed method could be applied to effectively extract DNA from real blood samples.

As described, the application of ABS formed with eutectic solvents has shown high extraction yields in the separation of organic compounds of different types (dyes, proteins, enzymes, amino acids or nucleic acids). The vast majority of papers have studied the partitioning of solutes in the two aqueous phases but it would be necessary in the future to study in greater depth the process of back-extraction and the reuse of ABS. Some of the works have already used real biological samples achieving good separation yields, so it is expected that for the future the application of eutectic solvent-based ABS will continue towards a larger scale application.

2.1.6. Extraction of Organic Compounds with Hydrophobic Eutectic Solvents (HES)

In 2015, van Osch et al. [130] published the first work on the use of hydrophobic eutectic solvents (HES). In this publication, six HES formed by decanoic acid as hydrogen bond donor and quaternary ammonium salts were described and used in the extraction of acetic, propionic and butyric acids from water. These innovative solvents showed extractive yields higher than those using trioctylamine. Since this first work, a large number of articles have focused on the use of HES in the extraction of different types of solutes, such as organic acids, alcohols, pesticides, antibiotics or dyes from aqueous solutions, as can be seen in Table 8.

The extraction of organic acids from water using HES has been addressed in several papers. Rodríguez-Llorente et al. (2019) studied the extraction of acetic, propionic, butyric and valeric acids using HES formed by DL-menthol or thymol and octanoic acid [26]. The performance of both HES in the extraction was compared with the results obtaining using three terpenoids: geraniol, eugenol and citral. The HES showed extractive properties similar to those using terpenoids but the recovery of the extracted acids from the HES using alkali solutions was not technically viable because of the formation of the octanoate ion. By contrast, the back-extraction of extracted organic acids was successfully done using geraniol. Therefore, the terpenoids seem to be more adequate to this purpose than the tested HES.

Van den Bruinhorst et al. (2019) also studied the extraction of volatile acids from water using the HES formed by trioctylphosphine oxide (TOPO) and dodecanoic acid or dihexylthiourea [131]. The HES composed of TOPO and dihexylthiourea showed good extraction performance at low acid concentrations and small S/F ratios. Therefore, this HES has great potential to be used in the volatile fatty acid extraction from fermentation broths. HES formed by TOPO and decanoic acid or dodecanoic acids have been recently used by Riveiro et al. [132] in the extraction of adipic, levulinic and succinic acid from water. The extraction efficiencies of the HES were compared with the results obtained using pure TOPO. According to the authors, the extraction capacity of TOPO was higher than those for the tested HES in the separation of the three acids.

Another very relevant application of HES has been the extraction of pollutants or biomolecules from aqueous effluents. Riveiro et al. (2015) proposed the use of HES formed by L-menthol and pyruvic, acetic, L-lactic or lauric acids in the recovery of caffeine, tryptophan, isophthalic acid and vanillin [14]. In this work, the partition of these biomolecules was studied and extensively compared with the partition obtained using organic solvents, ABS or ionic liquids from literature, obtaining competitive results using the HES.

Florindo et al. (2017) proposed the use of HES to separate pesticides from water [133]. In this work, HES formed by natural organic acids as hydrogen bond donors and DL-menthol or tetrabutylammonium chloride as hydrogen bond acceptors were employed. The extraction efficiencies of these HES were comparable to those obtained using hydrophobic imidazolium-based ionic liquids. In addition, the HES were used in four consecutive extraction cycles without regeneration, showing a decrease in the efficiency in each cycle. The extraction of five pesticides (bifenthrin, deltamethrin, fenpropathrin, permethrin, tetramethrin) from water has been recently studied by Mat Hussin et al. (2020) using HES formed by DL-menthol and thymol, 3-hydroxybenzoic acid or sesamol [134]. The highest extraction yields were obtained for the HES composed of DL-menthol and sesamol using a mole ratio of 1:1.

Table 8. Extraction of Organic Compounds Using Hydrophobic Eutectic Solvents.

Solute	Raffinate	Hydrophobic Eutectic Solvent	Year	Ref.
Volatile fatty acids	Water	Quaternary ammonium salts + decanoic acid	2015	[130]
Caffeine	Water	DL-Menthol + (pyruvic acid, acetic acid, L-lactic acid or lauric acid)	2015	[14]
Tryptophan				
Isophthalic acid Vanillin				
Pesticides	Water	DL-Menthol + natural organic acids	2017	[133]
Bisphenol A	Water	Tetrabutylammonium chloride + natural organic acids Fatty acids combined: octanoic acid, nonanoic acid, decanoic acid and dodecanoic acid	2018	[135]
Levofloxacin, Ciprofloxacin	Water	Quaternary ammonium salts + (hexanoic acid, octanoic acid, decanoic acid, n-butyl alcohol, cyclohexanol, 1-octanol, 1-dodecanol or 1-dodecanol)	2018	[136]
Ethanol	Water	DL-Menthol + dodecanoic acid	2018	[137]
1-Propanol				
1-Butanol				
Ethanol	Water	DL-Menthol + (decanoic acid or dodecanoic acid)	2018	[138]
1-Propanol				
1-Butanol				
Tyrosol	Olive oil mill wastewater	DL-Menthol + (octanoic acid or dodecanoic acid)	2019	[139]
Phenols				
N,N-Diethyl-4-nitroaniline	Water	10 Binary eutectic solvents formed by: menthol, camphor, borneol, thymol and trans-sobrerol	2019	[16]
Chloranilic acid				
Dyes	Tea beverages and fruit juices	Hexafluoroisopropanol as hydrogen-bond donor and L-carnitine or betaine as hydrogen-bond acceptor	2019	[140]
Pyrethroids				
Acetic acid	Water	(DL-Menthol or thymol) + octanoic acid	2019	[26]
Propionic acid				
Butyric acid				
Valeric acid				
Volatile fatty acids				
2-Chlorophenol	Water	(DL-Menthol, Thymol or dodecanoic acid) + (octanoic acid or decanoic acid)	2019	[141]
o-Cresol				
Phenol	Large volume water	Binary or ternary mixtures of carboxylic acids (C ₈ , C ₉ , C ₁₀ , C ₁₁ and C ₁₂).	2019	[142]
Trace phenolic compounds				
Bisphenol A	Water	Menthol or quaternary ammonium salts + (octanoic acid or decanoic acid)	2020	[143]
Carbamazepine	Water	Menthol + (formic acid or acetic acid)	2020	[144]
Pesticides: Bifenthrin, Deltamethrin, Fenpropathrin	Water	DL-Menthol + (thymol, 3-hydroxybenzoic acid or sesamol)	2020	[134]
Permethrin Tetramethrin				
Adipic acid Levulinic acid Succinic acid	Water	Triethylphosphine oxide (TOPO) + (decanoic acid or dodecanoic acid)	2020	[132]
Phenolic Compounds	Beverage samples	DL-Menthol + carboxylic acids (C ₈ , C ₉ , C ₁₀ , C ₁₁ and C ₁₂).	2020	[145]
Phenol				
2-Chlorophenol	Water	Menthol + (thymol or octanoic acid)	2020	[27]
2-Nitrophenol				

The use of HES in the extraction of pharmaceuticals from aqueous streams has been also studied. Tang et al. (2018) applied HES composed of quaternary ammonium salts and acids or alcohols in the extraction of two antibiotics: levofloxacin and ciprofloxacin [136]. The eutectic solvent formed by trioctylammonium chloride and 1-octanol exhibited extraction efficiencies of both antibiotics around 80–90%, being these values higher than those obtained using halogenated conventional solvents: CHCl_3 , CH_2Cl_2 , $\text{C}_2\text{H}_2\text{Cl}_4$ and $\text{C}_6\text{H}_5\text{Cl}$.

The extraction of carbamazepine has recently studied using HES composed of menthol and formic or acetic acid [144]. In this work, Pekel et al. used diethyl succinate as the diluent, obtaining extraction efficiencies higher than 90% in 30 min using the HES formed by menthol and acetic acid with 1:1 of molar ratio. Martins et al. (2019) proposed the use of HES formed by two terpenes, studying the solid–liquid equilibrium of 10 HES composed of: menthol, camphor, borneol, thymol and trans-sobrerol [16]. In this work, the effect of terpene proportion in the HES on the extraction efficiency of the selective separation of two dyes: *N,N*-diethyl-4-nitroaniline and chloranilic acid was studied. The maximum value of the separation factor of both dyes was 600, demonstrating the great capacity of these HES in the selective separation of dyes.

The extraction of linear and aromatic alcohols from water using HES has been also extensively studied. Verma et al. proposed the use of the HES formed by DL-menthol and dodecanoic acid to extract ethanol, 1-propanol and 1-butanol from water [137]. The HES exhibited substantially higher alcohol/water selectivities than the literature values for hydrophobic ionic liquids, whereas the alcohol distribution ratios for the HES were comparable to those of ionic liquids. These authors have proposed the recovery of the extracted alcohols from the HES by distillation, successfully simulating this process in Aspen Plus [138]. Florindo et al. have studied the extraction of bisphenol A from water using HES formed by binary mixtures of fatty acids [135] and mixtures of menthol or quaternary ammonium salts with octanoic or decanoic acid [143]. The mixture formed by octanoic and dodecanoic acids in a molar ratio of 3:1 showed a bisphenol A extraction efficiency of 88.32%. Better results were obtained using the HES formed by menthol or quaternary ammonium salts, achieving extraction efficiencies of bisphenol A close to 99% with the HES formed by tetraoctylammonium bromide and decanoic acid. In addition, this HES was used in five consecutive cycles with fresh feed without decreasing the extractive capacity.

Several papers have been focused on the extraction of phenols from aqueous solutions. Buldo et al. (2019) [139] applied the HES formed by DL-menthol and octanoic acid or dodecanoic acid, in the recovery of tyrosol and phenol from olive oil mill wastewater. Sas et al. (2019) also used the HES formed by DL-menthol, thymol or dodecanoic acid as hydrogen bond acceptors and octanoic acid or decanoic acid as hydrogen bond donors in the extraction of phenol, 2-chlorophenol and *o*-cresol from water [141]. Using the menthol-based HES, extraction yields higher than 80% for 2-chlorophenol and *o*-cresol were obtained and yields higher than 70% for the separation of phenol were achieved. Yang et al. (2019) have applied the binary and ternary HES formed by mixtures of C_8 – C_{12} carboxylic acids to extract trace phenolic compounds from real samples from the tap, lake and river waters [145]. Using the ternary HES formed by C_8 : C_9 : C_{12} carboxylic acids in molar ratio 3:2:1, extraction efficiency higher than 91.0% of phenolic compounds was achieved. Recently, Rodríguez-Llorente et al. (2020) have used the HES formed by thymol, menthol and octanoic acid to extract phenol, 2-chlorophenol and 2-nitrophenol from aqueous solutions [27]. These HES showed extraction efficiencies lower than those for three terpenoids: geraniol, linalool and citral and a conventional solvent: methyl isobutyl ketone. Because of this, the tested HES were discarded as potential solvents to be used in the extraction of phenols from industrial wastewater.

Finally, the HES has been used in the recovery of pollutants from beverages. The recovery of pyrethroids from tea beverages and fruit juices using eutectic solvents was proposed by Deng et al. (2019) [140]. In this work, new hydrophobic eutectic solvents composed of hexafluoroisopropanol as a hydrogen-bond donor and L-carnitine or betaine as hydrogen-bond acceptor was used. The obtained extraction efficiencies (85–109%) were similar to those using literature methods based on chlorobenzene or chloroform. Yang et al. (2020) [145] also used HES in the extraction of phenolic compounds from

beverage samples of fruit juice, tea drink and soda. Recoveries of bisphenol A higher than 95% were achieved using the HES formed by menthol and undecanoic acid in a molar ratio of 3:1 in the three studied beverages. Therefore, the HES has been revealed as very promising solvents to determine pollutants in beverages.

As described, the HES has been applied in the extraction of a wide variety of organic compounds from 2015. The majority of the works have used synthetic solutions of the compounds in water and real aqueous streams should be used to evaluate the potential of the HES to be applied in industrial applications. Studies on regeneration and reuse of HES are still very scarce and the fatty acid-based HES have been chemically unstable in solvent regeneration with alkalis. Hence, further studies should be conducted in the future with real streams and extraction and regeneration cycles to assess the performance of HES in the extraction of organic compounds from aqueous streams.

2.1.7. Extraction of Metals with Hydrophobic Eutectic Solvents (HES)

In 2016, Van Osch et al. proposed for the first time the use of hydrophobic eutectic solvents in the separation of metals from aqueous solutions [146]. Since this first work, several articles on the use of HES in the extraction of a large number of metals from aqueous solutions have been published, as can be seen in Table 9.

Table 9. Extraction of Metals using Hydrophobic Eutectic Solvents (HES).

Metals Extracted	Raffinate	Hydrophobic Eutectic Solvent	Year	Ref.
Li, Na, K, Co, Ni, Mn, Zn and Cu chlorides	Water	Decanoic acid + lidocaine in a 2:1, 3:1 and 4:1 molar ratio.	2016	[146]
Cu, Fe, Mg, Ca, Cr, Mn, Co and Ni	Mildly acidic solutions	(Menthol or thymol) + (C ₈ , C ₁₀ , C ₁₂ , C ₁₄ , C ₁₆ and C ₁₈) carboxylic acids	2018	[147]
Uranyl nitrate	Aqueous acid	Trioctylphosphine oxide (TOPO) + Phenol	2018	[148]
Pd, Pt, Cu, Co, Ni, Cr and Fe	HCl media	Thymol + trioctylphosphine oxide Trioctylphosphine oxide + capric acid Hydrocinnamic acid + capric acid	2020	[149]
Co and Zn	Water	[BMPYR][NTf ₂] + 2-methyl-2-butanol [HMPYR][Cl] + 1-decanol or [NBz _{1,1,18}][BTMPP] + lactic acid	2020	[150]

The HES formed by lidocaine and decanoic acid in three molar ratios was used in the extraction of Li, Na, K, Co, Ni, Mn, Zn and Cu from water. Van Osch et al. (2016) [146] concluded that the metal extraction occurs via an ion-exchange mechanism, transferring the protonated lidocaine to the water phase. In this work, high distribution coefficients were obtained for all tested metals, even for high Co²⁺ concentrations and low mass fractions of HES. In addition, the HES with a higher decanoic to lidocaine ratio (3:1 and 4:1) were successfully regenerated using sodium oxalate 0.1 M solutions.

Schaeffer et al. (2018) proposed the use of menthol and thymol-based HES in the selective extraction of Cu from Fe, Mg, Ca, Cr, Mn, Co and Ni in mildly acidic solutions [147]. Analyzing the metal distribution ratios obtained using the HES, authors concluded that Cu(II) and Fe(III) could be successfully extracted, whilst extraction of Mg(II), Ca(II), Cr(III), Mn(II), Co(II) and Ni(II) was negligible at the tested conditions. Because of this, the HES formed by thymol and decanoic acid was successfully used in the highly selective separation of Cu(II) from concentrated solutions containing other transition metals. In addition, this HES was used in five consecutive extraction and stripping cycles with constant extraction efficiency, using a 0.1 M H₂SO₄ solution as a stripping agent. Therefore, the HES based on terpenes (menthol or thymol) were revealed as a non-toxic and biodegradable alternative to conventional solvents in the extraction of Cu.

In 2018, Gilmore et al. proposed the use of HES formed by trioctylphosphine oxide (TOPO) and phenol in the extraction of uranyl nitrate from acidic solutions [148]. Using this HES, the distribution ratio was 500 using 250 ppm uranyl solutions and 5000 for the 2350 ppm solution, being these values similar to those reported for the commercial TRPO extraction process.

Schaeffer et al. (2020) have also used the HES formed by trioctylphosphine oxide and thymol or capric acid and the HES composed of hydrocinnamic and capric acids in the recovery and separation of platinum group and transition metals in HCl media [149]. The TOPO-based HES showed high values of selectivity towards Pt^{4+} , Pd^{2+} and Fe^{3+} , being promising solvents in the selective recovery of platinum-group metals from complex mixtures. Moreover, the tested HES showed selectivities and distribution ratios higher than literature values for TOPO in diluents or ionic liquids. The regeneration of the HES was studied using an acidic 0.1 M thiourea solution, obtaining a regeneration efficiency of 96%. After the extraction using HES, a 0.1 M NaCH_3COO aqueous solution was also used to form palladium nanoparticles with an average size of 5.7 ± 1.3 nm.

Finally, Lukomska et al. have recently studied the liquid–liquid extraction of Co(II) and Zn(II) from aqueous solutions using hydrophobic ionic liquids and HES formed by three ionic liquids: 1-butyl-1-methylpyrrolidinium bis{(trifluoromethyl)sulfonyl}imide ([BMPYR][NTf₂]), 1-hexyl-1-methylpyrrolidinium chloride ([HMPYR][Cl]) or benzyldimethyloctadecylammonium bis(2,4,4-trimethylpentyl)phosphinate ([NBz_{1,1,18}][BTMPP]) and three hydrogen bond donors: 2-methyl-2-butanol, 1-decanol or lactic acid [150]. The Co and Zn extraction efficiencies showed by the tested HES were substantially lower than those obtained for hydrophobic ionic liquids under the same conditions.

In summary, although the extraction of metals with HES has still been studied only in a few articles, the results obtained in the selective separation of metals is very promising, having studied the extraction under different operating conditions and having successfully reused HES with various stripping agents. It is expected that in the next few years the hydrophobic eutectic solvents will be applied in the separation of metals from real mixtures from the industry.

2.1.8. Predictive Methods in Liquid–liquid Extraction with Eutectic Solvents

Due to the great variety of eutectic solvents that have already been proposed in the literature, the use of predictive methods in the selection of the most suitable eutectic solvent in each application becomes increasingly necessary. Furthermore, to optimize and verify the viability of future processes using eutectic solvents, it is necessary to use thermodynamic models to correlate the liquid–liquid equilibrium data obtained experimentally and process simulators. For this reason, the following three sections review the predictive models, the thermodynamic correlation models and the simulators used to date in the literature on eutectic solvents.

Among the articles described in the previous categories, 25 articles were found in which predictive models have been used, with COSMO-based methods being the most widely used, followed by Perturbed-Chain Statistical Associating Fluid Theory (PC-SAFT) and molecular dynamics.

The use of predictive methods in the application of eutectic solvents in the separation of hydrocarbons has been widely studied. The quantum chemical method conductor-like screening model for real solvents (COSMO-RS) has been successfully employed in the prediction of ternary liquid–liquid equilibria in the separation of toluene from *n*-heptane [60], ethylbenzene from *n*-octane [64], ethylbenzene from styrene [65], BTEX aromatics from *n*-octane [54], quinoline or indoline from toluene and *n*-heptane [86], pyridine from *n*-hexane and *n*-heptane and *n*-octane [84] using eutectic solvents. The prediction of solute distribution ratios and selectivities has been also done with the COSMO-RS method in the separation of benzene from *n*-hexane [56], benzene from cyclohexane [57] and dibenzothiophene from *n*-octane [79]. In addition, the COSMO-RS method was used to understand the interactions between the eutectic solvents and thiophene [71] and to predict the toluene solubility in eutectic solvents [66]. Naik et al. (2018) used classical molecular dynamic simulation techniques to understand and predict the phase behavior of ternary systems composed of quinoline, *n*-heptane and eutectic solvents, obtaining predictions with low deviations from the experimental ternary liquid–liquid equilibria [87]. Finally, Warrag et al. (2018) used PC-SAFT theory to successfully predict the distribution coefficients and thiophene/alkane selectivities in the separation of thiophene from *n*-hexane and *n*-octane [72].

Predictive methods have been also used in the extraction of alcohols from hydrocarbons using eutectic solvents. The COSMO-RS method was applied to predict the liquid–liquid equilibria in the separation of ethanol from *n*-hexane, *n*-heptane or *n*-octane and the separation of methanol and ethanol from benzene [91,93]. The COSMO-SAC model was also used in the selection of choline chloride-based eutectic solvents to separate dimethylcarbonate from ethanol [96]. PC-SAFT was also applied in the separation of ethanol, propanol and butanol from acetates and propionates using the choline chloride + glutaric acid eutectic solvents, correctly describing the phase equilibria of binary and ternary systems [98].

In the selective separation of β -tocopherol from α -tocopherol, Bezold et al. (2017) used the COSMO-RS methodology to predict the partition coefficients of solutes in eutectic solvents [103]. This predictive method overestimated the partition coefficient of α -tocopherol but the predicted trend of the tocopherol distribution was reproduced for the experimental values. The COSMO-RS successfully predicted key thermodynamic parameters (selectivities, solute distribution ratios, mixing excess enthalpies and activity coefficients at infinite dilutions) in the separation process of the deterpenation of essential oils [45,46].

Finally, predictive models have been also applied in the use of hydrophobic eutectic solvents in liquid–liquid extraction. Verma et al. (2018) used the COSMO-SAC model to predict the solid–liquid equilibria of the HES formed by lauric acid and DL-menthol and the ternary liquid–liquid equilibria in the separation of ethanol, 1-propanol and 1-butanol from water using the cited HES [137]. The liquid–liquid equilibria of ternary systems formed by linear alcohols and water using HES with menthol were also successfully predicted by COSMO-based calculations in Aspen Plus and molecular dynamics simulations [138]. Martins et al. (2019) applied the COSMO-RS method to accurately predict the solid–liquid equilibria of HES composed of terpenes [16]. Rodríguez-Llorente et al. (2019) [26] used the COSMO-RS method to select the most adequate HES and terpenoids to be used in the extraction of volatile fatty acids from water, by calculating the infinite dilution activity coefficients of the solutes in a wide number of HES, terpenes and terpenoids. The same methodology has been applied in the solvent screening to select the most promising solvents for the separation of phenols from industrial wastewater using HES, terpenes and terpenoids [27]. Finally, the COSMO-SAC model has been recently used in the solvent screening for 1-butanol dehydration, estimating distribution coefficients and selectivities [151].

Therefore, different predictive methods have been used to date to predict thermodynamic equilibria in ternary systems containing eutectic solvents and they have also been used in solvent screening. To date, the most widely used predictive methods have been those based on COSMO calculations, obtaining predictions with high reliability. The use of these methods in future investigations may reduce the experimental efforts, using those eutectic solvents that have a greater potential for the studied application.

2.1.9. Correlation of Liquid–Liquid Equilibrium Using Eutectic Solvents

To simulate and optimize a liquid–liquid extraction process on an industrial scale, the correlation of experimental data is essential, since commercial process simulators can thus be used. Among the described papers on the use of eutectic solvents in liquid–liquid extraction processes, 33 papers have used thermodynamic models to correlate the obtained liquid–liquid equilibria, being the most applied the Non-random two liquids (NRTL) model followed by the Universal quasichemical (UNIQUAC) model.

In the separation of hydrocarbons, the NRTL thermodynamic model has been successfully used in the correlation of the ternary liquid–liquid equilibria obtained in the separation with eutectic solvents of benzene and toluene from cyclohexane [57,58], BTEX from *n*-octane [54], toluene from *n*-hexane, *n*-heptane or *n*-octane [51,52,62,63], ethylbenzene from *n*-octane [64], ethylbenzene from styrene [65], thiophene from *n*-hexane and *n*-octane, pyridine and toluene from *n*-hexane [82], pyridine or benzothiazole from *n*-hexane, *n*-heptane and *n*-octane [83,84] and tetralin from dodecane [85]. On the other hand, the UNIQUAC model was simultaneously used with the NRTL model in the correlation

of equilibria in the separation of toluene, quinoline and iodine from *n*-heptane [61,86] and in the extraction of benzene from thiophene and cyclohexane from hexadecane [59]. In these publications, the deviations between experimental and predicted data were similar using both thermodynamic models, being lower than 1%. Since the UNIQUAC model requires more complex mathematical modeling than the NRTL model and the results obtained are comparable, the NRTL model has been more widely used in the literature for the correlation of liquid–liquid equilibrium data of systems containing hydrocarbons and eutectic solvents.

In the extraction of alcohols, the NRTL model has adequately correlated the liquid–liquid equilibria in the extraction of methanol and ethanol from benzene [91], ethanol from *n*-hexane, *n*-heptane and *n*-octane [89,93,94], ethanol from dimethyl carbonate [96], ethanol from methyl ethyl ketone [92] and ethanol, propanol and butanol from ethyl, propyl and butyl acetates and propionates [97,98]. The UNIQUAC model was used together with the NRTL thermodynamic model in the separation of methanol from toluene or *n*-heptane [90], ethanol from *n*-hexane and *n*-heptane [95] and in the extraction of cresols from *n*-hexane [101]. In the separation of methanol or ethanol from *n*-alkanes, the deviations between experimental and fitted data of UNIQUAC model were slightly lower than those for the NRTL model [90,95], whereas the deviations of UNIQUAC model were almost double than those for the NRTL model in the extraction of cresols from *n*-hexane [101]. Therefore, in the extraction of alcohols from hydrocarbons both thermodynamic methods have shown similar reliability to be used in the correlation of ternary liquid–liquid equilibrium data using eutectic solvents.

The NRTL model has been also employed to correlate the thermodynamic equilibrium data obtained in the separation of alcohols from water using eutectic solvents. Verma et al. (2018) used the NRTL model in the extraction of ethanol, 1-propanol and 1-butanol from water using HES and Song et al. (2020) in the dehydration of 1-butanol using hydrophilic eutectic solvents [137,151]. Finally, the experimental tie-lines of the equilibrium obtained in the use of ABS formed by eutectic solvents were adequately correlated with the NRTL model, showing deviations lower than 1.7% using eutectic solvents formed by choline chloride and sugars (glucose, fructose or saccharose) [115] and deviations below 1.2% in the ABS formed by eutectic solvents composed of choline chloride and ethanol, *n*-propanol, 1,2-propanediol or ethylene glycol [119]. In both papers, potassium phosphate was used to form the ABS previously described, showing the NRTL model a high reliability to be used in the correlation of liquid–liquid equilibria in ABS formed by eutectic solvents.

Hence, the NRTL model has also demonstrated its applicability in liquid–liquid extraction using hydrophobic eutectic solvents and aqueous biphasic systems formed by eutectic solvents and, therefore, this model can be used in the simulations of extraction processes with eutectic solvents.

2.1.10. Simulation of Liquid–Liquid Extraction Processes with Eutectic Solvents

The vast majority of industrial liquid–liquid extraction processes use counter-current extractors with multiple equilibrium stages. On the contrary, experimental liquid–liquid extraction studies with eutectic solvents have been focused on obtaining equilibrium data in a single stage. Because of this, the simulation of liquid–liquid extraction processes is essential to determine the potential of these solvents to be used on an industrial scale and to optimize the extraction processes. However, a very small number have been published to date on simulating liquid–liquid extraction processes with eutectic solvents.

Jiao et al. (2016) use the Aspen Plus simulator to optimize the extractor in the separation of cresols from *n*-hexane via eutectic solvents formation using imidazole [101]. In these simulations, the parameters of the NRTL model obtained from the correlation of experimental data obtained in the same work were used. In the optimization, the number of equilibrium stages in the extractor and the mass flow of imidazole were varied to maximize the recovery of *o*-cresol.

Verma et al. (2018) also used Aspen Plus simulation software to optimize the whole process to separate 1-butanol from water using hydrophobic eutectic solvents [138]. In this work, the eutectic solvents were introduced to Aspen Plus as pseudo components using COSMO-based calculations. In the simulations, the extraction of 1-butanol from water with the HES formed by menthol and decanoic or dodecanoic acids and the subsequent solvent regeneration were optimized. A complete comparison of the proposed process using HES with the results and costs for a conventional process using mesitylene as solvent was also done using Aspen Plus simulations, concluding that the alternative process using HES is economically and technically competitive with the currently used process in the industry.

Aspen Plus simulator has been also used to simulate the dehydration of 1-butanol using the eutectic solvent formed by choline chloride and urea [151]. In the simulations done by Song et al., the parameters of the NRTL model obtained from the experimental data were used to optimize the extraction and the solvent recovery by flash distillation. In the extractor, the equilibrium stages and the mass flow of the solvent were optimized to maximize the extraction yield of 1-butanol and its purity, whereas pressure and temperature of flash distillation were optimized to regenerate the eutectic solvent.

A similar approach using Aspen Plus and NRTL thermodynamic model has been applied by Wu et al. (2020) in the simulation of the whole process of extraction of tetralin from dodecane [85]. In this work, the extractor was simulated to optimize the number of equilibrium stages and the solvent-to-feed ratio. In addition, the solvent recovery was simulated using back-extraction with water followed by a flash distillation to separate the eutectic solvent formed by tetrabutylphosphonium bromide and levulinic acid from water.

Therefore, the application of process simulation in liquid–liquid extraction with eutectic solvents has been little studied to date. However, very valuable results have been obtained using process simulators since it allows the optimization of the whole extraction and solvent regeneration processes. In addition, a comparison between the extraction processes using eutectic solvents with those already used in the industry could be done using simulators to evaluate the technical and economic potential to be employed at the industrial scale.

2.2. General Overview of the Use of Eutectic Solvents in the Development of Analytical Methods by Liquid–Liquid Extraction

As previously discussed, eutectic solvents are currently being used in the development of a large number of analytical methods based on liquid–liquid microextraction processes. This review is focused on the application of eutectic solvents, terpenes and terpenoids in liquid–liquid extraction processes that can be used at the industrial scale. For this reason, a general review of the applications of eutectic solvents in analytics will be carried out without analyzing the specific variables of each of the analytical methods. Recently, several reviews have been published on the application of eutectic solvents in analytical methods, detailing the analytical procedures [28–30].

The analytical methods based on extraction processes with eutectic solvents that are being developed are focused on the determination of organic compounds and metals in water, food and biological samples. In Figure 4, the percentage distribution of the published papers is shown in six categories as a function of the application.

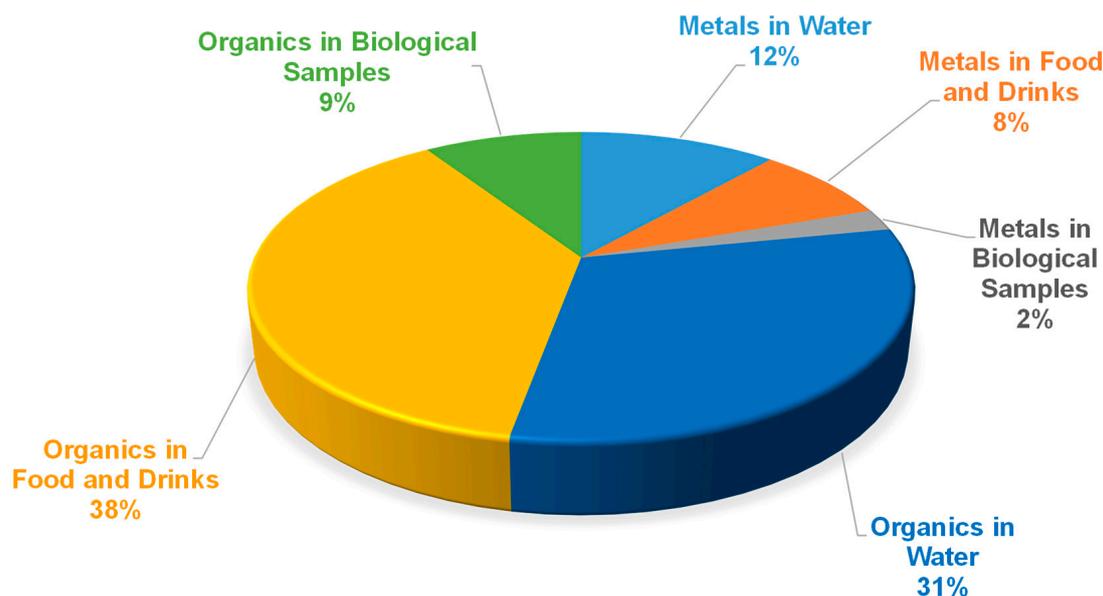


Figure 4. Percentage distribution of the published papers (2010–2020) on eutectic solvents in the development of analytical methods as a function of the application.

As seen, the determination of organic compounds in food is the most relevant application of eutectic solvents in the development of analytical methods. Specifically in the analysis of oils, the eutectic solvents have been used in the quantification of hexanal and heptanal [152], alkyl gallated [153], oxyphenylated phenylpropanoids [154], ferulic, caffeic and cinnamic acids [155], sesamol [156], tert-butylhydroquinone [157–159], chlorophenol, 2,3-dihydroxybenzoic acid, *p*-cresol, 4-chlorophenol, 2,4-dichlorophenol and 2,4,6-trichlorophenol [160] and bisphenol A [161].

The eutectic solvents have been also applied in analytical methods to quantify organic compounds in tea, fruit juices and milk. The organic compounds analyzed in drinks have been: antibiotics [162], curcumin [163,164], diazinon and fenitrothion [165], auxins [166], pesticides [167–169], β -carotene and lycopene [170], phthalates [171], bisphenol-A [172], caffeine [173] and synthetic pigments [174]. Pesticides and insecticides have been also quantified using eutectic solvent-based analytical methods in cucumber [175], tomato [176], honey [177] and cabbage leaves [178]. Finally, meats have been also analyzed to quantify polycyclic aromatic hydrocarbons [179] and antibiotics [180].

A wide variety of organic compounds in water have been analyzed using analytical methods based on microextraction using eutectic solvents, being the second most studied application. Some of the organic compounds analyzed have been: antibiotics [181], chlorophenols [182], microcystins [183], anti-inflammatory drugs [184], malachite green and crystal violet [185,186], polycyclic aromatic hydrocarbons [187,188], ultraviolet filters [189–191], parabens [192], steroids [193], benzene, toluene and ethylbenzene [194], benzylureas [195,196], methadone [197], sulfonamides [198–200], ciprofloxacin [201], agonists [202], organic acids [203] and pesticides [204,205].

Organic compounds have been also quantified in biological samples using eutectic solvent-based analytical procedures. These methods have been used to determine pesticides in urine and plasma [206], polycyclic aromatic hydrocarbons in urine and saliva of tobacco smokers [179], warfarin in urine and plasma [207], procainamide in human saliva [208], ketoprofen and diclofenac in liver [209] and nitrite in saliva and human urine [210].

Analytical methods based on microextraction with eutectic solvents have also been used to quantify metals. In water samples, the following metals were analyzed: arsenic [211], cadmium [212], cobalt [213], copper [214], chromium [215–217], nickel [213,218], palladium [219] and selenium [220]. In the analysis of food and drinks, the eutectic solvents have been applied in the quantification of copper, cadmium and lead in honey and milk [221,222], copper in vegetables [223], chromium (VI)

in beverages [224], cadmium and zinc in fruit juices [225], vanadium in tomato, cucumber, banana and apple [226] and a wide variety of heavy metals in vegetables irrigated with treated municipal wastewaters [227]. Finally, the eutectic solvents have been also used in the quantification of metals in biological samples, analyzing the chromium content in fishes and mushrooms species [228] and the cadmium, nickel and lead content in urine samples [229].

In all the analytical methods previously enumerated, the eutectic solvents have been used in microextraction processes to concentrate the solutes to be quantified. Once the solutes have been extracted, different conventional analytical techniques have been used. Figure 5 shows the percentage distribution of the analytical techniques used in the different articles described. As seen, the vast majority of articles have used high-performance liquid chromatography (HPLC), a technique especially used in articles focused on the quantification of organic compounds. The second most used technique has been atomic absorption, corresponding to articles in which the content of metals has been quantified in water, food and drinks or biological samples. The gas chromatography (GC) has been used to quantify volatile hydrocarbons in water and food and drinks, using flame ionization (FID) or mass spectrometry (MS) detectors. Ultraviolet-visible spectroscopy (UV-VIS) has been applied in the quantification of organic compounds in drinks and biological samples and to quantify the metal content in water and drinks. Finally, other more complex techniques, such as ion mobility spectrometry [180] and the electroanalysis [201] have been used together with eutectic solvents in analytical methods.

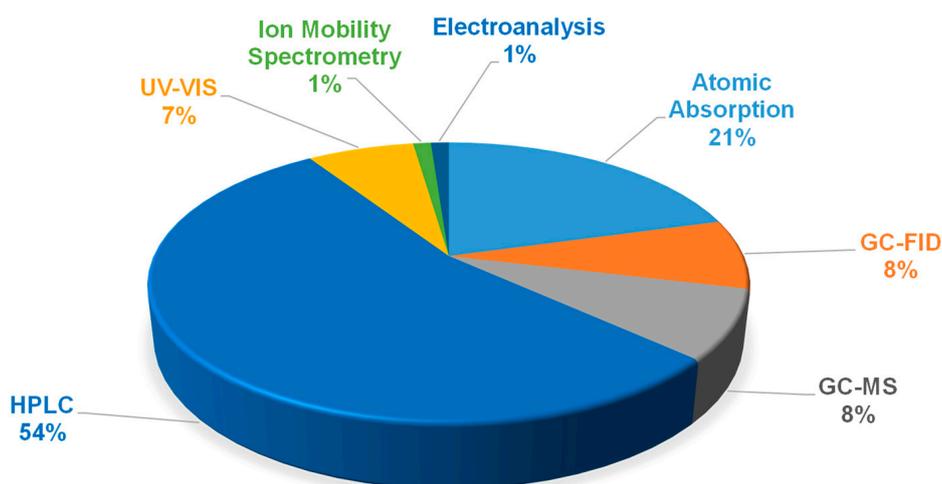


Figure 5. Percentage distribution of the published papers (2010–2020) on eutectic solvents in the development of analytical methods as function of the analytical method used after the extraction.

In this general review of the applications of eutectic solvents in the development of analytical methodologies using liquid–liquid microextraction processes, a large number of published works and a great variety of solutes analyzed have been revealed. Although these applications are not oriented to the development of industrial processes of separation by liquid–liquid extraction, some of the solutes that have been extracted in the described analytical methods could be carried out on a larger scale.

3. Application of Terpenes and Terpenoids in Extraction Processes

This section focuses on the use of terpenes and terpenoids as solvents in extraction processes. The use of terpenes and terpenoids has previously appeared in this paper in the formulation of hydrophobic eutectic solvents using menthol, thymol, camphor, borneol and sesamol as hydrogen bond donors or acceptors. In this section, it will be discussed the extraction processes using pure terpenes and terpenoids as solvents. According to the search performed, only 46 articles were found that study their application in extraction processes. Figure 6 shows the appearance of terpenes and terpenoids as solvents in the collected articles. Notably, limonene is the most studied followed by α -pinene, citral,

geraniol and *p*-cymene. Limonene is very widespread in nature and is also an agricultural by-product of the citric industry [18]. Its applications are mainly based on the substitution of conventional *n*-hexane. The rest of the terpenes with application in extraction processes that have been found are β -pinene, eucalyptol, linalool, β -citronellol, eugenol, pinane (and hydrogenated pinenes), carvone, menthol and *p*-menthane.

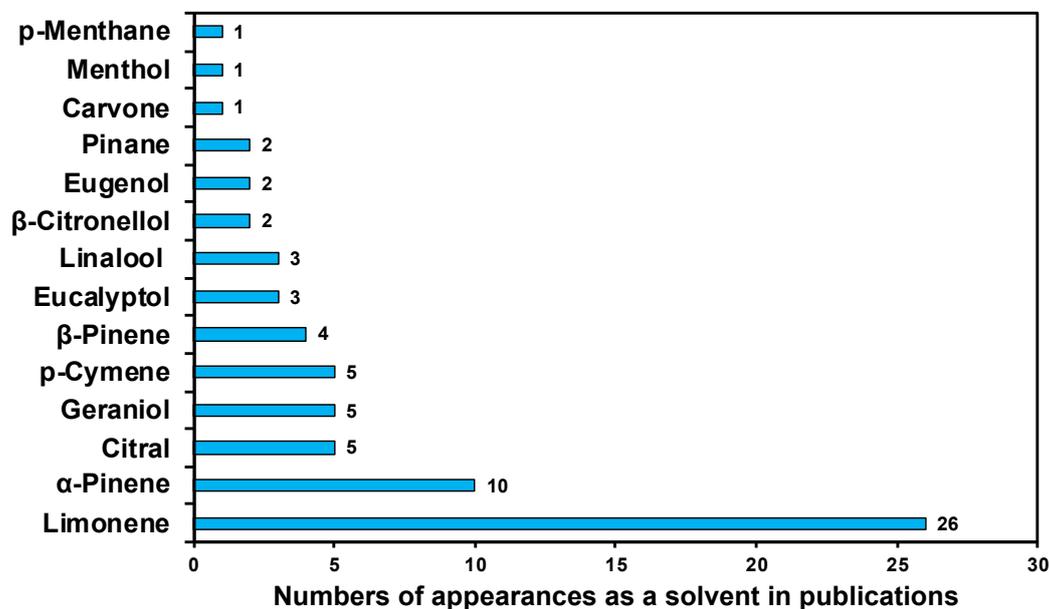


Figure 6. Numbers of appearances in the published papers of terpenes and terpenoids as solvents.

To analyze the different extraction processes with terpenes and terpenoids, the articles found were divided into 4 categories depending on the matrix to which solvents were applied. The selected matrices are the following:

1. Agricultural products
2. Microalgae
3. Aqueous streams
4. Others

As with eutectics solvents, a critical review of published articles on the application of terpenes and terpenoids as solvents has been made. A description of the uses and main results of the different articles has been performed, emphasizing the comparison with conventional solvents. Besides, the regeneration and reuse processes of the terpenes and terpenoids used by the different authors have been analyzed. At the end of the section, a review of the different predictive methods, the thermodynamic models used in the correlation of the liquid–liquid equilibria and the simulation methods of the separation processes with terpenes and terpenoids are described.

3.1. Extraction from Agricultural Products with Terpenes and Terpenoids

First applications of terpenoids as solvents were performed in the extraction of compounds from food products, specifically in lipid extraction. The most employed solvent is *n*-hexane, though for its hazardousness and being a petroleum-based compound, other solvents have been sought.

In 2004 and 2005, Mamidipally and Liu used limonene for the extraction of lipids from rice bran [230,231]. Limonene obtained almost equivalent yields of lipid extraction compared to the conventional solvent *n*-hexane. Also, the quality of crude oil was comparable. The optimal conditions for lipid extraction obtained were a solvent-to-bran ratio (wt./wt.) of 5:1 and an extraction time of 1 h.

Besides, a limonene recovery step was done through vacuum evaporation. Compared to the fresh solvent, oxidation products in the recovered limonene was <1% (wt.), thus allowing the limonene to be recycled. After obtaining these results with limonene in lipid extraction, other works were published with other matrices for substitution of *n*-hexane and other conventional solvents. The research papers concerning the extraction from agricultural products are collected in Table 10.

Table 10. Extraction Processes from Agricultural Products Using Terpenes and Terpenoids.

Solute Extracted	Agricultural Product	Terpene/Terpenoid as Solvent	Year	Ref.
Lipids	Rice bran	Limonene	2004	[230]
Lipids	Rice bran	Limonene	2005	[231]
Lipids	Olive seeds	Limonene	2008	[232,233]
Lipids	Peanuts, soy and sunflower seeds	α -Pinene	2013	[234]
Lipids	Rapeseed	Limonene, α -pinene, <i>p</i> -cymene	2014	[235]
Lipids	Rapeseed	Limonene, <i>p</i> -cymene	2015	[236]
Lipids, aromas, carotenoids	Caraway seed, carrot, rapeseed	Pinane	2016	[237]
Lipids, aromas, carotenoids, water	Caraway seed, carrot, rapeseed	<i>p</i> -Menthane	2019	[238]
Carotenoids	Tomato	Limonene	2010	[239]
Aromas	Blackcurrant bud	α -Pinene	2014	[240]
Aromas	Caraway seed	α -Pinene	2015	[241]
Aromas	Thyme	Limonene	2015	[242]
Water (Moisture determination)	Onion, garlic, minced meat, carrots, rosemary, mozzarella, mint, leeks and sage leaves	Limonene	2010	[243]
Water (Moisture determination)	Onion, garlic, carrot, leeks, olive, caraway and coriander seeds	α -Pinene	2012	[244]
Betulin	Birch bark	Limonene, pinane and turpentine	2018	[245]

In 2008 Virot et al. also reported a method for lipid extraction with limonene from olive seeds [232,233]. Soxhlet extraction and microwave-integrated Soxhlet extraction techniques were applied in lipid extractions. No differences in using *n*-hexane were obtained in terms of the quantity and quality of the extracts. Also, a regeneration stage was performed with Clevenger and microwave Clevenger distillation procedures. In Clevenger distillation almost 90% of limonene was recycled, surpassing 50% reached with *n*-hexane.

Other terpenes have been applied as solvents from the lipid extraction from oilseeds. Bertouche et al. in 2013 employed α -pinene for oil extraction from peanuts, soy and sunflower seeds with Soxhlet extraction [234]. As with previously published articles using limonene, the results achieved with α -pinene were comparable to *n*-hexane. Additionally, recycling rates of 90% were reached with α -pinene employing Clevenger distillation, obtaining also almost negligible degradation of the solvent. The terpenes limonene, α -pinene, *p*-cymene were used also in lipid extraction from rapeseed, in the work conducted by Li et al. in 2014 [235]. Soxhlet extraction and Clevenger distillation techniques were also applied. The highest oil extraction yield was obtained with *p*-cymene and limonene, surpassing isopropanol, butanol, *n*-hexane and ethanol solvents. Also, extraction yields with α -pinene outnumbered those obtained with *n*-hexane. On the other hand, in the work published by Sicaire et al. in 2015 [236], also applying *p*-cymene and limonene in oil extraction from rapeseeds with conventional Soxhlet, resulted in lower extraction yields for the terpenes than *n*-hexane. *n*-Hexane enabled 47 g

lipids/100 g dry matter and terpenes reached 80% of this quantity. Sicaire et al. highlighted the relevance of solvent diffusivity into the matrix in the results obtained.

Otherwise, valuable compounds as carotenoids have been extracted using terpenes and terpenoids. In 2010, Chemat-Djenni et al. applied limonene as solvent by the first time for the extraction of lycopene from tomato [239]. The limonene was obtained through steam distillation and deterpenation process from orange peels, thus remarking the valorization of this agricultural by-product. The results with limonene were also comparable with the use of conventional solvent dichloromethane.

Pure terpenes have also been applied in the extraction of aromas. Filly et al. conducted experimental and theoretical studies in the extraction of aromas from blackcurrant buds in 2014 [240] and caraway seeds in 2015 [241] with alternative solvents including α -pinene, for substitution of *n*-hexane. Besides, in 2015 Villanueva Bermejo et al. published a research work for the extraction of thymol from thyme using limonene and pressurized liquid extraction [242]. From *Thymus vulgaris* at 10 MPa, thymol recoveries obtained were 7–11mg/g and the highest thymol concentrations were obtained with limonene compared with ethanol and ethyl lactate.

In 2016, Yara-Varón et al. investigated the use of pinane in the Soxhlet extraction of lipids, carotenoids and aromas from rapeseeds, carrots and caraway seeds, respectively [237]. A mixture of *cis* and *trans* pinanes was obtained through catalytic hydrogenation of pinenes and turpentine oils. Pinanes were compared to *n*-hexane performance, obtaining similar extraction yields and lipids profiles in rapeseeds extraction. A maximum of 95.4% carotenoids extraction yield from carrots was reached with pinanes, while *n*-hexane extracted a maximum of 78.1%. Concerning aromas extraction, both extract compositions were similar using the two solvents. Continuing with this research, in 2019 Madji et al. studied the same solutes and matrices but with the employment of *p*-menthane. Analogously to the previous work, *p*-menthane was originated by catalytic hydrogenation of limonene. Mass yields in lipid extractions from rapeseeds were comparable using *p*-menthane (40.5%) and *n*-hexane (39.5%). In the extraction of aromas and carotenoids, similar yields and composition profiles were obtained with both solvents.

Terpenes have also been in water determination by Dean-Stark distillation for the substitution of toluene. In 2010 Veillet et al. [243] proposed the use of limonene instead of toluene for moisture determination of different food matrices (onion, garlic, minced meat, carrots, rosemary, mozzarella, mint, leeks and sage leaves). Comparable results were obtained using both solvents. Bertouche et al. in 2012 [244] also applied α -pinene in water extraction of food samples (onion, garlic, carrot, leeks, olive, caraway and coriander seeds). Analogously with the results obtained with limonene, performance with α -pinene was comparable to toluene. Besides, the use of *p*-menthane in the Dean-Stark procedure was performed by Madji et al. in 2019 [238]. Water extractions yields were similar with *p*-menthane and toluene, thus with *p*-menthane time needed to reach 100% water recovery was 55% lower than using toluene.

Finally, in 2018, Grazhdannikov et al. employed limonene, pinanes and hydrogenated turpentine in the extraction of betulin from birch bark [245]. The terpenes were proposed as green solvents in the purification of betulin. A separation of pure betulin of 95–97% and high yields of 75–82% were obtained.

Due to all the research that has been carried limonene, α -pinene, *p*-cymene and pinanes are promising candidates for the substitution of *n*-hexane in lipid extraction from oilseeds. Limonene has surpassed or matched *n*-hexane performance in lipid extraction, being able to replace it in this process. Though more studies must be done in fields of economic scope and solvent regeneration processes. Besides, more terpenes and terpenoids could be applied in this field. In the same way, the extraction of aromas and carotenoids research works could be expanded as there are no many studies, despite the results achieved. In Dean-Stark distillation, terpenes showed great performance comparable to toluene, being also good candidates in this technique.

3.2. Extraction from Microalgae with Terpenes and Terpenoids

In the same way that the extraction of lipids from oilseeds, terpenes have been applied in the extraction of oil from microalgae. Lately more applications have been developed. The research articles are collected in Table 11. In 2012, Dejoye Tanzi et al. applied for the first time terpenes in the extraction of lipids from microalgae (*Chlorella vulgaris*), using limonene, α -pinene and *p*-cymene [246]. Soxhlet extraction and solvent regeneration through Clevenger distillation were performed. The extraction yields of crude oil with terpenes resulted higher than those obtained *n*-hexane.

Continuing with this application of terpenes, in 2013, Dejoye Tanzi et al. also applied limonene, α -pinene and *p*-cymene in lipid extraction from *Nannochloropsis oculata* and *Dunaliella salina* [247]. A simultaneous distillation and extraction process with terpenes, Soxhlet extraction using *n*-hexane and Bligh & Dyer method employing a chloroform/methanol solvent mixture [248] were compared. Oil extraction yields of both microalgae using terpenes were slightly lower than those obtained from Bligh & Dyer method but higher than Soxhlet extraction with *n*-hexane. In 2015, Golmakani et al. [249] tested limonene in lipid extraction from *Spirulina*, *Phormidium* sp., *Anabaena planctonica* and *Stigeoclonium* sp. employed pressurized liquid extraction. They optimized the extraction process at 200 °C and 15 min. In agreement with the results obtained with Dejoye Tanzi et al. [247], lipid extraction yields with limonene were higher than those obtained with *n*-hexane from *Spirulina*. This phenomenon reported for several authors and also in lipid extraction from oilseeds could be related to a major polarity and higher density of limonene compared to *n*-hexane.

Castro-Puyana et al. in 2013 also proposed an alternative source of carotenoids using *Neochloris oleoabundans*, instead of focusing on lipid extraction [250]. The authors optimized the use of a limonene/ethanol mixture and pure solvents employing pressurized liquid extraction. The optimum conditions predicted by the statistical analysis were at 112 °C and using pure ethanol. Therefore, limonene was not a more suitable solvent than ethanol from carotenoid extraction.

Table 11. Extraction Processes from Microalgae using Terpenes and Terpenoids.

Solute Extracted	Microalgae	Terpene/Terpenoid as Solvent	Year	Ref.
Lipids	<i>Chlorella vulgaris</i>	Limonene, α -pinene, <i>p</i> -cymene	2012	[246]
Lipids	<i>Nannochloropsis oculata</i> and <i>Dunaliella salina</i>	Limonene, α -pinene, <i>p</i> -cymene	2013	[247]
Lipids	<i>Spirulina</i> , <i>Phormidium</i> sp., <i>Anabaena planctonica</i> and <i>Stigeoclonium</i> sp.	Limonene	2014	[249]
Carotenoids	<i>Neochloris oleoabundans</i>	Limonene	2013	[250]
Phenolic compounds	<i>Zonaria tournefortii</i>	Eucalyptol	2018	[251]

In 2018, Hamiche et al. [251] presented for the first time eucalyptol (1,8-cineole) as a candidate for the extraction of phenolic compounds from *Zonaria tournefortii*. The authors used a multistep liquid–liquid extraction with distilled water followed by the elimination of the aqueous phase after centrifugation and terpenoid recovery by steam distillation. The extraction yield with eucalyptol was (0.45% wt./vol.) notably lower than using a conventional solvent of a chloroform/methanol solvent mixture (2.16% wt./vol.). Nevertheless, solvent regeneration with steam distillation was successful as FTIR analysis showed no degradation of eucalyptol. Lastly, Hamiche et al. [251] recommended the use of more polar terpenoids for improving extraction performance.

As described, the lipid extraction of microalgae with limonene seems to be feasible and to be able to replace the use of *n*-hexane, as well as the previous extraction proposals in oilseeds. In the field of carotenoids and phenolic compounds using limonene and eucalyptol, they do not seem the most suitable solvents. However, these studies are still preliminary and scarce and it is necessary to investigate the use of different terpenes and terpenoids in order to optimize these processes.

3.3. Extraction from Aqueous Solutions with Terpenes and Terpenoids

Published papers about extraction using terpenes and terpenoids from aqueous solutions are collected in Table 12. Most of the studies determined the liquid–liquid equilibria of alcohols, terpenes or terpenoids and water. Subsequently, more studies have studied the extraction of other solutes.

Table 12. Extraction Processes from Aqueous Solutions with Terpenes and Terpenoids.

Solute	Raffinate	Terpene/Terpenoid as Solvent	Year	Ref.
Ethanol	Water	Limonene, citral	1995	[252]
Ethanol	Water	Limonene	2004	[253]
Ethanol	Water	Linalool	2005	[254]
Ethanol	Water	Citral	2007	[255]
Methanol	Water	Limonene, α -pinene, β -pinene	2005	[256]
Ethanol	Water	Limonene, α -pinene, β -pinene	2005	[257]
1-Butanol, 1-propanol	Water	Limonene, α -pinene, β -pinene	2008	[258]
Acetone	Water	Limonene, α -pinene, β -pinene	2010	[259]
Ethanol, methanol	Water	Geraniol	2012	[260]
Ethanol, methanol	Water	β -Citronellol	2012	[261]
Ethanol, methanol	Water	Linalool	2013	[262]
Ethanol	Water	Limonene, carvone	2013	[263]
Methanol	Water	Citral	2013	[264]
Acetone, 1-propanol	Water	β -Citronellol	2015	[265]
1-Butanol, ethanol, methanol, 1-propanol	Water	Eucalyptol	2016	[266]
1-Propanol	Water	Linalool, geraniol	2016	[267]
Phenol, <i>p</i> -cresol	Water	Eucalyptol	2016	[268]
β -Cyclodextrin	Pharmaceutical wastewaters	Limonene	2016	[269]
Acetic, propionic, butyric and valeric acids	Water	Citral, eugenol, geraniol	2019	[26]
Phenol, 2-chlorophenol, 2-nitrophenol	Water	Citral, eugenol, geraniol linalool	2020	[27]

Gironi et al. in 1995 [252] started to study binary systems (water + limonene) and (water + citral) and also the ternary systems (water + ethanol + limonene) and (water + ethanol + citral) at 293 K. Complete miscibility was observed with ethanol mass fraction greater than 0.73 for limonene system and 0.45 for citral system. Besides, Cháfer et al. in 2004 also studied the (water + ethanol + limonene) ternary system at temperatures 293.15 from 323.15 K [253]. In 2005 [254], Cháfer et al. published an article with the same temperatures for the (water + ethanol + linalool) ternary system. Lastly, in 2007 Gramajo de Doz et al. [255] also studied (water + ethanol + citral) ternary system at 303.15 K.

Tamura and Li published in 2005 [256] liquid equilibrium data of alcohols in ternary systems (water + methanol + limonene or α -pinene or β -pinene) and quaternary system (water + methanol + limonene + α -pinene) at 293.15 K. Analogously, the same year they presented a study [257] of (water + ethanol + limonene or α -pinene or β -pinene) and quaternary system (water + ethanol + limonene + α -pinene) at 293.15 K. Continuing with this work, in 2008 Tamura et al. [258] studied the ternary

systems (water + (1-butanol or 1-propanol) + limonene or α -pinene or β -pinene) at 293.15 K. Also, Li and Tamura published in 2010 [259] the equilibrium data of ternary system (water + acetone + α -pinene) at 288.15, 298.15 at 308.15 K and (water + acetone + limonene or β -pinene) at 298.15 K.

In 2012, Li et al. [260] published liquid–liquid equilibrium data of ternary systems (water + ethanol + citral) and (water + methanol + citral) at 283.15, 298.15 and 313.15 K. In the same year, Tianfie et al. [261] presented the data of the same systems but replacing citral with β -citronellol. Besides, Li et al. [262] published equilibrium data from (water + ethanol + linalool) and (water + methanol + linalool) ternary systems at 298.15 K. Also, in 2013 Huang et al. [264] studied ternary system (water + methanol + citral) at 283.15 and 313.15 K and Oliveira et al. [263] the quaternary system (water + ethanol + limonene + carvone) at 298.2 K.

More liquid–liquid equilibrium data with alcohols were published by Li et al. in 2015 [265] of (water + 1-propanol + β -citronellol) and (water + acetone + β -citronellol) systems at 283.15, 298.15 and 313.15 K. Also in 2016, Li et al. [266] presented the study of four alcohol systems with eucalyptol, (water + methanol or ethanol or 1-propanol or 1-butanol + eucalyptol) at 298.15 K. Lastly in 2016, Wan et al. [267] presented data from (water + 1-propanol + linalool) and (water + 1-propanol + geraniol) systems at 283.15, 298.15 and 313.15 K.

Another application of terpenes and terpenoids as solvents in liquid–liquid extraction is focused on the analytical field. Pourreza et al. published a research article in 2016 [269] applying limonene in dispersive liquid–liquid microextraction for the determination of cyclodextrin from pharmaceutical wastewater samples. In the same way that eutectic solvents are currently being used in the development of analytical methodologies to determine organic compounds in water, it is expected that terpenes and terpenoids can be applied in this field in the nearest future.

The extraction of phenolic compound from aqueous solutions using terpenes and terpenoids has been also studied. In 2017, Li et al. [268] studied the ternary liquid–liquid equilibria of (water + phenol + eucalyptol) and (water + *p*-cresol + eucalyptol) systems at 283.15, 298.15 and 313.15 K, showing phenol extraction efficiencies higher than 90%.

Recently, Rodríguez-Llorente et al. [27] have applied terpenoids in the extraction of phenol, 2-chlorophenol and 2-nitrophenol from aqueous solutions. Citral, eugenol, geraniol and linalool were applied in the multicomponent extraction of phenols and compared with the results obtained using eutectic solvents and conventional solvents such as toluene, diisopropyl ether (DIPE) and methyl isobutyl ketone (MIBK). Citral and geraniol archived higher extraction yields than DIPE, toluene and eutectic solvents and similar values to those using MIBK. Linalool also obtained high phenols extraction yield higher than DIPE and the eutectic solvents but lower than MIBK. Besides, a regeneration process was addressed with alkali back-extraction. Geraniol and linalool could be fully regenerated but back-extraction yields and FTIR analysis showed that citral and eugenol were not suitable for this process. Also, this regeneration capacity was tested through 3 cycles of extraction-regeneration, being the extraction yields higher to 94%. In addition, geraniol and linalool were applied in a parallel packed column extraction at different solvent-feed ratios obtaining similar yields than in vial. Lastly, Rodríguez-Llorente et al. also conducted countercurrent column simulations with Kremser and COSMO-based/Aspen Plus methodologies.

Rodríguez-Llorente et al. [26] also proposed the use of geraniol, citral and eugenol in the extraction of volatile fatty acids (acetic, propionic, butyric and valeric acids) from aqueous solutions, obtaining high yields of extraction. In this work, geraniol and eugenol showed extraction yields of volatile fatty acids greater than those reached experimentally by eutectic solvents formed by octanoic acid, thymol and menthol. Also, a back-extraction with NaOH and Na₂CO₃ for solvent regeneration was performed. As described for the extraction of phenols [27], consecutive cycles of extraction-regeneration were done, showing no decrease in extraction capacity after back-extraction. In addition, through experiments in parallel packed column extraction with geraniol, distribution coefficients were obtained and applied in countercurrent extraction by Kremser method simulations.

To summarize, liquid–liquid equilibria from alcohol–water–terpene systems have been extensively determined, though the studies are limited to some terpenes and terpenoids. Besides, alternative applications of terpenes and terpenoids in the extraction of different compounds as phenols or organic acids have been done, obtaining very promising results. In several cases, the results obtained using terpenoids have been higher to those using eutectic solvents and showing greater chemical stability. It is expected that studies on a greater scale could be performed for checking the feasibility of this extraction process. Also, research is still scarce, it could be amplified searching for new matrices and solutes for the extraction process.

3.4. Other Applications in Extraction of Terpenes and Terpenoids

This section includes works that use terpenes and terpenoids as solvents in other applications than those described in the three previous sections. In the development of novel analytical methodologies, some research articles have been focused on the use of terpenes and terpenoids. In 2013, Farajzadeh et al. [270] used menthol in dispersive liquid–liquid microextraction for extraction and concentration of phthalate esters in pharmaceutical samples. Through the solidification of menthol, analytes could be separated from water samples and concentrated. Faure et al. [271] in the same year proposed the use of limonene as a substitute of *n*-heptane in counter-current chromatography. Lastly, Medvedovici et al. in 2013 [272] published the use of limonene for the extraction of simvastatin, lovastatin and their metabolites from human plasma.

Moreover, Nikakhtari et al. in 2013 [273] applied limonene in the extraction of bitumen from oil sands. Different solvents were tested as cycloalkanes and aromatics solvents. Nevertheless, limonene showed the lowest results of the 13 solvents and mixtures employed.

3.5. Predictive Methods in Extraction with Terpenes and Terpenoids

Among the tools available for prediction of the most suitable solvents in extraction processes using terpenes and terpenoids, Hansen Solubility Parameters (HSP) and COSMO-based methods have been the most used. A total of 11 articles have been applied these methodologies in extraction processes with terpenes and terpenoids.

HSP can describe solvents in terms non-polar, polar and hydrogen bonding properties and can be a tool of selection and comparison of solvents. Dejoye Tanzi et al. [246] compared HSP parameters of limonene, α -pinene and *p*-cymene to *n*-hexane concluding that by their similar values, their behavior in the extraction of oil from microalgae likely also had to be similar. Besides, Li et al. [235] used HSP of limonene, α -pinene and *p*-cymene in the extraction of lipids from rapeseeds and predicted the differences in the extraction of the fatty acids, tocopherol and sterols. Also, HSP parameters have been used for prediction in the extraction of aromas using terpenes and terpenoids from blackcurrant buds [240], food [241] and caraway seeds [237].

COSMO-RS (Conductor-like Screening Model for Real Solvents) has served as a method for solvent screening in various applications of terpenes and terpenoids in extraction. Filly et al. [241] calculated sigma potential similarities of solvents and solutes for the comparison of the solvents in lipid extraction for caraway seeds, being the values in agreement with experimental results [241]. In addition, relative solubilities have been calculated and applied in prediction of the extraction of lipids from rapeseeds [236–238], carotenoids from carrots [237,238], aromas from caraway seeds [237,238] and betulin from birch bark [245] using terpenes. Lastly, as it was previously mentioned, Rodríguez-Llorente et al. applied the COSMO-RS method for calculating the infinite dilution activity coefficients as solvent screening of terpenes and terpenoids in extraction of volatile fatty acids from water [26] and separation of phenols from industrial wastewater [27], obtaining very similar trends in predictions and experimental data using various terpenes and terpenoids.

3.6. Correlation of Liquid–Liquid Equilibrium Using Terpenes and Terpenoids

Thermodynamic models as Non-random two liquids (NRTL) and UNIQUAC have been applied in the correlation of liquid–liquid equilibria of systems composed of water, alcohols, acetone or phenols and using terpenes and terpenoids as solvents. Between both models, UNIQUAC has been more extensively employed.

NRTL and UNIQUAC models have been applied satisfactorily in the correlation of the ternary systems formed by water, ethanol and terpenes as limonene [253] and linalool [254]. The quaternary system (ethanol + water + limonene + carvone) [263] was also fitted by NRTL and UNIQUAC models obtaining lower deviation using the NRTL model. In the correlation of equilibria of 1-propanol and water with linalool and geraniol, calculated root mean square deviations (RMSDs) were 0.97% and 1.07% for NRTL and UNIQUAC models, respectively [267]. Besides, RMSDs obtained values for NRTL and UNIQUAC were 0.59% and 0.54% in ethanol, 1-propanol and 1-butanol with eucalyptol systems [266]. On the other hand, eucalyptol equilibria data with water and phenol or *p*-cresol obtained RMSDs of 0.32% for both models [268]. Therefore, NRTL and UNIQUAC models can satisfactorily correlate liquid–liquid equilibria of systems formed by water, alcohols and terpenes.

The extended UNIQUAC model has been applied in correlation for equilibria of water, methanol and citral system, obtaining RMSDs lower than 1.12% [263]. Also, in the system of linalool with methanol and ethanol a satisfactory correlation was obtained with RMSDs lower than 1.35% [262]. On the other hand, a modified UNIQUAC model was applied by Li and Tamura in the correlation of liquid–liquid equilibria of limonene, α -pinene and β -pinene with acetone [259] and ethanol [257], obtaining a good agreement between experimental results and calculated values.

Extended and modified UNIQUAC models has been also employed simultaneously in the correlation of systems with alcohols. Both models could correlate satisfactorily limonene, α -pinene and β -pinene with 1-propanol and 1-butanol systems [258]. In the correlation of β -citronellol with methanol and ethanol with extended UNIQUAC and modified UNIQUAC mean RMSDs were 0.69% and 0.76%, respectively [261]. Also, in the β -citronellol with acetone and 1-propanol systems, equilibrium data with both models obtained mean RMSDs minor to 0.86% [265]. Lastly, Li et al. studied geraniol with methanol and ethanol systems obtaining mean deviations of 0.66% and 0.77% with the extended and modified UNIQUAC models, respectively [260].

Therefore, both the NRTL and UNIQUAC thermodynamic models have been used successfully in the correlation of liquid–liquid equilibrium data in systems that use terpenes or terpenoids as solvents. Both models could be used to simulate liquid–liquid extraction processes on an industrial scale with these solvents.

3.7. Simulation of Liquid–Liquid Extraction Processes with Terpenes and Terpenoids

Papers that address simulations in liquid–liquid extraction processes using terpenes and terpenoids are scarce and very recent. Firstly, Rodríguez-Llorente et al. in 2019 [26] applied the Kremser method in countercurrent extraction column simulations for the separation of volatile fatty acids from aqueous streams. The extraction (E_i) and reciprocal (U_i) factors of the Kremser method were obtained from experimental distribution ratios obtained in packed column extraction. Simulations showed that with 10 extraction stages in the extractor, a global acid extraction yield of 98% could be achieved using geraniol as solvent.

A similar approach was applied in the extraction of phenols from wastewaters by Rodríguez-Llorente et al. [27]. First, simulations using the Kremser method were performed using experimental data. These simulations served to compare and validate simulations using the predictive COSMO-based/Aspen Plus methodology. In this approach, terpenoids were described as pseudocomponents and the activity coefficients were calculated using the COSMOSAC model in Aspen Plus. Kremser and COSMO-based/Aspen Plus simulations showed close results validating this last methodology. According to the results obtained in the simulations, a complete separation of phenols

could be achieved using linalool and geraniol with a solvent-to-feed ratio of 0.5 and 10 equilibrium stages in the extractor.

The application of terpenes and terpenoids in liquid–liquid extraction processes as solvents is still very scarce. For this reason, the number of articles in which process simulation has been used is also very low. Taking into account the promising results recently obtained in the extraction of volatile fatty acids or phenols from aqueous streams, the applications of terpenes and terpenoids in extraction processes will be expanded in the nearest future.

4. Conclusions and Future Outlook of the Use of Eutectic Solvents, Terpenes and Terpenoids in Liquid–Liquid Extraction Processes

In 2007, the first article on the use of eutectic solvents in liquid–liquid extraction was published. In the early years, these solvents were used mainly in the extraction of organic compounds from oils and biodiesel and in the separation of hydrocarbons. Afterward, a wide variety of hydrophilic eutectic solvents were applied in the separation of alcohols from hydrocarbons and in the extraction of high added-value compounds. From 2014, aqueous biphasic systems based on eutectic solvents have been used in the separation of biomolecules and bioactive compounds. Another important novelty was the preparation of hydrophobic eutectic solvents (HES) in 2015. These HES are being currently studied in the extraction of organic compounds from aqueous streams and in the selective separation of metals.

In the extraction of glycerol from biodiesel using eutectic solvents, real biodiesel samples have been used and the solvents were successfully regenerated and reused. Also, the proposed processes achieved the requirements of international standards of biodiesel. Therefore, the degree of development of the process of extraction of glycerol from biodiesel with eutectic solvents is high and it would be necessary to increase the scale of the processes to develop a continuous process.

The extraction of hydrocarbons using eutectic solvent has been widely studied, being focused on the reduction of aromatic, nitrogen and sulfur contents in fuels. However, the extraction of hydrocarbons from real fuels has hardly been studied and few articles have studied the simultaneous extraction of hydrocarbons from multicomponent streams. To assess the feasibility of an extraction process of hydrocarbons using eutectic solvents, larger-scale extraction tests should be carried out and continuous extraction processes should be developed.

The eutectic solvents tested in the extraction of alcohols from alkanes have shown low extraction capacities compared to those of conventional solvents and ionic liquids. By contrast, higher alcohol/hydrocarbon selectivities were obtained using eutectic solvents than conventional solvents. Hence, these eutectic solvents could be used to remove alcohols with high purity from their mixtures with hydrocarbons. In the extraction of phenols from hydrocarbons, various salts have been tested to form eutectic solvents with the extracted phenols. In these applications, several extraction and regeneration cycles have been performed satisfactorily and larger scale extraction experiments will be required to confirm the technical viability of the processes.

One of the most promising applications of eutectic solvents in liquid–liquid separation processes is the formation of aqueous biphasic systems. Although the use of eutectic solvents in ABS is a recent application, significant results have been published to date. High extraction yields have been obtained using these systems in the separation of a wide variety of compounds: proteins, enzymes, dyes, amino acids and nucleic acids. To ensure the viability of these purification processes on the industrial scale, the back-extraction process of the solutes should be studied and technologies should be developed on a larger scale. Furthermore, the use of real biological samples and the comparison with other conventional or alternative technologies for the purification of these biomolecules will be essential in the future. In the application of eutectic solvents in the formation of ABS, the eutectic solvent integrity is destroyed and a nonstoichiometric partition of the hydrogen bond donor and acceptor can be found in the coexisting phases. Therefore, the distribution of the eutectic solvent on both phases must be checked to ensure their recovery and reuse.

The application of hydrophobic eutectic solvents in the extraction of organic molecules from water has also been widely studied in recent years. However, the vast majority of works have used synthetic mixtures formed by organic compounds and ultrapure water. The influence of the matrix of industrial aqueous streams or wastewaters should be studied in greater depth to confirm the viability of these solvents in the different proposed applications. Besides, continuous extraction and back-extraction processes should be carried out, studying the chemical stability of hydrophobic eutectic solvents, especially those formed by middle chain fatty acids that have shown low chemical stability. In the separation of metals with hydrophobic eutectic solvents, very promising results have been obtained, despite being a very recent application. Soon it is expected that real mixtures will be used to confirm the application of these solvents in the selective recovery of metals from waste.

To evaluate the application of eutectic solvents in liquid–liquid extraction processes on an industrial scale, it is essential to address the simulation of these processes. Using process simulators, the technical and economic feasibility of these alternative processes can be demonstrated and costs can be compared with conventional extraction processes. For this, it is essential to use both predictive methods and thermodynamic adjustment models that have shown high reliability. Until now, the NRTL and UNIQUAC thermodynamic models are suitable models for fitting ternary equilibrium thermodynamic data in systems composed of eutectic solvents. In addition, the COSMO-based calculations have been successfully used in solvent screenings and in predictions of liquid–liquid equilibria. PC-SAFT theory has been also successfully applied in the prediction of liquid–liquid equilibria of systems formed by eutectic solvents. These predictive and thermodynamic models should be applied to more realistic multi-component mixtures to adequately simulate and optimize complete extraction processes using eutectic solvents.

In the case of terpenes and terpenoids, their application in extraction processes is still scarce, even though they have proven to be competitive solvents with conventional solvents in some uses. Most of the articles on the application of terpenes and terpenoids in extraction have been focused on the separation of lipids and aromas from agricultural products and on the extraction of lipids from microalgae. Due to their hydrophobic character, terpenes and terpenoids have also recently been used as solvents in the liquid–liquid extraction of organic compounds from aqueous solutions.

In the extraction of lipids and aromas from agricultural products, terpenes have achieved results similar to those obtained with conventional solvents such as toluene and *n*-hexane. In addition, the regeneration and reuse of these solvents and their chemical stability have been confirmed. Similar results have been obtained in the extraction of liquids from microalgae, showing the terpenes extraction yields comparable to those of *n*-hexane.

In the application of terpenes and terpenoids in liquid–liquid extraction processes, these solvents have shown extraction performances superior to those of eutectic solvents in the extraction of volatile fatty acids and phenolic compounds from aqueous streams. Taking these preliminary results into account, terpenes and terpenoids have emerged as solvents with potential for the separation of organic compounds from aqueous streams due to their great ability to solubilize organic compounds and their hydrophobic nature. To confirm this potential as alternative solvents, terpenes and terpenoids should be used in the liquid–liquid extraction of contaminants from real aqueous streams, carrying out extraction experiments on a larger scale and developing continuous extraction and back-extraction processes.

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