Postprint of: Płotka-Wasylka J., Rutkowska M., de la Guardia M., Are deep eutectic solvents useful in chromatography? A short review, JOURNAL OF CHROMATOGRAPHY A, Vol. 1639 (2021), 461918, DOI: 10.1016/j.chroma.2021.461918

Are deep eutectic solvents useful in chromatography? A short review

Justyna Płotka-Wasylka[1,*], Małgorzata Rutkowska[1], Miguel de la Guardia[2]

[1] *Department of Analytical Chemistry, Faculty of Chemistry, Gdańsk University of Technology, PL-80-233 Gdańsk, Poland*

[2] *Department of Analytical Chemistry, University of Valencia, Valencia 46100, Spain*

*corresponding author: juswasyl@pg.edu.pl; plotkajustyna@gmail.com

Abstract

A literature update has been done concerning Deep Eutectic Solvents (DES) use in chromatography applications. The literature survey was based on the period from 2010 till 2020 and manuscripts reported in the data bases Web of Science and Scopus. The use of DES as mobile phase and mobile phase additives, stationary phases and solid phase modifiers and the use of DES as reaction solvents for chromatography use, were evaluated. Emphasis was placed on the differentiation of DES and Ionic Liquids (ILs) and the advanced green characteristics of the new solvents as compared with traditional organic solvents and ILs with a look into the drawbacks and future perspectives in the field of separation methods.

Keywords

Deep eutectic solvents; chromatography; green analytical chemistry; stationary phases; mobile phases; additives

1. Introduction

New approaches to green analytical chemistry are very often based on the use of new solvents to replace common organic solvents, which are toxic and highly volatile. In the last two decades, ionic liquids (ILs) have gained much scientific attention, due to their specific physicochemical properties and their applicability in very different areas [1]. However, the widespread use of ILs is limited by their high cost. Additionally, the green character of the ILs is often questioned, especially because of their poor biodegradability, biocompatibility and production sustainability [2]. A new generation of solvents, called deep eutectic solvents (DES) offer a more environment-friendly alternative than ILs. DES are defined as a mixture of two or several components, which may be liquid or solid and that at a particular composition present a high melting point depression staying liquids at room temperature [3]. DES may also be ionic but mainly consist of a mixture of organic compounds with a melting point significantly lower than that of any of the individual components. DES are easily available, inexpensive and biodegradable and can therefore be a viable eco-friendly substitute for conventional organic solvents [4]. Details on the advantages of the DES are shown in Figure 1.

Figure 1. The main advantages that characterize DES. Summarized from references [2,5–9].

The most popular DES are a combination of choline chloride (ChCl), carboxylic acids and other hydrogen bonds donors such as urea, citric acid, succinic acid and glycerol. ChCl is a low-costs, biodegradable and non-toxic quaternary ammonium salt that can be extracted from biomass or easily synthesized from fossil resources (4). DES formation can be done under simple operation conditions by directly mixing the components [6]. In 2007, DES was defined using a general formula of $\mathbf{R_1R_2R_3R_4N^+X^- \bullet Y^-}$, including in case a metal ion, M, and a Z anion and on this basis a classification of four types of these substances was proposed (Table 1) [10,11].

Table 1. Types of deep eutectic solvents

Type of DES	**Formula $\mathbf{R_1R_2R_3R_4N^+X^- \bullet Y^-}$**	**Description**	**Example**
DES Type I	Y = MClx M = Zn, Sn, Fe, Al, Ga	Combination of metal and organic salts	$ZnCl_2$ + ChCl
DES Type II	Y = MClx • yH_2O M = Cr, Co, Cu, Ni, Fe	A hydrate of metal salt and organic salt	$CoCl_2 \cdot 6H_2O$ + ChCl
DES Type III	Y =R_5Z Z = –$CONH^2$, -COOH, –OH	The hydrogen bond donor and organic salt	ChCl + urea
DES Type IV	-	Combination of metal chloride with a compound being the donor of a hydrogen bond	MClx + urea/ethylene glycol/ acetamide

DES can be synthesised as natural primary metabolites and therefore the toxicity of these systems should be significantly lower compared to ILs. The chemical structures of several compounds with the ability to form NDES are shown in Figure 2. After 2010, it was discovered that primary metabolites in many plants changed their state from solid to liquid when mixed in appropriate proportions. This led to the hypothesis that natural deep eutectic solvents (NADES) play a role as an alternative to water in living organisms and consequently to test a wide range of natural products, resulting in the discovery of over 100 NADES of natural origin [12].

Figure 2. Chemical structures of several of the most commonly used compounds (apart from ChCl) with the ability to form natural deep eutectic solvents.

2. Brief story of DESs

The first reports in the literature on the use of eutectic solvents date back to the end of 20th and the early 21st century. Several manuscripts published in the 1990s referred to some specific applications of these liquid mixtures. In 1994 eutectic mixtures were reported as substrates for enzymatic reactions [13,14], whereas in 1998 scientific developments in this field were described, as the use of heterogeneous eutectic mixtures for enzymatic synthesis [15]. It was one of the first studies in this area. In the following years DESs have been gaining more and an increasingly interest from scientists. A considerable amount of literature has been published on DES, their innovative solutions and their wide range of applications as

greener alternatives to organic solvents and ILs. In Figure 3, the landmarks of DES development are graphically depicted [3,16–18].

Figure 3. Landmarks of deep eutectic solvents development.

2.1. DESs as green medium

Over the past 20 years, green chemistry has rapidly expanded in almost every field of chemistry. Nowadays, green technology is one of the key issues in the field of chemistry, as it aims at minimizing environmental impact as well as reducing costs and improving safety and health of operators. With the introduction of the principles of green chemistry, the main efforts of many scientists have focused on the search and development of solvents that would have the highest possible greenness index - they would be the least toxic. Therefore, four directions towards ecological solvents have been developed: replacement of hazardous solvents with better environmental, health and safety solvents; application of "bio-solvents" produced from renewable sources; replacement of organic solvents with environmentally friendly supercritical liquids or application of ILs characterized by low vapour pressure [19]. To overcome the drawbacks of ILs, DESs have emerged as a new type of green solvents and natural origin products (NADES) are even more environmentally friendly compared to DES due to their easy renewal [20].

2.2. Application in analytical chemistry area

Due to their many advantages and innovative properties, DESs are widely used in many chemical fields [21] (Figure 4) including applications as valuable alternative solvents for Green Analytical Chemistry [8]. DES and NADES generally provide a network of hydrogen bond acceptor (HBA) and hydrogen bond donor (HBD) species, thereby enhancing the dissolution of target analytes [22]. The application of DES in analytical chemistry can be considered in several categories [9]. (I) (micro)extraction of target analytes from matrices with complex composition followed by determination using analytical instruments; (II) modification of nanoparticles, silica and other sorbents in order to increase the extraction efficiency; (III) dissolution or digestion of solid samples; (IV) eluent after a dispersive solid-phase extraction (DSPE) and further described in this review (V) chromatography as an additive or modifier of the mobile phase.

Figure 4. Chemistry fields where DES is applied.

DES-based (micro)extraction procedures are considered as a specific type of homogeneous liquid-liquid extraction, in which, after the addition of DES, a homogeneous solution is formed. In order to obtain a turbid solution, an emulsifying solvent must be added and phase separation is usually achieved by centrifugation [23]. On the other hand, in the DES-based DSPE extraction, the sorbent containing the analytes is collected by an external magnet, the aqueous phase is decanted and the analytes are eluted by a suitable solvent [24]. The combination of this method with gas chromatography (GC) with micro electron capture detector (ECD) was used for the ultra-trace analysis of organochlorine pesticides (OCP) in

environmental water samples obtaining low LOD values [25]. High selectivity and high sensitivity was characterized by the procedure using DES-based DSPE to extract dopamine, epinephrine and norepinephrine from biological samples prior to high-performance liquid chromatography (HPLC) determination [26]. There are also reports of air-assisted liquid-liquid micro-extraction based on DES for pre-concentration of methadone in water and biological samples, in combination with GC-FID (flame ionization detector) [27], liquid-liquid microextraction method for the extraction of polycyclic aromatic hydrocarbons from aqueous samples before determination with HPLC and diode array detection (DAD) [28] or DES-based dispersive liquid-liquid microextraction for the extraction of pesticide residues in fruit and vegetable juices preceded by a determination using GC-FID [29]. DES-based micro-extraction is also used to analyse solid samples. Among others, a method of DES-based headspace solid-phase microextraction, in combination with GC-FID has been proposed for determination of bioactive terpenoids [30] and microwave assisted DES extraction combined with head space-solid phase microextraction (HS SPME) followed by GC with mass spectrometry detection (MS) was used to determine volatile compounds in tobacco [18] [9]. Table 2 lists additional examples of DES applications in chemical analysis of solid and liquid samples. Both in the analysis of solid and liquid samples, ChCl is most commonly used as a HBA for the formation of DES in most of the described approaches. Whereas mainly organic acids, phenol and its derivatives, glycerol and urea were used as HBD for DES preparation. After extraction, the DES phase containing the target analytes was injected without pre-dilution directly into GC-MS, GC-FID or HPLC systems coupled with different types of detectors (UV, MS, FID, FLD, UV-Vis). Water is added to the mixture or heating is used to reduce the viscosity of the DES, especially when analysing solid samples. After extraction of the samples, filtration of the centrifuged suspensions is usually carried out before the determination [9].

There are literature reports which confirm that DES have great potential for routine analysis of trace metals in biological samples, which are characterized by a very complex matrix composition. DES were used, for example, during the determination Cu, Fe, and Zn in fish samples with the use of flame atomic absorption spectrometry (FAAS), where the extraction recovery of the metal elements in the DES was greater than 95% [31].

In the past few years, DES, as a new class of green solvents, has become very popular in many fields of science and technology. The use of DES in analytical chemistry is still in its infancy, but a significant increase in the number of scientific publications on this topic can be observed.

Table 2. Examples of use DESs for chemical analysis of solid and liquid samples.

Type of sample	Analyte	Sample matrix	DES composition	Detection method	LOD, [$\mu g L^{-1}$]	References
Liquid samples	BTE and PAHs	Water	ChCl:phenol	HPLC-UV	0.02–6.8	[32]
	Malachite green	Water	ChCl:phenol	UV-VIS	3.6	[33]
	Methadone	Water,	ChCl:TNO	GC-FID	0.7	[34]

		urine and plasma				
	Organochlorine pesticides	Water	ChCl:urea	GC-μECD	0.0004 – 0.0027	[35]
	Phenolic acids	Vegetable oils	ChCl:ethylene glycol	HPLC-UV	0.39 – 0.63	[36]
	Plant growth regulators	Edible oils	Tetramethylammonium chloride:ethylene glycol	HPLC-UV	5 –7.5	[37]
	Phenolic compounds	Virgin olive oil	ChCl:xylitol	HPLC-UV	-	[38]
	Total phenolic content Virgin	Virgin olive oil	Lactic acid:glucose:water	UV–Vis	-	[39]
	Cr(III/VI)	Water	ChCl:phenol	FAAS	550	[40]
	Co	Pharmaceutical supplement and tea samples	ChCl:phenol	FAAS	1.1	[17]
Solid samples	As, Cr, Mo, Sb, Se, V	Agricultural soi	ChCl:oxalic acid	ICP-OES	0.009–0.1	[41]
	Fe	Sheep, bovine and chicken liver	ChCl:lactic acid (1:1)	FAAS	0.026	[42]
	Mn	Vegetable samples	ChCl:tartaric, or oxalic or citric acids	ICP-OES	0.0034–0.0123	[43]
	Bioactive terpenoids	*Chamaecyparis obtusa* leaves	ChCl:ethylene glycol	GC-FID	0.02–0.03	[30]
	Flavonoids	*Chamaecyparis obtusa*	ChCl:1,4-butanediol, 30% water	HPLC-UV	0.07–0.09	[19]
	Ochratoxin A	Wheat and derived products	ChCl:urea, 40% water	HPLC-FLD	0.0009	[44]
	Phenolic compounds	*Pyrola incarnata* Fisch	ChCl:1,4-butanediol, 30% water	HPLC-UV	0.04 – 0.14	[45]
	Phenolic	*Cajanus cajan* leaves	ChCl:maltose, 20% (v/v) water	UPLC-UV	0.06 – 0.13	[46]
	Volatile compounds	Tobacco	ChCl:ethylene glycol	GC–MS	-	[18]
	Phenolic acids	*Herba Artemisiae* Scopariae	Tetramethyl ammonium chloride:urea mixed with methanol/water (60:40, v/v)	HPLC-UV	0.07–0.11	[47]

			ChCl:ethylene			
	PAH	Marine biological samples (fish	ChCl:oxalic acid	HPLC-FLD	0.005 – 0.03	[16]

3. Application of DESs in chromatography

DESs are mostly applied in the research on the stationary and mobile phases as well as mobile phase additives. Due to the role of DES in chromatography, there are three groups of applications, which are presented in the Figure 5. It also need to be mentioned, that DESs are pupular in counter current chromatography. All of these applications are briefly described with examples in this Section.

Figure 5. Application of DESs in chromatography.

3.1. DESs as mobile phases or mobile phase additives

Green solvents are applied widely to reduce the environmental problems connected with the application of conventional solvents in chemical production as well as to minimize cost and to improve safety and health. DESs as "eco-friendly" solvents are one of the most important subjects of the so-called "Green Chemistry" and they play a key role in environmentally friendly analytical techniques including their application as mobile phases or mobile phase additives. In such role, DESs can be used in liquid chromatography (LC) and HPLC.

Solvent selection rules for HPLC were developed over the past several decades, and acetonitrile as well as methanol have been permanently adopted as the most popular and applied organic modifiers in reversed phase RP-HPLC [48]. However, due to the growing environmental awareness brought about by the introduce of the "green chemistry" paradigm, new researches have been performed to find replacements to acetonitrile as well as other traditional organic solvents, as they are undesirable solvenst from a sustainable point of view [49,50]. Several problems associated with LC when green assessment is taken into consideration occur. Among them there is a large consumption of the organic solvents and other components and waste generation. It has been calculated that about 200 000 LC instruments are in use. With the simple assumption model when the typical column of 15 - 25 cm in length, 4,6 mm of i.d. packed with 5 μm particles is used, with the flow rate at the level of 1 mL/min, one can realize, that it creates around 0.5-1 L of waste per day, giving around 26,000,000–52,000,000 L of waste per year [51]. Due to this fact, green strategies and techniques targeted to the LC improvement are focused on solvent issue, including finding alternatives for organic solvents in HPLC. Other approaches applied to minimize organic solvents have been the introduction of surfactants or additives to the mobile phase [49]. Some of these additives have included DES (e.g. ChCl-Glycerol, ChCl-Ethylene Glycol), most of which can be environmentally considered as "green" solvents.

Only several works report the application of DESs as mobile phase in chromatography. The proposed mechanism is presented in Figure 6.

Figure 6. Schematic of application of DES as the mobile phase in RPLC.

The rare application of DESs as mobile phase in LC is due to the fact, that these solvents are characterized by a high viscosity and such parameter disqualifies DESs to be applied without dilution as mobile phase [52]. From the other side, addition of water impact on the decomposition of DESs into their constituent compounds. Such a process affects chromatography conditions. In this sense it must be mentioned that these effects do not concern DESs but the aqueous solutions of their components [52]. Additionally, there are other problems with application of DESs as mobile phase as presented in Figure 7. Due to these reasons, application of DESs as mobile phase in chromatography have not yet brought significant improvements. But what is worth to note, natural DESs, due to their characteristics, show greater potential in this area. Such application was presented by Sutton et al. [51]. Natural DES are shown to give chromatography performances in between those observed for ACN and MeOH when eluotropic strength, resolution, and peak capacity were taken into consideration, notwithstanding, the best overall performance for the mixtures tested in that study was presented by acetonitrile. However, it would be worth to investigate the addition of water as well as application of temperature which can impact on the decreasing viscosity as well as the eluotropic strength of the new mobile phases. Such solution could also result in fine tuning selectivity. Authors of presented work payed attention to the future research and stayed that the development of appropriate technologies must be considered essential before natural DES can be routinely used in HPLC analysis [51]. These improvements include: an improved pump system to generate high back-pressure, high-temperature endurable instrument, and stationary phases that allow the chromatographic analysis to operate at a high temperature to reduce the viscosity of DES.

Figure 7. Challenges to the use of DES as mobile phase

Although, the application of DESs as mobile phase is not successful yet, these solvents are widely used as mobile phase additives (Figure 8). Additives of mobile-phase are sometimes applied in order to optimize the chromatographic behaviours such as eliminating band tailing and increasing the number of theoretical plates [53]. It has been shown that even at a small amount, DESs can drastically improve the chromatographic performance in aspects of peak tailing, band broadening and resolution. It also need to be mentioned that the separation mechanism of DESs as mobile phase additives could be attributed to the combined effect of hydrogen acceptors as well hydrogen-bond donors [54]. In the reserach performed by Tan et al. [54], the following relationship has been shown: the single addition of hydrogen-bond donor cannot suppress peak tailing, while the single addition of hydrogen-bond acceptor showed a positive effect. Furthermore, the changes in the type of hydrogen-bond acceptor in DES impact on the alteration of retention ability of the chromatography column. In addition, DESs concentration was found to be a significant factor in chromatographic separation.

Figure 8. Schematic representation of the application of DES (in the example of ChCl/EG) as the mobile phase additive in an RPLC system.

In another work [53], it is noticed that DESs can act as mobile phase additives, and their components can simultaneously work as ions and play anion pairing role. The DESs cation would compete with the polar group of target analytes for the free silanol groups on the surface of stationary phase by the specific electrostatic interactions. The cation might be helpful for creating the ion pairs with the anion solutes. Contrary, depending on the anion, it could have less localized charge, lower degree of hydration and high polarizability (e.g. [Cl−]). In such case, the anion can disrupt the sheath of water molecules around the analytes by hydrogen bond, and the hydrophobicity of the analytes can increase noticeably [53,55]. Information on the application of DESs as mobile phase/mobile phase additives are presented in Table 3.

Table 3. Information on the application of DESs as mobile phase/mobile phase additives

Matrice	**Analyte(s)**	**DES (m.r.)**	**%DES in m.p.**	**Separation conditions**	**Analytical methodology**	**Ref.**
Herbal oral solution	Quaternary alkaloids	ChCl-EG (1:3)	1	Column: C18 Mobile phase: ACN:HCl (32:68 v/v); pH 3.3	HPLC-UV	[54]
Standard mixture	Quercetin	ChCl-EG (1:2)	0.2	Column: C18 Mobile phase: MeOH:water (60:40 v/v/)	HPLC-UV-VIS	[53]
Standard mixture	Caffeic acid	ChCl-glycerol (1:3)	0.1	Column: C18 Mobile phase: MeOH: water (18:82 v/v/)	HPLC-UV-VIS	[55]
Urine	Cardiovascular drugs	ChCl-EG-based NADES (2:1)	3.5	Mobile phase: SDS:buthanol:NADES:GAC (83:10:3.5:3.5 v/v/v/v/)	MLC-UV	[56]
Plasma	Cardiovascular drugs	ChCl-EG-based NADES (2:1)	3.5	Mobile phase: SDS:buthanol:NADES:GAC (83:10:3.5:3.5 v/v/v/v/)	MLC-UV	[56]
Milk	Melamine	ChCl-EG-based NADES (1:2)	4	Mobile phase: SDS:NADES:GAC	MLC-UV	[57]
Standard mixture	Nucleobases, nucleosides	ChCl-EG (1:3)	65	Column: C18 Mobile phase: Water:EtOH:NADES (30:5:65 v/v/v/)	UHPLC-DAD	[51]
Standard mixture	Caffeine, vanillin,coumarin, carvone, β-ionone, and β-carotene	L-menthol-levulinic acid (1:1)	5	Column: teflon Mobile phase: n-heptan: MeOH:DES	CPC	[58]
Standard mixture	Tocopherol mixture	ChCl-1,4-butanediol (1:1)	30	Mobile phase: heptane/EtOH/DES (30/40/30 wt/wt/wt)	CPC	[59]
Chelidonium maiusroot extract	Alkaloids	Menthol-phenol (1:1)	65	TLC Si60 plates; Mobile phase: DES/MeOH (65/35 wt/wt)	TLC	[60]
Standard mixture	Benzenes, PAHs, nucleosides, alkaloids	ChCl-IA: (2:1)	-	Electrolyte solution: ACN: phosphates buffers Column: Silica capillary:DES	CEC	[61]

ACN, acetonitrile; CEC, capillary electrochromatography; ChCl, choline chloride; ClChCl, chlorocholine chloride; CPC, centrifugal partition chromatography; EG, ethylene glycol; EGDMA, ethylene glycol dimethacrylate; GAC, glacial acetic acid; HI, hydrophilic interaction; HPLC, high performence liquid chromatography; IA, itaconic acid; MeOH, methanol; MLC, micellar liquid chromatography; NADES, natural deep eutectic solvent; PAHs, polycyclic aromatic hydrocarbons; SDS, sodium dodecyl sulphate; TLC, thin layer chromatography

m.p., mobile phase; m.r., molar ratio

252
253
254 *3.1.1. Application of DESs in countercurrent and centrifugal chromatography*

255 Countercurrent chromatography (CCC) is a separation technique based on the partition
256 of solutes between two different liquid phases. The technique is created by a multi-solvent
257 biphasic system, in which stationary phase is kept in the column with the aid of a centrifugal
258 field, while the mobile phase is pumped through the column. In practice, the CCC biphasic
259 system consists of three/four solvents which differ in polarity. In CCC, target analytes are
260 separated by application of changes in the ratio of the biphasic system components to adjust
261 their partition coefficients between both phases [62].
262 For the first time, DES were evaluated as solvents in CCC in 2016 [62]. In that research,
263 DESs have been shown to be a promising new class of solvents in CCC or CPC. They can be
264 used to substitute the water in biphasic systems composed of water and organic solvents.
265 From that time, several other studies have been published [58,59].
266
267 *3.1.2. Application of DESs in thin layer chromatography (TLC)*
268 In 2020, the results of a preliminary investigation of DES being employed as mobile phases in
269 thin layer chromatography (TLC) were published for the first time [60]. The work was
270 focused on the use of eutectic liquids allowing chromatographic separation of mixtures of
271 natural compounds, with particular regard to alkaloids. For this purpose several NADES
272 eutectic solvents were selected. In most of the tested modifications at least partial separation
273 of target analytes was achieved. The most successful mobile phase which enabled separation
274 of all the tested alkaloids was this where DES was diluted with the equimolar mixture of
275 menthol and phenol with a 35% addition of methanol. The study presents high potential of
276 DESs as mobile phase in TLC. However, future studies are highly recommended to explore
277 new methodological solutions and application possibilities.
278
279 ***3.2. DESs as stationary phases or surface modifiers***

280 Nowadays, the stabilization of DES on an appropriate matrix to act as chromatography
281 stationary phase is attempted. However only few papers focused on the application of DESs
282 as stiationary phase are available [61,63,64]. Considering results presented in these papers it
283 can be concluded that the modification of DES stability on matrix seems to be a key problem
284 in chromatography application. This is mainly due to the fact that although the hydrogen bond
285 acceptor can be covalently grafted to the matrix, the stabilization of hydrogen bond donor is
286 mainly based on the hydrogen bonding with HBA which can be easily break up by the rinse of
287 aqueous sample or elution [7]. Several methods could be used to regulation of the stability of
288 DES based stationary phase. In such way, several procedures have been proposed: i)

application of hydrophobic DES as stationary phase and elution with aqueous solvent, ii) co-polymerization of polymerizable HBAs and HBDs onto matrix, or iii) application of hydrophilic DES stationary phase in normal phase liquid chromatography.

A novel monolithic column, based on the copolymerization of ethylene dimethacrylate and a DES composed of ChCl and itaconic acid, was developed for capillary electrochromatography (CEC) by Wang et al. [61]. The basic research present a porous monolithic structure with good permeability. The developed column exhibited excellent performance for the separation of neutral compounds, phenols, toluidines, nucleosides, nucleotide bases and alkaloids. It was stated by the author that the potential retention mechanism might be attributed to synergistic effect of hydrophobic interaction, hydrogen bond interaction and electronic interaction [61]. The DES-based monolithic column was characterized by good analytical repeatability. The success of the research team of Wang indicates that organic polymer monolithic columns with DESs as functional monomers are a promising stationary phases in chromatography.

3.3. DESs as the reaction solvent or solvent additive for the preparation of chromatographic materials

DESs are widely used as substitute to traditional solvents in organic synthesis [65,66] and enzymatic reactions [67,68]. These successful applications inspired chromatography researchers to evaluate the possibility of DESs application as solvent for preparative chromatography. Preparation of stationary phases using DES as solvent is the most often performed reaction in this area (Table B), including: silanization reaction [69], surface radical chain-transfer reaction [70], and epoxy ring-opening reaction [71] (Table 4).

The first report on the silylation of silica particles was performed by Gu et al. using a classic DES of ChCl/urea and successful preparation a glucamine-modified silica stationary phase in DES [69]. The silica suspension can be maintained for 24 h in DES. However, it can be maintained only for less than 5 min in toluene. Fine dispersibility is probably due to the strong hydrogen bonding between hydrogen bond acceptor (ChCl) and hydrogen bond donor (silanol on the silica surface) as well as the appropriate viscosity of DES. It need to be mentioned that the stable suspension of silica is an advantage for the uniform modification of its surface.

A new stationary phase based on poly(itaconic acid)-grafted silica (Sil-PIA) was synthesized in DESs and characterized in detail [70]. Itaconic acid was homopolymerized on silica via surface radical chain-transfer using DESs as a green solvents. The results were compared with previous reported poly(acrylic acid)-grafted silica (Sil-PAA) stationary phase with satisfactory results. Sil-PIA provided shorter retention time but similar or higher selectivity for the separation of most polar compounds; such as bases, nucleosides, amino acids, and saccharides in hydrophilic interaction chromatography. In addition, Sil-PIA presented very good performance in the separation of eleven ginsenosides using isocratic elution in hydrophilic chromatography.

In another work, two homopolymeried and one copolymerized silica-based stationary phases were successfully prepared in DESs by the surface radical chain-transfer reaction by Yang et al. [72]. Through investigating the effects of different chromatographic conditions on retention of three stationary phases, it can be found that the retention of solutes on three stationary phases were based on both, partitioning mechanism and adsorptive interactions as

electronic interaction and hydrogen bonding. In comparison with the conventional solvents as chloroform and methanol, higher surface coverage was found in the case of DESs. In addition, similar results of elemental analysis were found for the materials prepared repeatedly in DESs. However, because of the application of some aliquote of other compounds (methanol and CCl_4) during column packing, the proposed method reduced the use of toxic solvents but it is still not 100% green method. However, this study presents the huge potential in the area of micro- or nano-materials preparation that could be used in separation science and other research fields.

Zgand et al. [73] published very interesting results focused on application of N-doped carbon dots (NCDs) modifiers of the spherical porous silica surface in DESs. The appropriate density and hydrophibility of DESs guaranteed the fine dispersibility of silica particles and NCDs, provided a homogeneous and thin layer of inmobilized NCDs. In comparison with conventional organic solvents (DMF and THF), increased surface coverage was obtained in the DES medium, proving its feasibility as a new kind of alternative solvent for hydrophilic nanomaterial-based surface modification of silica spheres. The new NCDs-silicaparticles (Sil-NCDs) were packed into chromatographic columns to study their initial feasibility as adsorbent material for LC. The results were satisfactory, and the new column presented a selective behavior for polar compounds in HILIC mode. It can be stated that the new Sil-NCDs stationary phases greatly broaden the application of carbon dots and give a typical example to design novel nano-on-micro materials in DESs. Moreover, this kind of NCDs decorated silica spheres are very promising to be used in other chemical and engineering fields.

After considering above mentioned studies, it must be stated that the high viscosity of DESs helps to create a stable dispersion of silica gel in comparison with organic solvents. Moreover, this parameter prevents particle aggregation, leading to an improved efficient modification.

It need to be also mentioned that no work has yet been presented on the application of DESs as stationary phases in GC. This is probably due to the fact that in GC high temperatures applied can weaken the hydrogen bonds in DESs, leading to their decomposition. However, it is still recommended to focus on this area as DESs are quite thermally stable compounds.

Table 4. Preparation reactions of stationary phases using DES as solvent

Reaction solvent	**Reaction type**	**Stationary phase**	**Application**	**Methodology**	**Ref.**
ChCl: EG (1:3)	Surface radical chain-transfer reaction	Sil-PIA	Nucleosides, nucleobases, amino acids, saccharides, ginsenosides	HILIC	[70]
ChCl:urea (1:2) ChCl:glycerol (1:2)		Sil-PIm; Sil-PAA; Sil-PIm-PAA	Nucleosides, saccharides, nucleobases, amino acids	HILIC	[72]

ChCl: EG (1:3)	Epoxy ring-opening reaction	Sil-PEI; Sil-PEICDs	Nucleosides, nucleobases, ginsenosides	HILIC	[71]
ChCl:EG (1:3)		Sil-NCDs	Tryptophan, nucleosides, nucleobases, saccharides	HILIC	[73]
ChCl:urea (1:2)	Silanization reaction	Sil-*N*-Glu	Sulfamides	HPLC	[69]

EG, ethylene glycol; ChCl, choline chloride; HILIC, hydrophilic interaction chromatography; NCDs, N-doped carbon dots; PEI, polyethyleneimine; PEICDs, PEI-functionalized carbon dots; Sil-N-Glu, N-methyl-glucamine-modified silic; Sil-PAA, poly(acrylic acid)-grafted silica; Sil-PIA, poly(itaconic acid)-grafted silica; Sil-PIm, poly(1-vinylimidazole)-grafted silica; Sil-PIm-PAA, poly(1-vinylimidazole-co-acrylic acid)-grafted silica

4. Conclusions and future perspectives

Promising perspectives of the use of DES in Chromatography are based on the easy availability of DES components and the fact that many of these are of natural origin and thus renewable. So, from the Green Analytical point of view these new solvents offer non-toxic sustainable alternatives to traditional organic solvents and ILs. However, the relative high viscosity, low volatility strong UV absorption and lack of HPLC grade purity of many of DES components create drawbacks on their use as mobile phases in LC or general use in GC. However, promising perspectives focused on the modification of stationary and mobile phases for GC or HPLC, additionally on the use of DES for sample preparation previously to their chromatography determination. So, it can be expected that in the next years the use of DES could be extended to the development of new robust and high performance chromatography methods. In this way it must be explored the effect of temperature and the presence of small amounts of water on the DES systems.

References

[1] R.D. Rogers, K.R. Seddon, Ionic Liquids - Solvents of the Future?, Science (80-.). 302 (2003) 792–793. doi:10.1126/science.1090313.

[2] A. Paiva, R. Craveiro, I. Aroso, M. Martins, R.L. Reis, A.R.C. Duarte, Natural deep eutectic solvents - Solvents for the 21st century, ACS Sustain. Chem. Eng. 2 (2014) 1063–1071. doi:10.1021/sc500096j.

[3] K. Owczarek, N. Szczepanska, J. Plotka-Wasylka, M. Rutkowska, O. Shyshchak, M. Bratychak, J. Namiesnik, Natural deep eutectic solvents in extraction process, Chem. Chem. Technol. 10 (2016) 601–606. doi:10.23939/chcht10.04si.601.

[4] C.M. Clouthier, J.N. Pelletier, Expanding the organic toolbox: A guide to integrating biocatalysis in synthesis, Chem. Soc. Rev. 41 (2012) 1585–1605. doi:10.1039/c2cs15286j.

[5] Z. Maugeri, P. Domínguez De María, Novel choline-chloride-based deep-eutectic-solvents with renewable hydrogen bond donors: Levulinic acid and sugar-based polyols, RSC Adv. 2 (2012) 421–425. doi:10.1039/c1ra00630d.

[6] B. Tang, K.H. Row, Recent developments in deep eutectic solvents in chemical

sciences, Monatshefte Fur Chemie. 144 (2013) 1427–1454. doi:10.1007/s00706-013-1050-3.
[7] T. Cai, H. Qiu, Application of deep eutectic solvents in chromatography: A review, TrAC - Trends Anal. Chem. 120 (2019) 115623. doi:10.1016/j.trac.2019.115623.
[8] Q. Zhang, K. De Oliveira Vigier, S. Royer, F. Jérôme, Deep eutectic solvents: Syntheses, properties and applications, Chem. Soc. Rev. 41 (2012) 7108–7146. doi:10.1039/c2cs35178a.
[9] A. Shishov, A. Bulatov, M. Locatelli, S. Carradori, V. Andruch, Application of deep eutectic solvents in analytical chemistry. A review, Microchem. J. 135 (2017) 33–38. doi:10.1016/j.microc.2017.07.015.
[10] A.P. Abbott, J.C. Barron, K.S. Ryder, D. Wilson, Eutectic-based ionic liquids with metal-containing anions and cations, Chem. - A Eur. J. 13 (2007) 6495–6501. doi:10.1002/chem.200601738.
[11] B. Kudłak, K. Owczarek, J. Namieśnik, Selected issues related to the toxicity of ionic liquids and deep eutectic solvents—a review, Environ. Sci. Pollut. Res. 22 (2015) 11975–11992. doi:10.1007/s11356-015-4794-y.
[12] Y. Dai, J. van Spronsen, G.J. Witkamp, R. Verpoorte, Y.H. Choi, Natural deep eutectic solvents as new potential media for green technology, Anal. Chim. Acta. 766 (2013) 61–68. doi:10.1016/j.aca.2012.12.019.
[13] R. López- Fandiño, I. Gill, E.N. Vulfson, Protease- catalyzed synthesis of oligopeptides in heterogenous substrate mixtures, Biotechnol. Bioeng. 43 (1994) 1024–1030. doi:10.1002/bit.260431105.
[14] I. Gill, E. Vulfson, Enzymic catalysis in heterogeneous eutectic mixtures of substrates, Trends Biotechnol. 12 (1994) 118–122. doi:10.1016/0167-7799(94)90088-4.
[15] M. Erbeldinger, X. Ni, P.J. Halling, Enzymatic synthesis with mainly undissolved substrates at very high concentrations, Enzyme Microb. Technol. 23 (1998) 141–148. doi:10.1016/S0141-0229(98)00039-8.
[16] Z. Helalat-Nezhad, K. Ghanemi, M. Fallah-Mehrjardi, Dissolution of biological samples in deep eutectic solvents: An approach for extraction of polycyclic aromatic hydrocarbons followed by liquid chromatography-fluorescence detection, J. Chromatogr. A. 1394 (2015) 46–53. doi:10.1016/j.chroma.2015.03.053.
[17] M.B. Arain, E. Yilmaz, M. Soylak, Deep eutectic solvent based ultrasonic assisted liquid phase microextraction for the FAAS determination of cobalt, J. Mol. Liq. 224 (2016) 538–543. doi:10.1016/j.molliq.2016.10.005.
[18] J. Nie, G. Yu, Z. Song, X. Wang, Z. Li, Y. She, M. Lee, Microwave-assisted deep eutectic solvent extraction coupled with headspace solid-phase microextraction followed by GC-MS for the analysis of volatile compounds from tobacco, Anal. Methods. 9 (2017) 856–863. doi:10.1039/c6ay03076a.
[19] W. Bi, M. Tian, K.H. Row, Evaluation of alcohol-based deep eutectic solvent in extraction and determination of flavonoids with response surface methodology optimization, J. Chromatogr. A. 1285 (2013) 22–30. doi:10.1016/j.chroma.2013.02.041.
[20] Y.H. Choi, J. van Spronsen, Y. Dai, M. Verberne, F. Hollmann, I.W.C.E. Arends, G.J. Witkamp, R. Verpoorte, Are natural deep eutectic solvents the missing link in understanding cellular metabolism and physiology?, Plant Physiol. 156 (2011) 1701–1705. doi:10.1104/pp.111.178426.
[21] B. Tang, H. Zhang, K.H. Row, Application of deep eutectic solvents in the extraction and separation of target compounds from various samples, J. Sep. Sci. 38 (2015) 1053–1064. doi:10.1017/CBO9781107415324.004.
[22] X. Li, K.H. Row, Development of deep eutectic solvents applied in extraction and

separation, J. Sep. Sci. 39 (2016) 3505–3520. doi:10.1002/jssc.201600633.
[23] A.N. Anthemidis, K.I.G. Ioannou, Recent developments in homogeneous and dispersive liquid-liquid extraction for inorganic elements determination. A review, Talanta. 80 (2009) 413–421. doi:10.1016/j.talanta.2009.09.005.
[24] G. Li, W. Tang, W. Cao, Q. Wang, T. Zhu, Molecularly imprinted polymers combination with deep eutectic solvents for solid-phase extraction of caffeic acid from hawthorn, Chinese J. Chromatogr. 33 (2015) 792–798.
[25] S.M. Yousefi, F. Shemirani, S.A. Ghorbanian, Deep eutectic solvent magnetic bucky gels in developing dispersive solid phase extraction: Application for ultra trace analysis of organochlorine pesticides by GC-micro ECD using a large-volume injection technique, Talanta. 168 (2017) 73–81. doi:10.1016/j.talanta.2017.03.020.
[26] T. Khezeli, A. Daneshfar, Dispersive micro-solid-phase extraction of dopamine, epinephrine and norepinephrine from biological samples based on green deep eutectic solvents and Fe3O4@MIL-100 (Fe) core-shell nanoparticles grafted with pyrocatechol, RSC Adv. 5 (2015) 65264–65273. doi:10.1039/c5ra08058d.
[27] N. Lamei, M. Ezoddin, K. Abdi, Air assisted emulsification liquid-liquid microextraction based on deep eutectic solvent for preconcentration of methadone in water and biological samples, Talanta. 165 (2017) 176–181. doi:10.1016/j.talanta.2016.11.036.
[28] M.A. Farajzadeh, M.R. Afshar Mogaddam, B. Feriduni, Simultaneous synthesis of a deep eutectic solvent and its application in liquid-liquid microextraction of polycyclic aromatic hydrocarbons from aqueous samples, RSC Adv. 6 (2016) 47990–47996. doi:10.1039/c6ra04103e.
[29] M.A. Farajzadeh, M.R. Afshar Mogaddam, M. Aghanassab, Deep eutectic solvent-based dispersive liquid-liquid microextraction, Anal. Methods. 8 (2016) 2576–2583. doi:10.1039/c5ay03189c.
[30] B. Tang, W. Bi, H. Zhang, K.H. Row, Deep eutectic solvent-based HS-SME coupled with GC for the analysis of bioactive terpenoids in Chamaecyparis obtusa leaves, Chromatographia. 77 (2014) 373–377. doi:10.1007/s10337-013-2607-3.
[31] E. Habibi, K. Ghanemi, M. Fallah-Mehrjardi, A. Dadolahi-Sohrab, A novel digestion method based on a choline chloride-oxalic acid deep eutectic solvent for determining Cu, Fe, and Zn in fish samples, Anal. Chim. Acta. 762 (2013) 61–67. doi:10.1016/j.aca.2012.11.054.
[32] T. Khezeli, A. Daneshfar, R. Sahraei, Emulsification liquid–liquid microextraction based on deep eutectic solvent: An extraction method for the determination of benzene, toluene, ethylbenzene and seven polycyclic aromatic hydrocarbons from water samples, J. Chromatogr. A. 1425 (2015) 25–33. doi:10.1016/j.chroma.2015.11.007.
[33] F. Aydin, E. Yilmaz, M. Soylak, A simple and novel deep eutectic solvent based ultrasound-assisted emulsification liquid phase microextraction method for malachite green in farmed and ornamental aquarium fish water samples, Microchem. J. 132 (2017) 280–285. doi:10.1016/j.microc.2017.02.014.
[34] N. Lamei, M. Ezoddin, K. Abdi, Air assisted emulsification liquid-liquid microextraction based on deep eutectic solvent for preconcentration of methadone in water and biological samples, Talanta. 165 (2017) 176–181. doi:10.1016/j.talanta.2016.11.036.
[35] S.M. Yousefi, F. Shemirani, S.A. Ghorbanian, Deep eutectic solvent magnetic bucky gels in developing dispersive solid phase extraction: Application for ultra trace analysis of organochlorine pesticides by GC-micro ECD using a large-volume injection technique, Talanta. 168 (2017) 73–81. doi:10.1016/j.talanta.2017.03.020.
[36] T. Khezeli, A. Daneshfar, R. Sahraei, A green ultrasonic-assisted liquid-liquid

microextraction based on deep eutectic solvent for the HPLC-UV determination of ferulic, caffeic and cinnamic acid from olive, almond, sesame and cinnamon oil, Talanta. 150 (2016) 577–585. doi:10.1016/j.talanta.2015.12.077.
[37] T. Tan, Z. Li, X. Mao, Y. Wan, H. Qiu, Deep eutectic solvent-based liquid-phase microextraction for detection of plant growth regulators in edible vegetable oils, Anal. Methods. 8 (2016) 3511–3516. doi:10.1039/c6ay00053c.
[38] A. García, E. Rodríguez-Juan, G. Rodríguez-Gutiérrez, J.J. Rios, J. Fernández-Bolaños, Extraction of phenolic compounds from virgin olive oil by deep eutectic solvents (DESs), Food Chem. 197 (2016) 554–561. doi:10.1016/j.foodchem.2015.10.131.
[39] V.M. Paradiso, A. Clemente, C. Summo, A. Pasqualone, F. Caponio, Towards green analysis of virgin olive oil phenolic compounds: Extraction by a natural deep eutectic solvent and direct spectrophotometric detection, Food Chem. 212 (2016) 43–47. doi:10.1016/j.foodchem.2016.05.082.
[40] E. Yilmaz, M. Soylak, Ultrasound assisted-deep eutectic solvent based on emulsification liquid phase microextraction combined with microsample injection flame atomic absorption spectrometry for valence speciation of chromium(III/VI) in environmental samples, Talanta. 160 (2016) 680–685. doi:10.1016/j.talanta.2016.08.001.
[41] J.M. Matong, L. Nyaba, P.N. Nomngongo, Determination of As, Cr, Mo, Sb, Se and V in agricultural soil samples by inductively coupled plasma optical emission spectrometry after simple and rapid solvent extraction using choline chloride-oxalic acid deep eutectic solvent, Ecotoxicol. Environ. Saf. 135 (2017) 152–157.
[42] E. Yilmaz, M. Soylak, Ultrasound assisted-deep eutectic solvent extraction of iron from sheep, bovine and chicken liver samples, Talanta. 136 (2015) 170–173. doi:10.1016/j.talanta.2014.12.034.
[43] E. Bağda, H. Altundağ, M. Soylak, Highly Simple Deep Eutectic Solvent Extraction of Manganese in Vegetable Samples Prior to Its ICP-OES Analysis, Biol. Trace Elem. Res. 179 (2017) 334–339. doi:10.1007/s12011-017-0967-5.
[44] L. Piemontese, F.M. Perna, A. Logrieco, V. Capriati, M. Solfrizzo, Deep eutectic solvents as novel and effective extraction media for quantitative determination of Ochratoxin A in wheat and derived products, Molecules. 22 (2017) 1–9. doi:10.3390/molecules22010121.
[45] X.H. Yao, D.Y. Zhang, M.H. Duan, Q. Cui, W.J. Xu, M. Luo, C.Y. Li, Y.G. Zu, Y.J. Fu, Preparation and determination of phenolic compounds from Pyrola incarnata Fisch. with a green polyols based-deep eutectic solvent, Sep. Purif. Technol. 149 (2015) 116–123. doi:10.1016/j.seppur.2015.03.037.
[46] Z. Wei, X. Qi, T. Li, M. Luo, W. Wang, Y. Zu, Y. Fu, Application of natural deep eutectic solvents for extraction and determination of phenolics in Cajanus cajan leaves by ultra performance liquid chromatography, Sep. Purif. Technol. 149 (2015) 237–244. doi:10.1016/j.seppur.2015.05.015.
[47] H.E. Park, B. Tang, K.H. Row, Application of Deep Eutectic Solvents as Additives in Ultrasonic Extraction of Two Phenolic Acids from Herba Artemisiae Scopariae, Anal. Lett. 47 (2014) 1476–1484. doi:10.1080/00032719.2013.874016.
[48] C.S. Funari, R.L. Carneiro, A.J. Cavalheiro, E.F. Hilder, A trade off between separation, detection and sustainability in liquid chromatographic fingerprinting, J. Chromatogr. A. 1354 (2014) 34–42. doi:10.1016/j.chroma.2014.05.018.
[49] A.I. Olives, V. González-Ruiz, M.A. Martín, Sustainable and Eco-Friendly Alternatives for Liquid Chromatographic Analysis, ACS Sustain. Chem. Eng. 5 (2017) 5618–5634. doi:10.1021/acssuschemeng.7b01012.
[50] M. Tobiszewski, J. Namieśnik, F. Pena-Pereira, Environmental risk-based ranking of

549 solvents using the combination of a multimedia model and multi-criteria decision
550 analysis, Green Chem. 19 (2017) 1034–1042. doi:10.1039/c6gc03424a.
551 [51] A.T. Sutton, K. Fraige, G.M. Leme, V. da Silva Bolzani, E.F. Hilder, A.J. Cavalheiro,
552 R.D. Arrua, C.S. Funari, Natural deep eutectic solvents as the major mobile phase
553 components in high-performance liquid chromatography—searching for alternatives to
554 organic solvents, Anal. Bioanal. Chem. 410 (2018) 3705–3713. doi:10.1007/s00216-
555 018-1027-5.
556 [52] A. Shishov, A. Pochivalov, L. Nugbienyo, V. Andruch, A. Bulatov, Deep eutectic
557 solvents are not only effective extractants, TrAC - Trends Anal. Chem. 129 (2020)
558 115956. doi:10.1016/j.trac.2020.115956.
559 [53] F. Gao, L. Liu, W. Tang, K.H. Row, T. Zhu, Optimization of the chromatographic
560 behaviors of quercetin using choline chloride-based deep eutectic solvents as HPLC
561 mobile-phase additives, Sep. Sci. Technol. 53 (2018) 397–403.
562 doi:10.1080/01496395.2017.1388257.
563 [54] T. Tan, M. Zhang, Y. Wan, H. Qiu, Utilization of deep eutectic solvents as novel
564 mobile phase additives for improving the separation of bioactive quaternary alkaloids,
565 Talanta. 149 (2016) 85–90. doi:10.1016/j.talanta.2015.11.041.
566 [55] G. Li, T. Zhu, Y. Lei, Choline chloride-based deep eutectic solvents as additives for
567 optimizing chromatographic behavior of caffeic acid, Korean J. Chem. Eng. 32 (2015)
568 2103–2108. doi:10.1007/s11814-015-0054-6.
569 [56] A.M. Ramezani, G. Absalan, Employment of a natural deep eutectic solvent as a
570 sustainable mobile phase additive for improving the isolation of four crucial
571 cardiovascular drugs by micellar liquid chromatography, J. Pharm. Biomed. Anal. 186
572 (2020) 113259. doi:10.1016/j.jpba.2020.113259.
573 [57] A.M. Ramezani, R. Ahmadi, G. Absalan, Designing a sustainable mobile phase
574 composition for melamine monitoring in milk samples based on micellar liquid
575 chromatography and natural deep eutectic solvent, J. Chromatogr. A. 1610 (2020)
576 460563. doi:10.1016/j.chroma.2019.460563.
577 [58] F. Bezold, M. Minceva, A water-free solvent system containing an L-menthol-based
578 deep eutectic solvent for centrifugal partition chromatography applications, J.
579 Chromatogr. A. 1587 (2019) 166–171. doi:10.1016/j.chroma.2018.11.083.
580 [59] F. Bezold, M.E. Weinberger, M. Minceva, Computational solvent system screening for
581 the separation of tocopherols with centrifugal partition chromatography using deep
582 eutectic solvent-based biphasic systems, J. Chromatogr. A. 1491 (2017) 153–158.
583 doi:10.1016/j.chroma.2017.02.059.
584 [60] D. Raj, Thin-layer chromatography with eutectic mobile phases—preliminary results, J.
585 Chromatogr. A. 1621 (2020) 0–5. doi:10.1016/j.chroma.2020.461044.
586 [61] R. Wang, Z. Mao, Z. Chen, Monolithic column with polymeric deep eutectic solvent as
587 stationary phase for capillary electrochromatography, J. Chromatogr. A. 1577 (2018)
588 66–71. doi:10.1016/j.chroma.2018.09.046.
589 [62] S. Roehrer, F. Bezold, E.M. García, M. Minceva, Deep eutectic solvents in
590 countercurrent and centrifugal partition chromatography, J. Chromatogr. A. 1434
591 (2016) 102–110. doi:10.1016/j.chroma.2016.01.024.
592 [63] Y. Hu, T. Cai, H. Zhang, J. Chen, Z. Li, L. Zhao, Z. Li, H. Qiu, Two copolymer-grafted
593 silica stationary phases prepared by surface thiol-ene click reaction in deep eutectic
594 solvents for hydrophilic interaction chromatography, J. Chromatogr. A. 1609 (2020)
595 460446. doi:10.1016/j.chroma.2019.460446.
596 [64] B. Tang, H.E. Park, K.H. Row, Preparation of chlorocholine chloride/urea deep
597 eutectic solvent-modified silica and an examination of the ion exchange properties of
598 modified silica as a Lewis adduct, Anal. Bioanal. Chem. 406 (2014) 4309–4313.

599 doi:10.1007/s00216-014-7817-5.
600 [65] D. Brenna, E. Massolo, A. Puglisi, S. Rossi, G. Celentano, M. Benaglia, V. Capriati,
601 Towards the development of continuous, organocatalytic, and stereoselective reactions
602 in deep eutectic solvents, Beilstein J. Org. Chem. 12 (2016) 2620–2626.
603 doi:10.3762/bjoc.12.258.
604 [66] A. Kumar, R.D. Shukla, D. Yadav, L.P. Gupta, Friedel-Crafts alkylation of indoles in
605 deep eutectic solvent, RSC Adv. 5 (2015) 52062–52065. doi:10.1039/c5ra08038j.
606 [67] T.F. Adepoju, Optimization processes of biodiesel production from pig and neem
607 (Azadirachta indica a.Juss) seeds blend oil using alternative catalysts from waste
608 biomass, Ind. Crops Prod. 149 (2020) 112334. doi:10.1016/j.indcrop.2020.112334.
609 [68] J. Hoppe, R. Drozd, E. Byzia, M. Smiglak, Deep eutectic solvents based on choline
610 cation - Physicochemical properties and influence on enzymatic reaction with β-
611 galactosidase, Int. J. Biol. Macromol. 136 (2019) 296–304.
612 doi:10.1016/j.ijbiomac.2019.06.027.
613 [69] T. Gu, M. Zhang, J. Chen, H. Qiu, A novel green approach for the chemical
614 modification of silica particles based on deep eutectic solvents, Chem. Commun. 51
615 (2015) 9825–9828. doi:10.1039/c5cc02553b.
616 [70] Y. Hu, T. Cai, H. Zhang, J. Chen, Z. Li, H. Qiu, Poly(itaconic acid)-grafted silica
617 stationary phase prepared in deep eutectic solvents and its unique performance in
618 hydrophilic interaction chromatography, Talanta. 191 (2019) 265–271.
619 doi:10.1016/j.talanta.2018.08.072.
620 [71] T. Cai, H. Zhang, J. Chen, Z. Li, H. Qiu, Polyethyleneimine-functionalized carbon dots
621 and their precursor co-immobilized on silica for hydrophilic interaction
622 chromatography, J. Chromatogr. A. 1597 (2019) 142–148.
623 doi:10.1016/j.chroma.2019.03.026.
624 [72] B. Yang, T. Cai, Z. Li, M. Guan, H. Qiu, Surface radical chain-transfer reaction in deep
625 eutectic solvents for preparation of silica-grafted stationary phases in hydrophilic
626 interaction chromatography, Talanta. 175 (2017) 256–263.
627 doi:10.1016/j.talanta.2017.07.038.
628 [73] H. Zhang, X. Qiao, T. Cai, J. Chen, Z. Li, H. Qiu, Preparation and characterization of
629 carbon dot-decorated silica stationary phase in deep eutectic solvents for hydrophilic
630 interaction chromatography, Anal. Bioanal. Chem. 409 (2017) 2401–2410.
631 doi:10.1007/s00216-017-0187-z.
632