Chinese Chemical Letters 34 (2023) 107750

Contents lists available at ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Responsive switchable deep eutectic solvents: A review

Jingyu Zhang[a], Shang Li[b], Liping Yao[a], Yuexing Yi[a], Lingqi Shen[a], Zuguang Li[a,*], Hongdeng Qiu[c,*]

[a] College of Chemical Engineering, Zhejiang University of Technology, Hangzhou 310014, China
[b] College of Materials Science and Engineering, Zhejiang University of Technology, Hangzhou 310014, China
[c] CAS key laboratory of Chemistry of Northwestern Plant Resources/Key Laboratory for Natural Medicine of Gansu Province, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, China

ARTICLE INFO

Article history:
Received 24 May 2022
Revised 30 July 2022
Accepted 15 August 2022
Available online 17 August 2022

Keywords:
Deep eutectic solvents
Switchable solvents
Reversible phase transition
Sample preparation
Review

ABSTRACT

Deep eutectic solvents (DESs) have drawn considerable attention as a new type of green solvent since they were reported. Subsequent studies have shown that DESs have the potential to be used as "designable" solvents, which means that the precursors of DESs with different structures and properties can be screened to customize DESs for specific functions. Researchers have found that during the sample preparation process involving DESs, the specific properties of some "smart" DESs can be switched by directing external driving forces, leading to a reversible phase transition of the target solution. These "smart" DESs are called switchable deep eutectic solvents (SDESs). The advent of SDES simplifies the sample pretreatment steps, reduces the use of organic solvents, and makes solvents easy to recycle, which matches the concept of green and sustainable chemistry. Compared with the number of previous experimental studies, the reviews and summaries on SDESs are rare. Therefore, this review made a summary of the concept and research progress of SDESs based on some related works in the past decade, including composition and type, characterization, switching mechanism, *etc.* It is expected to provide a certain reference and guidance for the subsequent in-depth research of SDESs in the analytical sample pretreatment.

1. Introduction

Eco-environmental friendliness is the theme of the development of human society since the 21st century. The benign needs of society for ecology have promoted the birth of green industries and products. The sample pretreatment process in analytical chemistry also tends to be greener and more efficient, in which the green improvement of the solvent is relatively much important. Abbott *et al.* [1,2] first proposed the concept of deep eutectic solvents (DESs). DES has been gradually developed as a new type of green solvent to substitute traditional organic solvents and ionic liquids (ILs) [3–5]. This is a deep eutectic mixture formed by intermolecular hydrogen bonding between hydrogen bond acceptor (HBA) and hydrogen bond donor (HBD), which has a melting point lower than that of pure HBD and pure HBA [6–8]. From the solid-liquid phase diagram of the basic binary DES (Fig. 1), the hydrogen-bonded mixture composed of precursor A and precursor B exhibits a triple point (lowest eutectic point). This phenomenon was first observed in a hydrogen-bonded mixture of choline chloride (m.p. 302 °C) and urea (m.p. 133 °C) in a molar ratio of 1:2, which was heated at 80 °C for a period of time and a clear liquid with a melting point of 12 °C was formed after cooling to room temperature [1]. Another potential feature of DESs is that HBAs and HBDs with appropriate properties can be screened to design DESs that can match specific target, and exhibit low toxicity and environmental friendliness [9,10]. Nowadays DES has been widely used in sample pretreatment [11–14], development of *in-situ* formation of efficient eutectic systems [15], extraction and separation of natural products [16–19], and preparation of chromatographic materials [20] and nanomaterials [21].

The researchers subsequently attempted to synthesize DESs with different compositions [22,23]. Smith *et al.* [24] summarized and proposed a general formula for describing the composition of DESs: Cat^+X^-zY, which Cat^+ represents the cation of various sulfonium, phosphonium or ammonium salts, X^- is the halide salt anion, and Y is Lewis acid or Brönsted acid, z is the number of moles of Y. According to the several types of HBA and HBD, DESs can be divided into the four categories represented in Fig. 2. Microscopi-

* Corresponding authors.
E-mail addresses: lzg@zjut.edu.cn (Z. Li), hdqiu@licp.cas.cn (H. Qiu).

https://doi.org/10.1016/j.cclet.2022.107750
1001-8417/

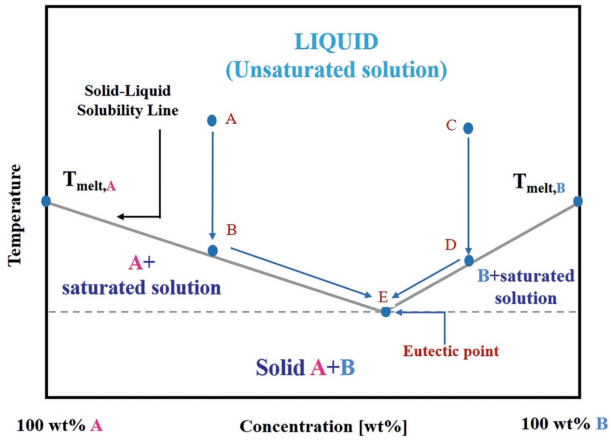

Fig. 1. A binary solid-liquid phase diagram with a eutectic point [7]. The solid-liquid two-phase equilibrium line of compound A and compound B has a triple point (minimum eutectic point) after forming a hydrogen-bonded mixture (DESs). Reproduced with permission [7]. Copyright 2021, American Chemical Society.

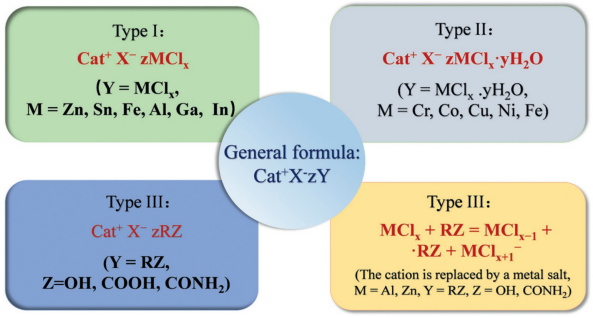

Fig. 2. General formula and four basic categories of DESs.

cally, the interaction force between HBA and HBD includes hydrogen bonding, electrostatic force, and Van der Waals force, among which the key role that constitutes DES is intermolecular hydrogen bonding interaction. The structural analysis of four ChCl-based DESs by Perkins *et al.* [25] showed that hydrogen bonding interactions mainly occur between HBD and anion (HBA). The extensive hydrogen bond grid structure between the two makes DES liquid at room temperature and has a lower lattice energy than before, which reduces the stability of the ionic crystal and leads to a lower melting point of the mixture. Therefore, DESs are considered as a new and special type of ILs.

The preparation process of DESs is simple, rapid and mild, with no by-products and purification requirements. The choice of synthetic method is generally determined by experimental conditions and available instrumentation. The most common preparation method is to mix the HBA and HBD with heating and stirring until a homogeneous transparent liquid is formed. Other methods for preparing DESs include vacuum evaporation, freeze drying and microwave assisted method with high efficiency [26,27]. Dai *et al.* [28] added an appropriate amount of distilled water to the mixture of the components required for the synthesis of DESs. The solution was placed in a rotary evaporator to remove the solvent, and a homogeneous and stable clear liquid was obtained after treatment. Gutiérrez's group [29] prepared DESs with urea and choline chloride (mole ratio at 2:1) by mixing and freezing at 77 K and 253 K, respectively, finally freeze-dried to obtain a transparent and viscous liquid.

Recently, the dynamic transformation of solution systems between single phase and dual phase has aroused great attention. Completing the extraction and separation process by inducing reversible switching of the single-phase and dual-phase system has become the focus of studies. The current research topic is how to combine the advantages of high activity and high selectivity of homogeneous reaction with easy separation and purification of heterogeneous reaction into the sample pretreatment process. It has been found that applying dynamic two-phase switch in ILs driven by temperature or CO_2/N_2 can induce phase transitions, and achieve greater efficiency in separation and purification [30]. ILs were gradually replaced by DESs in subsequent studies [31,32], not only because DESs had comparable properties to ILs (low flammability, volatility and better thermal stability), but also had some unique advantages, including low toxicity and cost, easy preparation, excellent green sustainability and biodegradability, as well as the "designability" [33] and on-line switch ability of DES. The switchable feature of DES is the focus of this review. DES has been widely used in catalysis [6,34], separation and purification [35]. In particular, the system composed of DES and aqueous phase has a great prospect in the extraction and separation of analytes [36]. The reversible control of phase transitions in homogeneous systems and liquid-liquid separation systems by external driving forces is of great significance for some applications of DESs [37].

The concept of switchable solvent (SS) was first proposed by Philip. G. Jessop in 2005 [38]. Such green solvents can be converted between two forms with different physical properties by driving external factors and applied to the pretreatment of analytes. The physical properties of SS that can be switched include polarity, solubility, conductivity, *etc.* Therefore, compared with traditional organic solvent, SS has more advantages in sample pre-treatment process [39,40]. Each step in the traditional sample preparation process often requires a specific optimal active solvent, and the solvent used in the previous step must be completely removed before proceeding to the next step, which will increase the cost of the entire process and produce waste solvents and other pollutants. SS can be used in several continuous pretreatment steps by changing its solvent properties online, which reduces the use of other solvents and achieve greater efficiency in separation and purification, reflecting the idea of green and sustainable.

Research on the combination of solvent switch ability and ILs/DESs has been gradually developed in recent years. The reversible switching of ILs by CO_2 as a driving factor is well established [41–43]. Design and application in sample preparation of switchable ILs provides theoretical support for the research of switchable deep eutectic solvents (SDESs) [44–46]. SDES refers to a type of DES whose physical properties can be switched abruptly in response to external driving forces (such as changing the temperature of the system [47], the pH of the system [48,49] and alternating CO_2/N_2 bubbling [50–52]). In the last decade, the number of published research on switchable and reversible DESs is on a sharp upward trend and is forecast to grow continuously (Fig. 3). The SDES-related research and development has brought the development of DES into a new stage [53,54]. This novel solvent has excellent performance in the extraction and separation of target analytes, and further solves the problem that solvents are difficult to be effectively recovered and recycled in sample pretreatment process [55]. Although there is almost no research to explain the specific concept of SDESs, and no systematic and clear summary of its properties and applications, researchers have found the advantages of polarity-switchable DESs in experiments and are building on this keep exploring.

Lu *et al.* [56] synthesized dozens of SDESs and finally selected SDES synthesized by tetrabutylammonium bromide and octanoic acid as the optimal solvent then combined with the DLLME and solidified floating organic droplet (SFO) method to extract UV filters of the water sample. The pH of the solution was adjusted by Na_2CO_3 to switch the hydrophobicity of SDES to hydrophilicity. H_2SO_4 was added to restore the hydrophobic SDES *in*

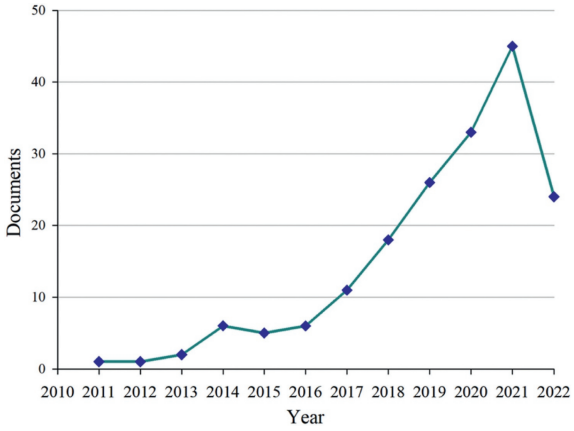

Fig. 3. Trends in the number of research on switchable and reversible DESs published in the last decade (Scoups, 2010.4-2022.4).

situ after SDES is miscible in water and the hydrophobic UV filters was extracted to SDES phase. Stupar *et al.* [57] synthesized a series of fatty acid-based hydrophobic NADESs combined with ultrasound-assisted method to extract β-carotene from pumpkin. A hydrophilic miscible system was formed *in situ* after adding ammonium hydroxide to the mixed phase of DES and target analyte, then the miscible system was subjected to a series of separations to obtain β-carotene.

Based on the previous studies, this review attempts to summarize the research progress and practical application such as the composition and categories of SDESs, the factors that driving SDESs switching, the characterization of structural changes before and after SDESs synthesis and switching, and the switching mechanism of SDESs. Finally, we try to propose possibilities for SDES development. This review is expected to provide a certain reference and guidance for subsequent research in related fields.

2. Composition and categories of SDESs

The investigation and screening of hydrogen bond acceptor (HBA) and hydrogen bond donor (HBD) to design SDESs has become the main theme of DESs development [58], which is one of the highlights of SDESs research. Researchers need to have a basic understanding of the composition and properties of existing SDESs before they set out to develop a new SDES. Based on some published studies, we briefly summarize and enumerate the precursors and the driving factors for switching of some main SDESs in Table 1, and which targets are used for preprocessing. Studies have shown that the composition of DESs fundamentally affects its role in extraction, catalysis and other processes [10]. Researchers have spent effort studying the types and molar ratios of HBDs and HBAs to design SDESs with specific uses [2,9]. In some research involved in this review, HBAs that can successfully synthesize switchable DESs include secondary amines, tertiary amines, quaternary ammonium (salts), amidines, guanidine and other nitrogen-containing bases and fatty acids, phenols, and other compounds. HBDs include fatty acids, alcohols, phenolic compounds, *etc.* A brief overview of our classification of these SDESs precursors can be seen in Fig. 4. Unfortunately, the sources of precursors for the synthesis of SDESs have certain limitations, and some raw materials (such as phenolic substances) may have certain toxicity. Therefore, it is needed to explore possible combinations of SDESs or greener and simpler

Table 1
Summary of representative features of some major SDESs.

Num.	DES components (HBA/HBD)	Research target	Driving factor	Ref.
1	$[N_{4,4,4,4}]$Cl/Octanoic acid	Detection of six UV-filters in surface and bathing waters	pH	[56]
2	Octanoic acid/Decanoic acid	Recovery of β-carotene from pumpkin	pH	[57]
3	Ethanolamine/4-methoxyphenol	Extraction and preconcentration of chlorobenzenes from aqueous solutions	CO_2	[67]
4	Ethanolamine/4-methoxyphenol	-	CO_2	[68]
5	TMG/DL-Menthol	Extraction lipids from micro-algae	CO_2	[50]
6	Octanoic acid/Lauric acid	Extraction of triacyl glycerides from sunflower oil	Amine CO_2	[61]
7	Choline chloride/Octanoic acid	Determination of anthraquinones in fried Cassia semen tea infusions	pH	[69]
8	*N*,*N*-Dimethyl cyclohexanamine/2-methoxyphenol	Sustainable separation of petroleum hydrocarbons pollutant	CO_2	[51]
9	Diethanolamine/4-chlorophenol	Selective separation of aromatic amino acids in water	Temperature	[60]
10	DL-Menthol/4-aminophenol	Extraction of pyrethroid pesticides from milk	pH	[70]
11	Thymol/Octanoic acid	Determination of strobilurin fungicides in water, juice, wine, and vinegar samples	pH	[71]
12	Imidazole/Ethylene glycol	-	CO_2	[52]
13	$[N_{4,4,4,4}]$Cl/Hydroquinone	Microextraction of three phenolic antioxidants from oil samples	pH	[48]
14	Thymol/Hexanoic acid	Extraction of antibiotics from environmental water	pH	[72]
15	Imidazole/Hexanoic acid	Oil lipid dissolution and recovery	Ratio of imidazole hexanoic acid	[55]
16	Choline chloride/Sodium hexanoate	Sustainable valorization of papaya peels for thrombolytic cysteine protease isolation	CO_2	[73]
17	Ethanolamine/*p*-Cresol	Extraction of polysaccharides from Ganoderma lucidum	Temperature	[66]
19	Diethanolamine/Hexanoic acid	Preconcentration of liposoluble constituents in Salvia Miltiorrhiza	pH	[74]
19	Lidocaine/Oleic acid	Extraction of dyes from water	Temperature	[64]
20	Choline chloride/$[N_{4,4,4,4}]$Cl	Extractive fermentation of ultrapure fibrin digesting enzyme from Bacillus subtilis	pH	[54]
21	Choline chloride/Salicylic acid	Catalytic degradation of lignin	Temperature	[47]
22	Hendecanoic acid/Nonanoic acid	Extraction of trace phenolic compounds in large volume water samples	pH	[75]
23	DL-Menthol/Lauric acid	Determination of phthalate esters in the packed milk samples	pH	[76]
24	DL-Menthol lauric acid, decanoic acid	Determination of testosterone and methyltestosterone in milk	pH	[65]
25	Nonanoic acid, decanoic acid, hendecanoic acid	Determination of β-carotene and lycopene in fruit juices	pH	[49]
26	4-Methoxyphenyl, 3-amino-1-propanol	Determination of the chiral fungicide mefentrifluconazole in water, fruit juice, and fermented liquor	pH	[77]

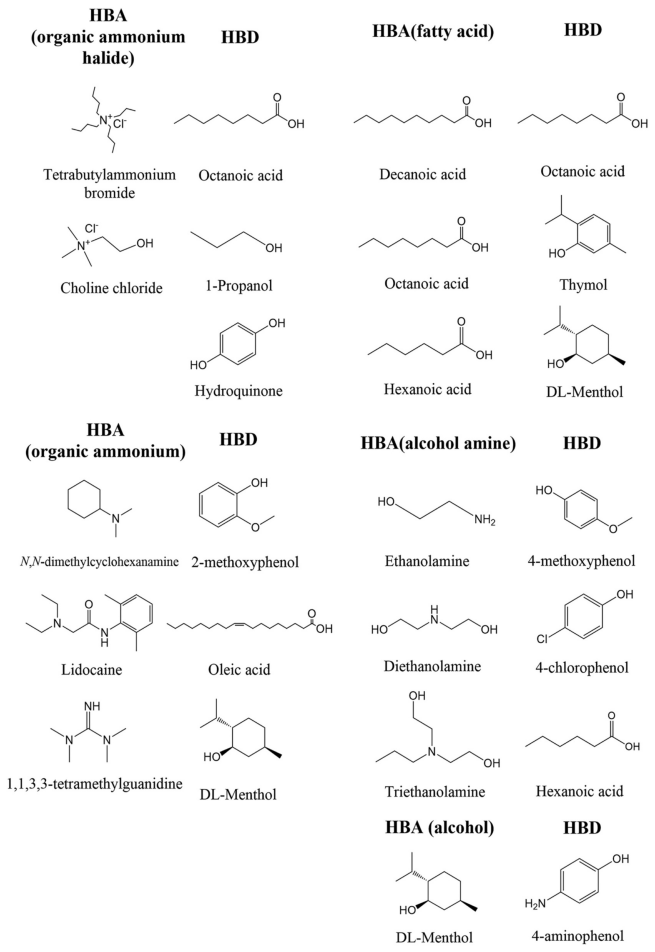

Fig. 4. Categories of HBAs and HBDs (and their classifications) capable of synthesizing SDESs.

SDESs precursors for HBA and HBD [59] while exploring more applications of SDESs.

Another research highlight of SDES is that its possibility to reversibly switch in response by external driving forces, so that miscible/immiscible transitions can be generated in the system that combined with DESs and sample solution and then utilized to enrich or separate. It simplifies the sample pretreatment process, achieves the effect of applying the only solvent to different chemical processes, saves energy and meets the requirements of green environmental protection. These responsive switchable properties can be polarity, solubility, conductivity, density, *etc.* Most of the published studies are based on polarity-switchable DESs, with only a few studies describing the phenomenon of solubility-based switching of DESs with aqueous solutions under temperature regulation [60]. Natural switchable deep eutectic solvent (NASDES) was first introduced and summarized as two basic modes by Sed's group [61]. The forward mode: The insoluble is filtered out after the hydrophobic target is extracted with hydrophobic NADES-Y, and an amine solution is added to the DES phase to switch it to hydrophilic form and separate from the hydrophobic extract. The hydrophilic DES is then mixed with the aforementioned insoluble (hydrophilic) for extraction. CO_2 was introduced after another filtration to restore the hydrophobicity of DESs and separate it from the extract. The reverse mode: Hydrophobic NADES-Y is converted to hydrophilic by mixing with amine solution. The insoluble was filtered after the hydrophilic substances were extracted, and CO_2 was introduced to restore the DESs to the hydrophobic NADES-Y, the hydrophilic extracts were obtained after layering. NADES-Y was mixed with hydrophobic insoluble for extraction, and the separation was completed after switching. This switchable system can achieve beneficial effect of using the same kind of solvent to extract different substances separately. This lays a theoretical foundation for the subsequent research and progress of SDESs.

According to the difference of driving factors that induce SDES to switch and the switching mechanism of SDES, we can divide SDES into CO_2/N_2-driven SDES [62], pH-driven SDES [63], and temperature-driven SDES [64]. Different driving factors gain different mechanisms of behavior of SDES. The recent research on this part is clear and progressive. We divided SDES into extraction-type, separation-type, and extraction/separation-type SDES according to the different switching purposes in the pretreatment process. For example, the extraction-type SDES completes the extraction by switching the polarity into the sample matrix, and finally obtains a mixed phase of the target analytes and SDESs [65]. The separation-type SDES switched after the extraction of the target, with the purpose of separating the target extract and recovering the SDES [51]. The extraction/separation-type SDES switched twice during the extraction and separation of the analyte to complete the extraction and separation of the target and recover the SDESs [66]. According to the different switching characteristics of SDESs in previous studies [47,67–70], it can be divided into polarity switchable DESs [71–75] and solubility switchable DESs [60–64]. There are relatively few proofs about this kind of classification, mainly due to most of the SDESs have switched and transformed based on the principles of hydrophobicity and hydrophilicity [76,77], and few studies have designed and described the phenomenon of solubility switching of DES in solution systems [66]. Novel SDESs with different switchable mechanisms and properties are yet to be explored and hope to be developed in the future for their great potential.

2.1. CO_2/N_2 as a driving factor

CO_2/N_2 has become a well-established trigger for switchable solvent. In a published study [78], CO_2 can dramatically switch the properties of certain switchable materials, include solvents, surfactants, catalysts, polymers, gels, *etc.* The CO_2-responsive SDES can be designed to use nitrogen-containing compounds (alkyl chain alcohol amines, polyamines, tertiary amines, quaternary ammonium salts) as HBAs, and HBDs usually select phenols or alcohols. There are also cases where fatty acids are selected for both HBA and HBD. The basis for selection is closely related to the switching mechanism of CO_2-responsive SDES. The most attractive advantage of CO_2/N_2-driven SDESs is that SDESs can be recycled [50]. CO_2 is greener and more sustainable compared with other external driving factors and is easy to obtain and remove. CO_2-driven SDESs can also function as solvents for CO_2/SO_2 capture and absorption, reducing the environmental emissions of exhaust gases [79–81]. Polyamine hydrochloride and thymol were selected to synthesize CO_2-responsive hydrophobic SDESs [62]. The excess free amino groups on the polyamine hydrochloride structure can serve as sites for CO_2 capture and absorption at low CO_2 partial pressures. The hydrophilicity and hydrophobicity of SDES switches when it absorbs CO_2, and its properties are reversibly restored when N_2 is introduced. It has a good absorption effect on CO_2 and can also recover SDES.

The SDESs system using CO_2 to switch was first discovered by Sed *et al.* [61]. After mixing the hydrophobic NADES that composed of fatty acids with weak amine solutions, fatty acid anions tend to form complexes with amines, resulting in the cleavage of DES hydrogen bonds and the formation of a homogeneous solution. After CO_2 was bubbled in, the interaction between H_2CO_3 and amine became stronger, so the original complex structure was broken, and the hydrophobicity of DES was restored after the fatty

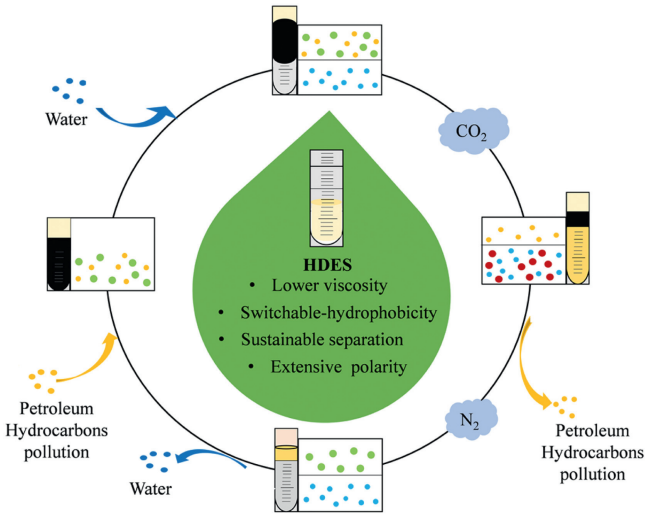

Fig. 5. Sustainable extraction and separation process of petroleum hydrocarbons pollutant in waste oil by CO_2/N_2 driven SDESs. Reproduced with permission [51]. Copyright 2021, Elsevier.

acid anion was protonated. The proficiency in these principles provides the basis and ideas for the subsequent research based on CO_2 switching DES. A subsequent study [68] synthesized a series of hydrophilic SDES based on chain alkanolamines as HBA and phenolic compounds as HBD. After the SDES and the water phase formed a homogeneous system, the SDES was driven to switch between hydrophilicity and hydrophobicity by alternately bubbling CO_2/N_2, and the result showed that it changed miscible to immiscible with the water phase. This process eliminates the need for additional solvents such as dispersants used in microextraction. Finally, the switching process was explained from the reversible formation and destruction of ammonium salts in the aqueous phase by means of FT-IR and ^{13}C NMR. Nazraza and co-workers [67] correlated experimentally validated performance of SDESs in homogeneous liquid-liquid microextraction (HLLME). The chlorobenzene in the water sample was preconcentrated using a SDES based on monoethanolamine/4-methoxyphenol, followed by CO_2 to form an emulsion, and centrifugation to separate the DES phase containing chlorobenzene. After dilution, the sample can be directly injected for analysis. This achieved greater efficiency in separation and preconcentration.

Li *et al.* [51] developed a CO_2/N_2-switched hydrophobic SDES for sustainable separation of petroleum hydrocarbons from oily wastes. The process is shown in Fig. 5. After the extraction, CO_2 was introduced into the SDES phase containing petroleum hydrocarbons to switch the SDES to hydrophilicity and separated with petroleum hydrocarbons, then N_2 was introduced to reversibly return SDES to hydrophobicity. FT-IR was used to characterize the SDES before and after CO_2 treatment, and it was confirmed that CO_2 destroyed the hydrogen bonds of the hydrophobic DES to convert it into a hydrophilic form of salt, and the resulting phase transition was caused by CO_2 making HBA (tertiary amine group) protonation and HBD (phenolic hydroxyl group) deprotonation in HCO_3^- solution.

Balaraman *et al.* [73] studied the thrombolytic cysteine protease extracted and purified from Papaya based on natural SDES. The hydrophilic SDES was synthesized using choline chloride and the corresponding sodium salt of long-chain fatty acids, and the conversion of SDES and matrix fluid into two phases was promoted under the action of CO_2. The top phase was quantified and purified using immobilized metal affinity chromatography to obtain ultrapure target compounds. After the influence factor optimization, the extraction time for the first stage was set as 15 min, the purity multiple after purification by immobilized metal affinity chromatography was 48.6, and the specific enzyme activity was 112.5. It is noticeable that this kind of study has important implications for the extraction of bioactive substances from natural products by SDES.

2.2. pH (acid-base) as a driving factor

The separation of a homogeneous solution system generally requires a certain temperature or high energy input from the outside to trigger its phase transition. The reversible phase transition mode that relies on the introduction of CO_2/N_2 requires the use of specific gas bubbling equipments, which increases the cost and energy consumption, and the operation is relatively complicated and difficult to control. The precursors that make up the CO_2-responsive SDESs may be toxic substances such as phenolic compounds, which reduce the greenness of the process. Otherwise, the addition of CO_2 will lead to the polarity difference between hydrophobic and hydrophilic compounds in the homogeneous phase, which may limit the selective extraction and separation performance of complex matrices in target solutions, making this method difficult to apply widely. Therefore, switching the properties of DES by regulating the pH of the solution system to triggering the reversible phase transition have gradually achieved the attention of researchers, and the mechanism of action of this pH-regulated SDES was investigated [82]. By adding appropriate proton donors and deprotonation reagents to the solution system containing the analyte to adjust the pH value of the system to complete the switching of SDES, the extraction and separation of the target analyte can be continuously completed in the solution system without additional equipments [76]. The HBAs used in the design of pH-responsive SDES were mainly quaternary ammonium salts, medium-chain fatty acids, menthol and thymol. Medium and long-chain fatty acids are used in most cases of HBDs, but alcohol and phenolic substances are also good choices. The specific situation should be selected according to the switching purpose of the SDES.

Yang reported a pH-regulated hydrophobic SDES to extract trace phenolic compounds from water samples [75]. After $NH_3{\cdot}H_2O$ was added to the SDES/water system as an emulsifier, the two phases were gradually converted into a homogeneous phase. HCl is then added to break the demulsification, and SDES was generated *in situ* to extract and separate phenolic compounds. The experiments evaluated the extraction efficiency of binary SDES and ternary SDES composed of fatty acids for phenolic substances. Under the optimal extraction conditions, the proposed method was applied to the analysis of four phenolic compounds in real water samples, with recoveries ranging from 87.4% to 106.6%.

Jia *et al.* [71] used pH-regulated SDES to pretreat and determine methoxy acrylate fungicides in water, fruit juice, wine, and vinegar samples. A strong hydrophobic DES was synthesized from thymol and caprylic acid, and the polarity of SDES which was switched by NH_4OH and citric acid in effervescent tablet ($NaHCO_3$+citric acid) to achieve one-step extraction and separation. The detection limits and the recoveries of this method applied in real samples analysis was ranged from 0.15 μg/L to 0.38 μg/L, and 77.4% to 106.9%, respectively. Li and co-workers [49] used the same principal method to extract β-carotene and lycopene from fruit juice. The standard curves ranged from 0.1 μg/mL to 100 μg/mL (lycopene) and 0.025 μg/mL to 5.00 μg/mL (β-carotene) has a good linearity in the range. The limits of detection (LODs) for lycopene and β-carotene were 0.05 μg/mL and 0.0021 μg/mL, respectively.

The pH-driven SDES has a good prospect in the extraction and separation of active components of natural products. Wang *et al.* [74] pre-concentrated and extracted four fat-soluble components in Salvia miltiorrhiza based on SDES combined with HCl. Hydrophilic

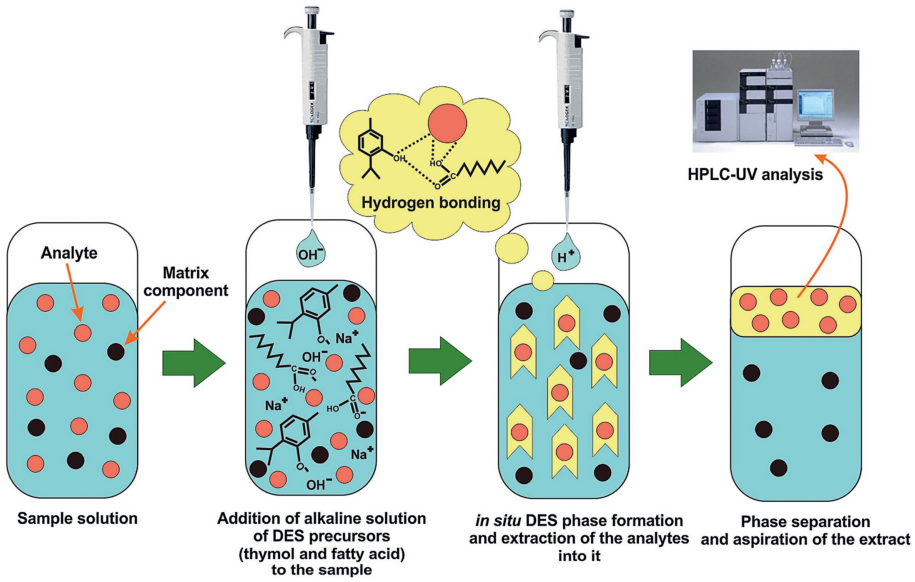

Fig. 6. Schematic illustration of pH-responsive SDES based on thymol and fatty acids for extraction of sulfonamides from milk. Copied with permission [63]. Copyright 2021, Elsevier.

SDES was synthesized by alkanolamine and fatty acid. After adding inorganic strong acid HCl, DES was switched to hydrophobic dispersion to form an emulsion, then the upper phase was formed and separated after centrifugation. Under optimal conditions, the enrichment factors of diterpene quinones ranged from 59 to 274, are showed good linearity ($R^2 \geq 0.9963$) and precision (relative standard deviation, 0.5%-8.6%) with relatively high spiked recoveries (94.6%-104.6%), which the detection limits are from 0.5 ng/mL to 0.7 ng/mL.

There were some studies attracted attention that involved natural product thymol as HBA to synthesize SDESs [63]. In this work, SDES with good pH responsiveness was synthesized using thymol as HBA and caprylic acid as HBD. For the first time, it was proved that the SDES combination of natural product terpenoids and medium-chain fatty acids can be miscible with the solution in an alkaline aqueous environment, and DES droplets are formed *in situ* and the sulfonamides in the milk are dispersed and extracted after adding acidic factors. The detailed process is shown in Fig. 6. The target exhibits good mass transfer from matrix to extractant and the mass transfer extraction of the target can be completed in 30 s with the enrichment factor ranged from 22 to 103. The detection limits of sulfamethazine, sulfaquinoxaline, sulfame-thoxazole and sulfadiazine were 1 μg/L, 1 μg/L, 3 μg/L and 5 μg/L, respectively in this study.

Constructing pH-driven SDES systems with high-efficiency extraction and separation capabilities may be an effective way to address the elevated temperature, high energy, and specific equipment issues required for current switchable phase transition processes. Adjusting the pH of the system by adding additional non-toxic reagents to the system should be regarded as one of the key research directions of SDES in the phase separation and extraction of solution systems.

2.3. Temperature (heat) as a driving factor

Although adding acid-base compounds sequentially to change the pH of the system or alternately bubbling CO_2/N_2 shows a good property switching effect for SDESs, but both switching pathways require the introduction of additional substances (gas, inorganic, or organic reagents) to accomplish phase switching. This may negatively affect the analysis of some specific targets. Furthermore,

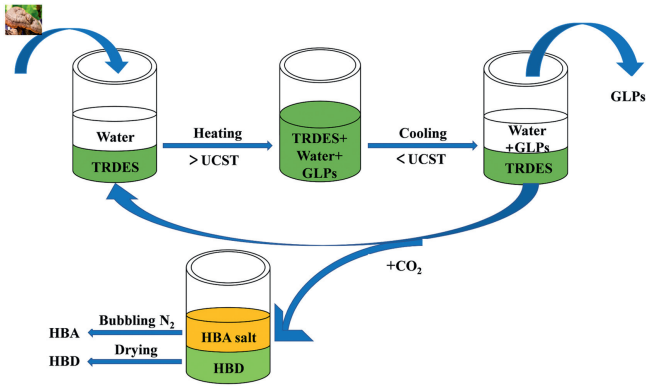

Fig. 7. Extraction and separation process of polysaccharides from Ganoderma lucidum by SDES with UCST-type phase behavior. Reproduced with permission [66]. Copyright 2020, Elsevier.

researchers are considering realizing the reversible switching of SDESs in the solution system of target analytes from the direction that no additional substances are introduced at all, and the solvent can be separated after the reaction. In recent years, studies have shown that in the two-phase system formed by the hydrophobic DESs and the water phase, the miscibility of the hydrophobic DESs and water can be driven by changing the system temperature called temperature-responsive deep eutectic solvents (TRDESs) [60,66]. On the basis of previous research, the subsequent design of temperature-responsive SDESs (TRDESs) should mainly select alkanolamines as HBA and phenols as HBD, and exhibit two types of behaviors [83,84], such as the upper critical solution temperature (UCST)-type phase behavior and the lower critical solution temperature (LCST)-type phase behavior. For the hydrophobic TRDESs with UCST (Fig. 7), the DES and the aqueous phase delaminated at low temperature and miscible at elevated temperature when the temperature was changed. The phase transition behavior of LCST-type TRDESs is to form a homogeneous phase with water at low temperature, and to achieve separation from the water phase by heating up. Furthermore, because of the entropy, the temperature increase usually tends to help the two phases to mix, so the performance of LCST is relatively rare. When several types of inter-

actions coexist and compete in the mixture, the presence of LCST can eventually be observed in the system. TRDES is used in the extraction and separation of water compounds and the catalysis of biomass conversion [47].

It should be noted that, whether it is UCST-type TRDES or LCST-type TRDES, although the existence state of DES and the water phase has changed (transition between single-phase and double-phase), the hydrogen bonds inside DES are not completely destroyed. The hydrophilicity and hydrophobicity were also unchanged relative to the target extract, and the hydrogen bonding interactions within the DES and the hydrogen bonding interactions between the DES and water were changed. Therefore, the formation of homogeneous phase of DES with water does not hinder its extraction of hydrophobic substances. Some attempts were made to explain this part of the mechanism in the following part. By studying the relationship between the thermodynamic properties and phase transitions of HBA/HBD and the water phase, we can select and design TRDESs that can exhibit UCST or LCST-type phase behavior and use them for other special extraction and separation processes.

Longeras *et al.* [64] reported the first application of lidocaine (LD) and oleic acid (OA) to synthesize DES with exhibition of LCST phase behavior. The TRDES stratified with water to form two phases at elevated temperature (above LCST) and mixed with water to form a stable homogeneous phase at ambient temperature. It was determined that the ionic forms of both the amine and oleic acid used in the study were more soluble in water than their neutral forms. According to studies [85,86], oleic acid is chosen as HBD because the phase behavior of oleic acid and water system can change with temperature. Furthermore, lidocaine (LD) is an amphiphilic amine with a highly temperature-sensitive pK_a value (p$K_a = 8$). The change of pK_a caused by temperature change will affect the ionic strength in the system and then change the solubility of DES in water. This provides that ionic state of the TRDES/water system can be significantly changed and the solubility of DES in water can be changed by temperature. Moreover, the slight change in the temperature induces phase separation, indicating that the DES is highly sensitive to temperature changes.

Depending on the application and switching purpose of SDES, different precursors can be selected for the design of SDES. Therefore, an accurate understanding of the relationship between the composition and switching properties of the SDES can help us customize the suitable SDES. Research on the synthesis of temperature-responsive SDESs by selecting HBAs and HBDs with specific thermodynamic properties has great potential. Exploring the possible applications and properties of TRDES in other systems is a topic worthy of effort. There are cross-overlapping substances (quaternary ammonium salts and phenols) in the precursors of the above three types of SDESs. Therefore, it was observed that the UCST-type TRDES based on alkanolamines and *p*-substituted phenols can be switched by temperature to extract and CO_2/N_2 bubbling to separate and recycle SDES precursors. [66]. Whether there are other cases in which the same SDES can be switched by one or more driving factors remains to be further investigated. TRDES can not only complete the extraction by switching the phase transition, but also achieve a better solvent recovery without introducing additional chemicals into the system at all. It has certain advantages in the choice of solvent.

3. Characterization of SDESs during synthesis and switching

Since the discovery that SDESs can be designed by distinct categories of HBA and HBD, the characterization of its mircro-structure has been the focus of related research [87,88]. To scientifically prove the formation of internal hydrogen bonds, eutectic point of SDES and the transformation of properties of SDES during its application, it is necessary to characterize and measure the molecular structures and properties of HBA, HBD and SDES. Among them, differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FT-IR), hydrogen/carbon nuclear magnetic resonance spectroscopy (^{1}H NMR/^{13}C NMR), turbidity test, *etc.* are widely used in the synthesis and characterization of DESs [72,89]. The purpose of characterizing SDES is to study its switching mechanism. It is needed to focus on the relative dominance of the induction effect and the conjugation effect during the formation of hydrogen bonds, mainly discussing the difference in electronegativity between the two atoms forming hydrogen bonds and the changes in the microstructure before and after the formation of hydrogen bonds, in order to understand and explain the switching mechanism of SDES.

3.1. Characterization of SDESs before/after synthesis

FT-IR is selected to measure the infrared characteristic absorption peaks of HBA, HBD and their hydrogen bond complex (SDES), respectively, and then compare the changes of the infrared characteristic absorption peaks of the three at the hydrogen bond formation sites such as N–H, C–N, O–H, to determine whether a hydrogen bond grid structure is formed between HBA and HBD [90]. It should be noted that due to the differences in structure and physicochemical properties between HBA and HBD, the structural effects of hydrogen bonding interactions between them are also different. Therefore, the shift phenomenon of the infrared vibration absorption peaks of some chemical structures produced by this process is relative. Even though, it can roughly infer the changes in the infrared spectra after the formation of hydrogen bonds between different HBA and HBD precursors by analyzing the structure and properties of the compounds, such as the electronegativity of functional groups, electron cloud density, and bond force constants, to judge whether the target SDES is synthesized.

Shi *et al.* [69] performed FT-IR characterization after synthesizing SDES with choline chloride (ChCl) and caprylic acid (Fig. 8A). O–H and C–N vibrational peaks in pure ChCl were found to be located at 3322 cm^{-1} and 1085 cm^{-1}, respectively, and O–H (3291 cm^{-1}) and =CO (1704 cm^{-1}) were observed in the FT-IR spectrum of pure octanoic acid vibration absorption peak. In the spectrum of SDES, not only the characteristic absorption peaks of octanoic acid and ChCl were found, but also the O-H vibration peak originally located at 3291 cm^{-1} of pure octanoic acid was shifted to 3230 cm^{-1} in SDES. It is speculated that the O–H of octanoic acid participates in the formation of hydrogen bonds, which leads to the migration of some electrons from oxygen atoms to the direction of hydrogen bonds, resulting in the reduction of the force constant of the O–H bond of the carboxyl group and the red-shift phenomenon. The results proved that hydrogen bonding force does exist between HBA and HBD. Xiong *et al.* [60] compared the FT-IR spectra of 4-chlorophenol, diethanolamine (DEA) and SDES synthesized from 4-chlorophenol/DEA and found that the O–H vibrational peaks on the benzene ring of 4-chlorophenol were at blue-shifted from 3273 cm^{-1} to 3298 cm^{-1} after SDES synthesis. This is because the electronegativity of the alkanol group in DEA is weaker than the electronegativity of the chlorobenzene group in 4-chlorophenol for the H atom in the N–H–O hydrogen bond, which causes electrons to move towards the phenolic hydroxyl group, a larger force constant for the O–H bond, and a blue shift of the vibrational absorption peaks, The N–H vibrational peak in DEA is red-shifted from 3301 cm^{-1} in pure DEA to 3298 cm^{-1} in 4-chlorophenol/DEA mixture. The C–H vibrational peaks in $-OCH_2$ and $-NCH_2$ are blue-shifted from 2916 cm^{-1} and 2835 cm^{-1} in pure DEA to 2933 cm^{-1} and 2850 cm^{-1} in mixture, respectively. These results all indicate that the hydrogen bond is formed between DEA and 4-chlorophenol, and the inductive effect dominates

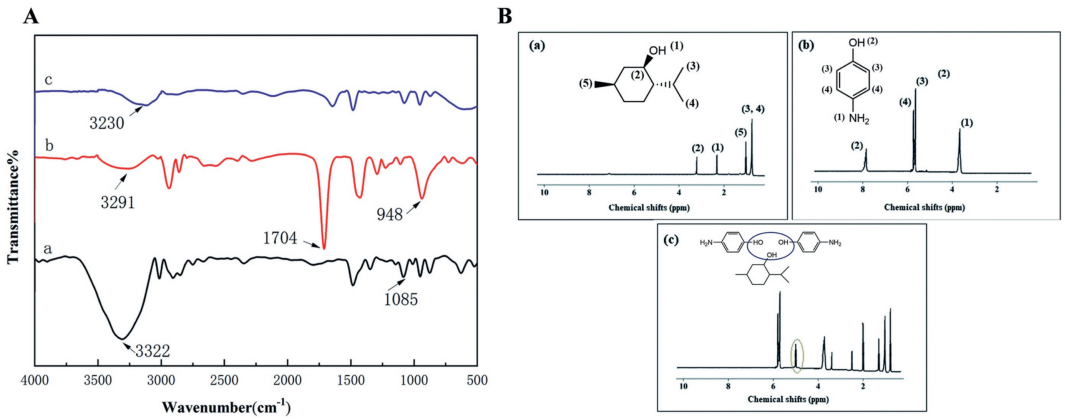

Fig. 8. (A) FT-IR spectra of SDES and its precursors: (a) choline chloride, (b) octanoic acid, (c) HSDES. Reproduced with permission [69]. Copyright 2021, the Royal Society of Chemistry. (B) ^{1}H NMR spectra of (a) menthol, (b) *p*-aminophenol, and (c) *p*-aminophenol DES. Reproduced with permission [70]. Copyright 2021, the Royal Society of Chemistry.

the change of the force constant and the shift of the absorption peak in this process.

^{1}H NMR is chosen to analyze the structure of HBA, HBD and SDES by chemical shift (δ) and integrated value of resonance absorption peak. By comparing the chemical shifts of hydrogen atoms related to the formation of hydrogen bonds among the three, it can be inferred whether hydrogen bonds are formed between HBA and HBD. Wan *et al.* [68] investigated the ^{1}H NMR of monoethanolamine (MEA) and MEA/*p*-methoxyphenol SDES by external standard method. It was found that the H signals of the two chemical environments on the alkyl of MEA (NH_2-CH_2-CH_2-OH) shifted from 3.58 ppm and 2.76 ppm to 3.25 ppm and 2.39 ppm in DES, respectively, which could be explained by the formation of hydrogen bonds. Niroumandpassand *et al.* [70] characterized the ^{1}H NMR spectra of menthol, *p*-aminophenol, and menthol/*p*-aminophenol SDES and found no peaks related to -OH groups in SDES ($\delta_{OH} = 7.98$ ppm in *p*-aminophenol), but a new singlet was found at 5.1 ppm (Fig. 8B). It is speculated that the offset may be related to the formation of intermolecular hydrogen bonds between menthol and the O-H of *p*-aminophenol. Mogaddam *et al.* [48] compared the ^{1}H NMR spectra of tetra-butylammonium chloride (TBAC), *p*-diphenol and TBAC/*p*-diphenol SDES and found that DES showed a new peak at chemical shift 7.48 ppm. It is speculated that this peak represents H in the intermolecular hydrogen bond of DES. The chemical shift of O–H, which does not participate in hydrogen bonding, is shifted from 8.19 ppm to 9.23 ppm. The rest of the structures of HBA and HBD can be observed in the SDES hydrogen spectrum. It is well proved that the hydrogen bond is formed between TBAC and *p*-diphenol.

Differential scanning calorimetry (DSC) was used to detect the thermal absorption peaks of HBA, HBD and SDES, respectively. Internationally, the intersection of the extension line of the baseline in the DSC thermogram and the tangent at the maximum slope before the peak is usually used as the reference melting temperature when the substance undergoes solid-liquid phase transition [91]. Comparing the reference melting temperature of the three statuses can prove that the synthesized SDES has a deep eutectic point. Differential scanning calorimetry analysis of the synthesized SDES was reported [56]. The study showed that the thermal absorption peaks of tetrabutylammonium bromide (HBA) and octanoic acid (HBD) were detected at 103.46 °C and 15.57 °C. The melting point (0 °C) of DES synthesized from both is lower than that of tetrabutylammonium bromide (m.p. 117 °C) and octanoic acid (m.p. 16 °C) (Fig. 9). Therefore, it can be speculated that the formation of hydrogen bonds reduces the lattice energy of the mixture, resulting in a eutectic point between HBA and HBD.

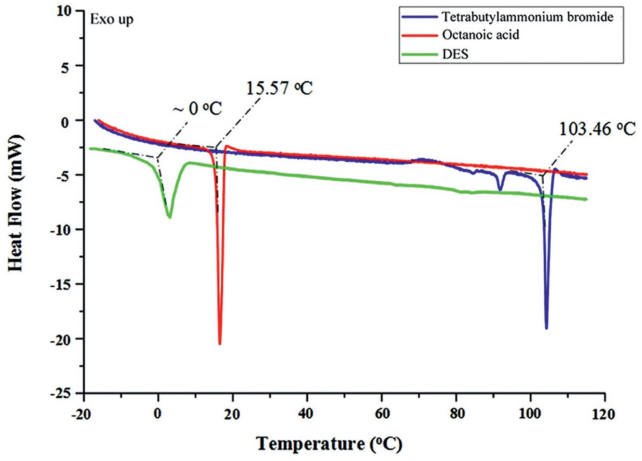

Fig. 9. DSC thermogram of optimized DES (HBA:HBD = 1:2.6, 61 °C, 108 min and 819 rpm) and its precursors. Copied with permission [56]. Copyright 2021, Elsevier.

3.2. Characterization before and after SDESs switching

SDESs are a class of structurally simple mixtures that bind primarily through hydrogen bonding forces. The changes in the molecular structure of SDES before and after switching can be observed by ordinary characterization methods, which can help to understand the mechanism of SDES switching and design SDES with specific functions and functions. Through characterization methods such as FT-IR, ^{1}H NMR and ^{13}C NMR, and observing the law of absorption peak changes in the spectrum, we can speculate what microstructure changes occurred in SDES during the feature switching [50,51].

Cai *et al.* [50] synthesized SDES with tetramethylguanidine/menthol (molar ratio at 3:1), and then characterized the SDES before and after CO_2 and N_2 bubbling by FT-IR, ^{1}H NMR, and ^{13}C NMR (Fig. 10). FT-IR results showed that a new peak appeared at 1634 cm^{-1} after CO_2 was bubbled in, and the peak disappeared after N_2 was introduced. It is speculated that the menthol hydroxyl group may be deprotonated to form a carbonyl group. The results of ^{1}H NMR showed that the H in different chemical environments in SDES did not change significantly before and after CO_2 injection. The results of ^{13}C NMR showed that a new peak appeared at 158 ppm after bubbling CO_2, which also disappeared after bubbling N_2. From these results, we can speculate that the SDES is responsive to CO_2/N_2.

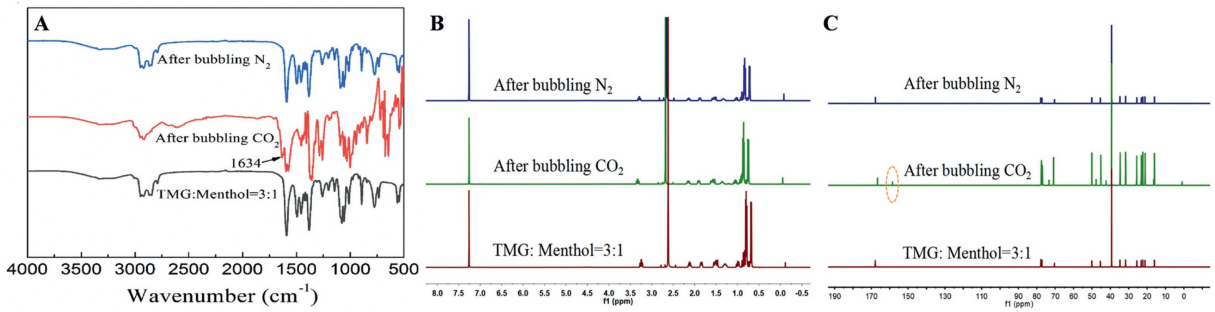

Fig. 10. The (A) FT-IR, (B) ^{1}H NMR, and (C) ^{13}C NMR for the DES (tetramethylguanidine:menthol = 3:1) before and after bubbling CO_2. Reproduced with permission [50]. Copyright 2021, Elsevier.

Some researchers have reported the use of SDESs to capture and absorb CO_2 in the environment and complete the recovery and reuse of SDESs. CO_2-responsive hydrophobic SDES was synthesized using polyamine hydrochloride and thymol. From the FT-IR spectrum, the structural changes of the SDES combination of triethyltetramine chloride ($[TETA]^+Cl^-$)/thymol before and after absorbing CO_2 were observed, and it was found that the SDES appeared at 1641 cm^{-1} after absorbing CO_2. And strong peaks were found at 1330 cm^{-1} and 1584 cm^{-1}, which presumably formed the carbamate anion structure of -NHCOO$^-$. Thus, it was proved that the SDES could absorb CO_2 and convert it into a hydrophilic salt [60].

Liu and colleagues [52] synthesized a series of hydrophobic SDESs based on imidazole as HBA and ethylene glycol as HBD to study the switching mechanism of CO_2/N_2 on hydrophobic DES. The FT-IR spectrum of SDES showed that a new peak appeared at 1635 cm^{-1} after CO_2 bubbling. It is speculated that it may be due to the formation of a carbamate (-NHCOO$^-$) structure after imidazole absorbs CO_2, which leads to the appearance of asymmetric stretching. A new peak was also found at 2350 cm^{-1}, and it was speculated that the physical absorption of CO_2 might lead to the appearance of asymmetric stretching. Interestingly, these two signals were not found in the FT-IR spectrum of SDES after N_2 bubbling. From the ^{13}C NMR spectrum, new peaks ('C' of '–NHCOO$^-$') appeared at 159.2 ppm and 67.2 ppm after CO_2 bubbling. The intensity of this peak decreases after N_2 bubbling due to the destruction of the carbamate structure by C—N bonding (CO_2 and N_2). In addition, the electrical conductivity of the SDES was measured before and after CO_2/N_2 bubbling. Due to the formation of the carbamate structure, the conductivity of the DES after CO_2 bubbling was significantly improved (from 31.2 μs/cm to 2000 μs/cm). This property change was recovered after N_2 was introduced. The above results indicate that CO_2/N_2 can make the SDES undergo a reversible transformation of properties.

4. SDESs switching mechanism

4.1. The switching mechanism of CO_2/N_2 responsive SDESs

The research on the mechanism of CO_2 switching DES has never been interrupted. CO_2 mainly destroys the hydrogen bond structure inside SDES through intermolecular interaction with nitrogen-containing HBA or phenolic HBD, decomposes SDES and changes its hydrophilicity and hydrophobicity for extraction and separation. The addition of N_2 will offset the structural effect of CO_2 on DES and restore the structure and properties of the original DES.

After characterizing the SDES before and after CO_2 bubbling, Wan *et al.* [68] proposed a possible mechanism for the miscible/immiscible transition of the CO_2-switched SDES with the aqueous phase. CO_2 exists in the form of H_2CO_3 after entering the aqueous solution. Since the acidity of H_2CO_3 is stronger than that of

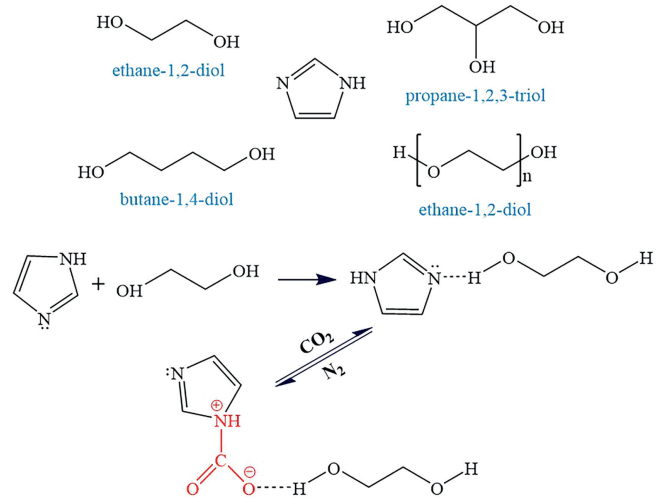

Fig. 11. SDES composed of imidazole/alcohol and its CO_2/N_2 switching mechanism.

4-methoxyphenol, H_2CO_3 can form hydrogen bonds with MEA to replace 4-methoxyphenol. Therefore, after the introduction of CO_2, part of the hydrogen bonds of the SDES were broken, and the MEA combined with CO_2 to form a carbamate (–NHCOO$^-$) structure. In addition, there are bicarbonate and carbonate in the solution system. The salting-out effect brought about by these substances promotes the accumulation of 4-methoxyphenol in the lower phase, while the carbonate of MEA accumulates in the upper phase. The -NHCOO$^-$ structure was destroyed after the introduction of N_2, and the homogeneous system was restored with water after the *in-situ* generation of SDES.

After characterization of SDES before and after switching by FT-IR and ^{13}C NMR, Liu *et al.* [52] attempted to microscopically explain the mechanism of phase switching of imidazole/alcohol SDES in response to CO_2/N_2 (Fig. 11) and further use the same system to separate olive oil from the SDES/olive oil emulsion. After CO_2 is bubbled in, due to the relatively stronger binding force of C-N bond, CO_2 will break the hydrogen bond between imidazole and alcohol and interact with nitrogen atom of imidazole to form an anion-cation complex of carbamate. The structural polarity increases and the SDES switches to the hydrophilic form and delaminates with the hydrophobic phase (olive oil). After separation, N_2 was introduced into the DES phase to combine with CO_2 to form a C–N bond and break the carbamate structure, allowing the imidazole to restore its original structure and form a hydrogen bond with the free alcoholic hydroxyl group. In this way, the purpose of recycling SDES is achieved.

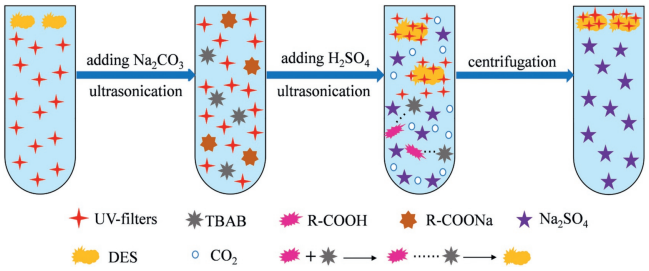

Fig. 12. The mechanism of Na_2CO_3/H_2SO_4 switching SDES. Reproduced with permission [56]. Copyright 2021, Elsevier.

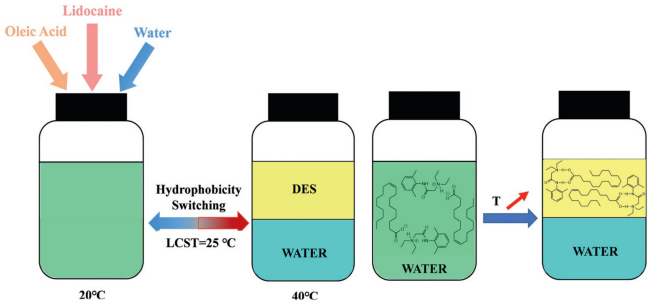

Fig. 13. Extraction and separation process and mechanism of LCST-type TRDES. Reproduced with permission [64]. Copyright 2020, American Chemical Society.

4.2. The switching mechanism of pH-responsive SDESs

The mechanism of switching SDES by adjusting the pH of solution system can be explained by the breaking and formation of ionic or covalent bonds in the solution system. After characterizing the structural changes of pH-regulated SDES before and after switching by ^{1}H NMR, Lu *et al.* [56] proposed the possible switching mechanism of hydrophobic SDES synthesized based on tetra-butylammonium bromide (TBAB) and octanoic acid in aqueous phase (Fig. 12). The basic salt Na_2CO_3 was added to the solution to raise the pH of the system. The acid-base interaction between octanoic acid and Na_2CO_3 breaks the hydrogen bond inside the hydrophobic SDES through competition, and TBAB is released. When the pH was raised to the pK_a of HBD, octanoic acid mostly existed in the form of water-soluble sodium salt (R-COONa) (R-COOH + Na_2CO_3 → R-COONa + $NaHCO_3$). The presence of octanoate, bicarbonate and TBAB increases the ionic strength of the system and promotes the miscibility of SDES with water. H_2SO_4 was then added to reduce the pH below the pK_a of octanoic acid. The increase of H^+ in the system led to the protonation of R-COONa and $NaHCO_3$, octanoic acid was recovered in the system and CO_2 was generated *in situ* (2R-COONa + H_2SO_4 → 2R-COOH + Na_2SO_4) ($2NaHCO_3 + H_2SO_4 \rightarrow Na_2SO_4 + CO_2 + H_2O$). With the assistance of ultrasound, the hydrogen bond network structure between TBAB and octanoic acid was reconstructed, and the hydrophobic SDES was generated *in situ* and dispersed as tiny droplets in the aqueous phase to form an emulsion. With the assistance of *in-situ* CO_2, the salting out of Na_2SO_4 promoted the mass transfer of the hydrophobic UV filter in the water phase to the SDES, and the SDES phase carrying the target substance could be separated from the water after demulsification.

Yang *et al.* [75] proposed a possible mechanism of action for SDES extraction of phenolic compounds from water based on fatty acids as HBA and HBD. The hydrophobic SDES is used as an extractant and mixed with water to form two phases, and $NH_3 \cdot H_2O$ is added to react with the fatty acid-based DES to cause an acid-base reaction and break the hydrogen bonds inside the DES (DES-COOH + $NH_3 \cdot H_2O$ → DES-$COONH_4$ + H_2O). SDES is converted into a hydrophilic form of fatty acid amine salts to form a homogeneous phase with water, and then HCl is added to react with fatty acid amine salts to generate fatty acids in water. Hydrophobic SDES was recovered by hydrogen bond reconstruction between fatty acid molecules and dispersed in water for extraction. After centrifugation, the upper DES phase was extracted for analysis.

4.3. The switching mechanism of temperature-responsive SDESs

The hydrophilicity and hydrophobicity of the TRDES relative to the extraction target did not change when the TRDES and the aqueous system underwent a monophasic/biphasic transition. In fact, it is the hydrogen bonding within DES and between DES/H_2O that change with temperature, which leads to the change of the solubility of DES in water. The temperature-switching behavior of TRDESs is divided into two cases, namely the upper critical solution temperature (UCST) type phase behavior and the lower critical solution temperature (LCST) type phase behavior.

For UCST-type TRDESs (Fig. 7) [60,66], there is almost no hydrogen bonding between DES and water at low temperature, and the solubility of DES in the aqueous phase is extremely low. The hydrogen bonding interaction between HBA and HBD that make up the TRDES gradually weaken with increasing temperature. And H_2O begin to gather around groups (–NH, –OH) that can form hydrogen bonding sites in DES. The FT-IR spectrum of the heated DES shows a higher infrared vibrational wavenumber than the original DES, which indicates that a hydrogen bond structure is formed between DES and H_2O, and finally miscible with water. In this process, part of the hydrogen bonds between TRDES are destroyed to expose HBD and HBA, which can achieve the goal of recycling HBA and HBD. After heating to a certain temperature (UCST), DES and water completely form a homogeneous phase and the hydrogen bond strength between DES and water is the largest. For LCST-type TRDESs (Fig. 13) [64], the hydrogen bonding interaction between DES and water is extremely weak above the LCST, thus forming two phases with water. When the temperature started to decrease and dropped below the LCST, most of the exposed hydrogen-bonding sites on DES formed hydrogen-bonding interactions with H_2O, and some of the DES was decomposed into HBA and HBD, thus ultimately miscible with water.

Compared with SDESs that introduces additional compounds as driving factors, TRDESs can achieve no or less doping in the chemical process, which improves the greening degree in the switching process and switching principle. However, the dis-advantages of temperature-responsive SDESs are also obvious in the research, such as the low extraction efficiency of some compounds and the low recovery rate of TRDESs, which need to be improved through follow-up research and design.

5. Applied techniques and methods related to SDESs

The widely used sample pretreatment methods include liquid-phase extraction, solid-phase extraction [92–94], gas-liquid microextraction, which need to use multiple organic solvents, resulting in problems such as low environmental friendliness, small enrichment multiples, complicated operation steps, and long extraction time. Liquid phase microextraction (LPME) was proposed in 1996, whose principle is to use the difference in the distribution ratio of the target between the two phases to concentrate and separate, with the advantages of less reagents usage, shorter extraction time, and higher enrichment factors [95–98]. Application of SDES can greatly simplifies the extraction step when combined with liquid-liquid microextraction technique. The hydrophobic SDES was converted into a hydrophilic state and frequently contacted with the sample, and then the conditions can be changed to convert the

SDES into a hydrophobic state. The target components are retained in a small amount of SDES phase, and the separation and enrichment can be completed without additional organic solvents, which has a good application prospect.

In one study [48], the determination of three phenolic antioxidants in oil samples was performed by first extracting the target compounds into an alkaline solution by elevated temperature liquid-liquid microextraction. Dispersion liquid-liquid microextraction was performed using SDES. After the hydrogen bonds are broken, the SDES is thoroughly mixed with the solution. DES was generated *in situ* in the solution to complete the dispersion when the pH was adjusted to make the solution acidic. The mass transfer of phenolic antioxidants to DES achieved a good separation and enrichment effect. Microextraction of sulfonamides in milk by pH-responsive SDES has been studied. The SDES precursors and the sample solution were mixed uniformly under alkaline conditions, and the pH was adjusted to acidity to form hydrophobic SDES droplets *in situ* in the solution. Finally, sulfonamides were retained in a small amount of SDES phase to complete the separation and enrichment [63]. In addition, for facilitating the dispersion of SDES into the sample solution and the mass transfer of target analytes to the SDES, the extraction process could combine with some assistant methods such as ultrasonic-assisted technique, microwave-assisted technique, effervescent-assisted technique, and solidification of floating organic droplet.

Ultrasonic-assisted extraction (UAE) technique uses the comprehensive effects of cavitation, vibration, fragmentation, and mixing generated by ultrasonic waves in the medium to destroy the plant cell wall, which has advantages in reducing the mass transfer resistance of the target extract and accelerating its diffusion to the extractant. Through the combination of UAE-SDES, a short-time and high-efficiency extraction effect can be achieved. UAE also showed potential in the extraction application of natural product components with the characteristics like green and low energy consumption [99]. Balaraman *et al.* [73] synthesized SDESs based on choline chloride and long-chain fatty acids, and isolated and purified thrombolytic cysteine protease from papaya peel using ultrasonic-assisted dispersive liquid phase microextraction technique. Alena Stupar *et al.* [57] prepared switchable natural deep eutectic solvents based on C_8 and C_{10} fatty acids for the recovery of β-carotene from squash. In order to strengthen the extraction and recovery process of β-carotene, SDESs were combined with UAE, and the extraction process in the experiment was carried out in an ultrasonic water bath.

Effervescent-assisted dispersion liquid-liquid microextraction (EA-DLLME) was proposed in 2014 [100]. The CO_2 generated by the effervescent reaction can be used as the dispersing force of the dispersive extraction to promote the full contact between the extractant and the sample solution, so that the target components can quickly enter the extractant. The consumption of dispersants or dispersing auxiliary instruments in DLLME is reduced. It is more common to apply effervescent technique to the extraction process of pH-responsive SDESs. It is proved as a fast, economical and easy-to-operate combined technique. Shi *et al.* [69] prepared a pH-responsive SDES for the determination of anthraquinones in fried cassia seeds. With no consumption of organic solvent and auxiliary equipment, CO_2 is generated *in situ* by the effervescent reaction of H_2SO_4 and Na_2CO_3 to facilitate the dispersion of the extractant. H_2SO_4 and Na_2CO_3 are not only pH regulators, but also effervescent agents and electrolytes. The salts generated by the effervescent reaction can also be used as electrolytes to promote the phase separation of SDES. Jia *et al.* [71] used pH-responsive SDESs for the extraction of strobilin fungicide from water, fruit juice, wine and vinegar samples. The extractant was dispersed in the sample solution with the help of pH adjustment and effervescent reaction and easily collected after solidification in an ice bath.

Solidified floating organic droplet (SFO) is a separation method in sample preprocessing [101], which using the difference of freezing points between the solvent and the sample matrix solution to solidify and separate the solvent from the matrix solution. In recent years, SFO-based dispersion liquid-liquid microextraction (DLLME-SFO) was proposed for separation of extractants. However, most of the extractants that can match DLLME-SFO are traditional organic solvents. Combining DESs with SFO can make up for the shortcomings of traditional solvents [102]. DES can achieve a good match with DLLME-SFO because of its low freezing point and easy curing at low temperature. DES-based DLLME-SFO was used for preconcentration and extraction of organophosphorus pesticides in edible oils [103]. The analytical target was enriched in the DES phase after centrifugation, the upper phase was solidified in an ice bath, and then dissolved at room temperature to obtain the organic phase of the target. In the follow-up research, this method was optimized by designing and synthesizing SDES with lower freezing point. Niroumandpassand *et al.* [70] extracted five pyrethroid insecticides from milk by preparing a pH-responsive DES of menthol and *p*-aminophenol. Menthol was released *in situ* after pH change and dispersed into milk samples for extraction. After layering, the upper phase was solidified in an ice bath, and then was taken out with tweezers and melted to obtain the target. The DLLME-SFO combined with SDES solves the problem of how to separate a small amount of SDES phase from the sample matrix liquid, so that SDES can produce better results in the sample preparation process.

According to the development trend of analytical extraction techniques, a type of DES-based eco-friendly mechanochemical extraction (DESs-MCE) method is in a rapid development rate [104,105]. MCE is a room temperature extraction method that provides a unique motion to disrupt the cell wall structure of natural products relying on the action of mechanical force to make the plant material reach the state of ultra-fine pulverization, which promotes the release of active ingredients and provide prerequisites for the interaction with solid phase extraction reagents, and the solubility of active substances in specific solvents can be improved by introducing solid-phase chemical reactions [106]. Theoretically, the combination of SDES and MCE may be able to achieve a convenient and efficient extraction and separation process, and the SDES can be recovered and reused by switching, which further improves the environmental protection degree of the pretreatment process. This approach may have considerable potential for future development.

6. Conclusions

With the popularization of the concept of green analytical chemistry, researchers began to design new sample preparation methods based on efficient and environmentally friendly solvents. DES is one of the most popular green solvents in recent years, and its development follows the recommended orientation of efficient and green analytical method. The emergence of SDES has expanded and optimized the application of DES in sample preparation, and has now become one of the most potential and valuable research issues in the sample pretreatment process due to its efficient extraction and separation effect, green extraction principle and multi-functional advantage. Designing highly active and selective SDESs by HBAs and HBDs with different properties and performance to optimize traditional pretreatment process involving multi-solvent are both opportunities and challenges.

Based on some published studies, this paper summarizes the research progress of SDESs, and hopes to pave a way for subsequent research in related fields. The improvements and enhancements to the disadvantages and innovation of SDES are of great significance, such as: (1) SDES precursors are investigated and selected to design SDESs with novel driving factors (light) or switch-

ing properties (conductivity) by means of computational chemistry; (2) Developing SDES switched by multiple driving factors for different purposes; (3) Construct a switchable system of great advantage combining SDESs with other compounds or design a switchable deep eutectic system to substitute SDESs; (4) Complete the *in-situ* configuration of SDESs in the system without additional preparation and so on. Some existing problems and difficulties need to be solved in follow-up research. The synthesis efficiency of SDES is not particularly high, and the synthesis of some SDES based on ammonium salts is relatively unstable with a long-time cost. It may be solved by inputting external energy (*e.g.*, microwave) to assist. The SDES obtained after extraction is difficult to recover with negative influence to instrument detection and analysis, and has certain limitations (such as not suitable for GC-MS analysis). If a gasifiable SDES can be designed, it will improve the universality of SDES. To further demonstrate the practical application value of SDES, it should propose solutions based on existing problems and challenges in future.

Considering the current research status of SDESs and the possible follow-up research directions and their innovation, we have faith to anticipate that the future of SDEDs is promising.

Declaration of competing interest

The authors declare no conflict of interests.

Acknowledgments

This study was financially supported by the National Natural Science Foundation of China (No. 22174129), the Natural Science Foundation of Zhejiang Province (No. LZY21E030001).

References

[1] A.P. Abbott, G. Capper, D.L. Davies, R.K. Rasheed, V. Tambyrajah, Chem. Commun. 1 (2003) 70–71.
[2] A.P. Abbott, G. Capper, S. Gray, ChemPhysChem 7 (2006) 803–806.
[3] H. Zhang, J.M. Vicent-Luna, S.X. Tao, et al., ACS Sustain. Chem. Eng. 10 (2022) 1232–1245.
[4] H.Y. Wang, B. Tan, J.J. Wang, Z.Y. Li, S.J. Zhang, Langmuir 30 (2014) 3971–3978.
[5] A.P. Abbott, D. Boothby, G. Capper, D.L. Davies, R.K. Rasheed, J. Am. Chem. Soc. 126 (2004) 9142–9147.
[6] L.F. Peng, Z.F. Hu, Q.C. Lu, et al., Chin. Chem. Lett. 30 (2019) 2151–2156.
[7] B.B. Hansen, S. Spittle, B. Chen, et al., Chem. Rev. 121 (2021) 1232–1285.
[8] M.A.R. Martins, S.P. Pinho, J.A.P. Coutinho, J. Solut. Chem. 48 (2019) 962–982.
[9] C. Florindo, L.C. Branco, I.M. Marrucho, ChemSusChem 12 (2019) 1549–1559.
[10] J. Cao, M. Yang, F.L. Cao, J.H. Wang, E.Z. Su, J. Clean. Prod. 152 (2017) 399–405.
[11] X.F. Han, J. Chen, H.J. Zhang, Z. Li, H.D. Qiu, Sci. Sin. Chim. 48 (2018) 1548–1560.
[12] H.M. Liu, P. Jin, F.C. Zhu, L. Nie, H.D. Qiu, Trends Anal. Chem. 134 (2021) 116132.
[13] T. Tan, Z. Li, X.J. Mao, Y.Q. Wan, H.D. Qiu, Anal. Methods 8 (2016) 3511–3516.
[14] T. Gu, M. Zhang, T. Tan, et al., Chem. Commun. 50 (2014) 11749–11752.
[15] M. Liu, D. Cao, W.T. Bi, D.D.Y. Chen, ACS Sustain. Chem. Eng. 9 (2021) 12049–12057.
[16] M.C. Ali, J. Chen, H. Zhang, et al., Talanta 203 (2019) 16–22.
[17] L.X. Zhang, H. Yu, H.B. Yu, Z. Chen, L. Yang, Chin. Chem. Lett. 25 (2014) 1132–1136.
[18] Q.S. Chen, L.X. Chai, H, X.P. Yao, et al., ACS Sustain. Chem. Eng. 9 (2021) 10083–10092.
[19] D. Cao, Q. Liu, W.Q. Jing, et al., ACS Sustain. Chem. Eng. 8 (2020) 19169–19177.
[20] T. Cai, H. Qiu, Trends Anal. Chem. 120 (2019) 115623–115632.
[21] J. Chen, M.C. Ali, R. Liu, et al., Chin. Chem. Lett. 31 (2020) 1584–1587.
[22] M.C. Ali, R. Liu, J. Chen, et al., Chin. Chem. Lett. 30 (2019) 871–874.
[23] C. Florindo, L. Romero, I. Rintoul, L.C. Branco, I.M. Marrucho, ACS Sustain. Chem. Eng. 6 (2018) 3888–3895.
[24] E.L. Smith, A.P. Abbott, K.S. Ryder, Chem. Rev. 114 (2014) 11060–11082.
[25] S.L. Perkins, P. Painter, C.M. Colina, J. Chem. Eng. Data 59 (2014) 3652–3662.
[26] Y. Chen, F.X. Xu, M.M. Pang, et al., Sustain. Chem. Pharm. 27 (2022) 100695.
[27] F.X. Xu, J.Y. Zhang, J. Jin, et al., J. Oleo Sci. 70 (2021) 1481–1494.
[28] Y.T. Dai, E. Rozema, R. Verpoorte, Y.H. Choi, J. Chromatogr. A 1434 (2016) 50–56.
[29] M.C. Gutierrez, M.L. Ferrer, C.R. Mateo, F.D. Monte, Langmuir 25 (2009) 5509–5515.
[30] D.Z. Xiong, G.K. Cui, J.J. Wang, et al., Angew. Chem. Int. Ed. 54 (2015) 7265–7269.
[31] S.L. Desset, D.J. Cole-Hamilton, Angew. Chem. Int. Ed. 48 (2009) 1472–1474.
[32] Q.X. Zhou, Y.Y. Gao, Chin. Chem. Lett. 25 (2014) 745–748.
[33] K.K. Kow, K. Sirat, Chin. Chem. Lett. 26 (2015) 1311–1314.
[34] M.R. Bhosle, L.D. Khillare, S.T. Dhumal, R.A. Mane, Chin. Chem. Lett. 27 (2016) 370–374.
[35] T. Tan, X.M. Xu, Y.Q. Wan, Chin. Chem. Lett. 30 (2019) 1182–1185.
[36] K.J. Xua, P.L. Xu, Y.Z. Wang, Talanta 213 (2020) 120839.
[37] W.Y. Tang, K.H. Row, J. Clean. Prod. 268 (2020) 122306.
[38] P.G. Jessop, D.J. Heldebrant, X.W. Li, C.A. Eckert, C.L. Liotta, Nature 436 (2005) 1102.
[39] G.L. Aragonés, R. Lucena, S. Cárdenas, M. Valcárcel, Talanta 131 (2015) 645–649.
[40] J.R. Vanderveen, J. Durelle, P.G. Jessop, Green Chem. 16 (2014) 1187–1197.
[41] W.Y. Tang, K.H. Row, Bioresour. Technol. 296 (2020) 122309–122318.
[42] T. Yu, T. Yamada, G.C. Gaviola, R.G. Weiss, Chem. Mater. 20 (2008) 5337–5344.
[43] X.Y. Pei, D.Z. Xiong, Y.C. Pei, H.Y. Wang, J.J. Wang, Green Chem. 20 (2018) 4236–4244.
[44] J.D. Jimenez, S. Jung, E.J. Biddinger, J. Electrochem. Soc. 162 (2015) 460–465.
[45] V.M. Blasucci, R. Hart, P. Pollet, C.L. Liotta, C.A. Eckert, Fulid Phase Equilib. 294 (2010) 1–6.
[46] I. Anugwom, V. Eta, P. Virtanen, et al., ChemSusChem 7 (2014) 1170–1176.
[47] S.Z. Wang, Y.B. Li, X.F. Wen, et al., Ind. Crops Prod. 177 (2022) 114430.
[48] M.R.A. Mogaddam, M.A. Farajzadeh, M. Tuzen, A. Jouyban, J. Khandaghi, Microchem. J. 168 (2021) 106433.
[49] H. Li, C.X. Zhao, H. Tian, Y.L. Ling, W.Y. Li, Food Anal. Methods 12 (2019) 2777–2784.
[50] C.Y. Cai, X.Y. Chen, F.F. Li, Z.J. Tan, Sep. Purif. Technol. 279 (2021) 119685.
[51] X.J. Li, L.T. Sun, X. Lv, et al., J. Environ. Chem. Eng. 9 (2021) 106280.
[52] F.J. Liu, Z.M. Xue, X. Lan, Z.H. Liu, T.C. Mu, Chem. Commun. 57 (2021) 627–630.
[53] L. Zhong, C. Wang, G.H. Yang, et al., Bioresour. Technol. 343 (2022) 126022.
[54] R. Muniasamy, B.S. Balamurugan, D. Rajamahendran, S. Rathnasamy, Sci. Rep. 12 (2022) 903–917.
[55] C. Lo, J. Semerel, C.V.D. Berg, R.H. Wijffels, M.H.M. Eppink, RSC Adv. 11 (2021) 8142–8149.
[56] Y. Lu, X.D. Wang, H.D. Gu, M. Gao, Microchem. J. 169 (2021) 106626.
[57] A. Stupar, V. Seregelj, B.D. Ribeiro, et al., Ultrason. Sonochem. 76 (2021) 105638.
[58] D.O. Abranches, J.A.P. Coutinho, Curr. Opin. Green Sustain. Chem. 35 (2022) 100612.
[59] H. Balaraman, R. Selvasembian, V. Rangarajan, S. Rathnasamy, ACS Sustain. Chem. Eng. 9 (2021) 11290–11313.
[60] D.Z. Xiong, Q. Zhang, W.J. Ma, et al., Sep. Purif. Technol. 265 (2021) 118479.
[61] G. Sed, A. Cicci, P.G. Jessop, M. Bravi, RSC Adv. 8 (2018) 37092–37097.
[62] Y.X. Gu, Y.C. Hou, S.H. Ren, Y. Sun, W.Z. Wu, ACS Omega 5 (2020) 6809–6816.
[63] A. Pochivalov, K. Cherkashina, A. Shishov, A. Bulatov, J. Mol. Liq. 339 (2021) 116827.
[64] O. Longeras, A. Gautier, K.B. Busserilles, J.M. Andanson, ACS Sustain. Chem. Eng. 8 (2020) 12516–12520.
[65] X. Li, T. Yuan, T. Zhao, X.M. Wu, Y.L. Yang, J. Chromatogr. Sci. 58 (2020) 880–886.
[66] C.Y. Cai, Y.N. Wang, W. Yu, et al., J. Clean. Prod. 274 (2020) 123047.
[67] M. Nazraz, Y. Yamini, A.M. Ramezani, Z. Dinmohammadpour, J. Chromatogr. A 1636 (2021) 461756.
[68] W.R. Wan, D.Z. Xiong, Q. Zhang, J.J. Wang, ACS Sustain. Chem. Eng. 7 (2019) 17882–17887.
[69] Z.H. Shi, X.Y. Li, Y.H. Tian, et al., Anal. Methods 13 (2021) 4739–4746.
[70] A. Niroumandpassand, A. Javadi, M.R.A. Mogaddam, Anal. Methods 13 (2021) 1747–1756.
[71] L.Y. Jia, X. Huang, W.F. Zhao, H.H. Wang, X. Jing, Food Chem. 317 (2020) 126424.
[72] W.W. Ma, K.H. Row, Microchem. J. 160 (2021) 105642.
[73] H.B. Balaraman, G. Viswanathan, R. Muniasamy, T. Gayatri, S.K. Rathnasamy, Microchem. J. 175 (2022) 107118.
[74] X.P. Wang, R.Q. Wang, X.Y. Pan, et al., J. Chromatogr. A 1666 (2022) 462858.
[75] D.Z. Yang, Y.D. Wang, J.B. Peng, C. Xun, Y.L. Yang, Ecotoxicol. Environ. Safe. 178 (2019) 130–136.
[76] X.L. Wang, Y.G. Lu, L.Y. Shi, Z D, Y.L.Yang Yang, Microchem. J. 159 (2020) 105332.
[77] H.J. Jiang, X. Huang, H.Y. Xue, et al., Chirality 34 (2022) 1–9.
[78] P.G. Jessop, S.M. Mercera, D.J. Heldebrant, Energy Environ. Sci. 5 (2012) 7240–7253.
[79] Z. Li, L.L. Wang, C.P. Li, et al., ACS Sustain. Chem. Eng. 7 (2019) 10403–10414.
[80] G. Cui, M. Lv, D.Z. Yang, Chem. Commun. 55 (2019) 1426–1429.
[81] K. Zhang, S.H. Ren, X. Yang, et al., Chem. Eng. J. 327 (2017) 128–134.
[82] F.O. Farias, H. Passos, J.A.P. Coutinho, M.R. Mafra, Ind. Eng. Chem. Res. 57 (2018) 16917–16924.
[83] A. Ejraei, S. Shirvani, M.A. Aroon, M.A. Khansary, S. Khalaj, Fluid Phase Equilib. 425 (2016) 465–484.
[84] Y.R. Zhao, J.Y. Ma, X. Yu, M.H. Li, J. Hu, Chin. Chem. Lett. 32 (2021) 548–552.
[85] J.J. Janke, W.F.D. Bennett, D.P. Tieleman, Langmuir 30 (2014) 10661–10667.
[86] E. Durand, J. Lecomte, P. Villeneuve, Biochimie 120 (2016) 119–123.
[87] H. Ghaedi, M. Zhao, M. Ayoub, et al., J. Chem. Thermodyn. 137 (2019) 108–118.
[88] F.S. Mjalli, G. Murshid, S. Al-Zakwani, A. Hayyan, Fluid Phase Equilib. 448 (2017) 30–40.
[89] Y.T. Liu, Y.A. Chen, Y.J. Xing, Chin. Chem. Lett. 25 (2014) 104–106.

[90] E Yang, W.J. Zhang, S.X. Pei, et al., Sci. China Ser. B: Chem. 36 (2006) 218–226.
[91] T. Lever, P. Haines, J. Rouquerol, et al., Pure Appl. Chem. 86 (2014) 545–553.
[92] H. Qi, L.Y. Jiang, Q. Jia, Chin. Chem. Lett. 32 (2021) 2629–2636.
[93] H.Q. Li, Y.Z. Wang, X.Y. He, et al., Talanta 230 (2021) 122341.
[94] F.T. Xu, Y.Z. Wang, Z.W. Liu, et al., Anal. Chim. Acta 1137 (2020) 125–135.
[95] Z.M. Liu, X.H. Zang, W.H. Liu, C. Wang, Z. Zhang, Chin. Chem. Lett. 20 (2009) 213–216.
[96] Y.C. Fan, Z.L. Hu, M.L. Chen, C.S. Tu, Y. Zhu, Chin. Chem. Lett. 19 (2008) 985–987.
[97] Q.X. Zhou, G.H. Xie, L. Pang, Chin. Chem. Lett. 19 (2008) 89–91.
[98] W.F. Zhang, X.X. Lin, H.F. Li, Z.H. Wang, J.M. Li, Chin. Chem. Lett. 25 (2014) 1225–1229.
[99] H.B. Zhu, Y.C. Fan, Y.L. Qian, et al., Chin. Chem. Lett. 25 (2014) 465–468.
[100] G.L. Aragonés, R. Lucena, S. Cárdenas, Molecules 25 (2020) 6053–6073.
[101] C.X. Wu, Q.H. Wu, C. Wang, Z. Wang, Chin. Chem. Lett. 22 (2011) 473–476.
[102] A.K. El-Deen, K. Shimizu, Molecules 26 (2021) 7406–7430.
[103] E. Zahiri, J. Khandaghi, M.A. Farajzadeh, M.R.A. Mogaddam, J. Chromatogr. A 1627 (2020) 461390.
[104] M. Wang, J.Q. Wang, Y.Yi. Zhou, et al., ACS Sustain. Chem. Eng. 5 (2017) 6297–6303.
[105] M. Wang, J.Q. Wang, Y. Zhang, et al., J. Chromatogr. A 1443 (2016) 262–266.
[106] M. Wang, W.T. Bi, X.H. Huang, D.D.Y. Chen, J. Chromatogr. A 1449 (2016) 8–16.