Analytica Chimica Acta xxx (2018) 1–10

Contents lists available at ScienceDirect

Analytica Chimica Acta

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

Review

Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments

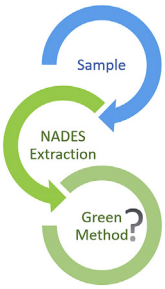
María de los Ángeles Fernández, Joana Boiteux, Magdalena Espino, FedericoJ.V. Gomez**, María Fernanda Silva*

Instituto de Biología Agrícola de Mendoza (IBAM-CONICET), Facultad de Ciencias Agrarias, Universidad Nacional de Cuyo, Mendoza, Argentina

HIGHLIGHTS

- Contributions regarding NADES as extraction media are analyzed in terms of energy, time, sample and solvent consumption.
- Strategies to make NADES-mediated approaches even greener are presented.
- The review underlines the relevance of developing sustainable analytical methodologies.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 23 February 2018
Received in revised form
20 July 2018
Accepted 24 July 2018
Available online xxx

Keywords:
Natural deep eutectic solvents
Extraction
Green analytical chemistry
Sample prep
Microextractions

ABSTRACT

The concept of sustainable development has impacted in analytical chemistry changing the way of thinking processes and methods. It is important for analytical chemists to consider how sample preparation can integrate the basic concepts of Green Chemistry. In this sense, the replacement of traditional organic solvents is of utmost importance. Natural Deep Eutectic Solvents (NADES) have come to light as a green alternative. In the last few years, a growing number of contributions have applied these natural solvents proving their efficiency in terms of extraction ability, analyte stabilization capacity and detection compatibility. However, the arising question that has to be answered is: the use of NADES is enough to green an extraction process? This review presents an overview of knowledge regarding sustainability of NADES-based extraction procedures, focused on reported literature within the timeframe spanning from 2011 up to date. The contributions were analyzed from a green perspective in terms of energy, time, sample and solvent consumption. Moreover, we include a critical analysis to clarify whether the use of NADES as extraction media is enough for greening an analytical methodology; strategies to make them even greener are also presented. Finally, recent trends and future perspectives on how NADES-based extraction approaches in combination with computational methodologies can contribute are discussed.

Contents

* Corresponding author. Instituto de Biología Agrícola de Mendoza (IBAM-CONICET), Facultad de Ciencias Agrarias, Universidad Nacional de Cuyo, Almte. Brown 500, (CP 5505), Chacras de Coria, Mendoza, Argentina.
** Corresponding author. Instituto de Biología Agrícola de Mendoza (IBAM-CONICET), Facultad de Ciencias Agrarias, Universidad Nacional de Cuyo, Almte. Brown 500, (CP 5505), Chacras de Coria, Mendoza, Argentina.
E-mail addresses: fedeg33@gmail.com (FedericoJ.V. Gomez), msilva@fca.uncu.edu.ar (M.F. Silva).

https://doi.org/10.1016/j.aca.2018.07.059
0003-2670/

1. Introduction 00
2. NADES-mediated extraction methodologies 00
2.1. NADES physicochemical properties affecting extraction parameters 00
3. It is enough to use NADES to "green" an extraction process? 00
3.1. Computational approach for greening analytical methodologies 00
3.2. Other strategies to make NADES-mediated techniques even greener 00
4. Challenges and concluding remarks: "Green" nature of NADES in analytical sample preparation 00
Acknowledgements 00
References 00

1. Introduction

Nowadays, global sustainability challenges are intimately interconnected being human health and environmental impact the main concerns. In this context, it is not possible to deal with analytical chemistry in isolation [1]. Bearing in mind that analytical chemistry methods are used to solve problems, only holistic and disruptive approaches integrating research, development, and innovation in interdisciplinary and transdisciplinary studies will make revolutionary advances. Over the last few years, scientific chemistry community has been mobilized on the development of green practises. Concerning the contemporary goals of analytical chemists, the great challenge is to align the principles of Green Analytical Chemistry (GAC) with the twelve principles of Green Chemistry [1–3].

Despite unquestioned advances in analytical instrumentation, sample prep is the bottleneck of every analytical procedure. The adverse environmental impact of analytical procedures can be overcome applying the following strategies: miniaturizing the analytical scale and/or replacing hazardous solvents by safer alternatives. Although the ideal situation is the development of "solvent-free" extraction schemes [4], this concept is still rather utopic. Therefore, the search for alternative solvents is of utmost important [5].

Over the past two decades, ionic liquids (ILs) gained great attention as green media. Nevertheless, their "greenness" is often argued, due to their poor biodegradability, biocompatibility, and sustainability [6]. Later, a new kind of solvents based on the eutectic behaviour of their counterparts, emerged as an alternative to ILs. Deep eutectic solvents (DES) were introduced by Abbott et al. [7], showing a wide liquid range and interesting properties to be used as a solvent. Eutectic system, from the Greek "ευ" (eu = easy) and "Τήξις" (teksis = melting) is denoting a mixture of substances forming a joint super-lattice that melts and freezes at a single temperature that is lower than the melting points of the separate constituents. The application of DES has been focused to organic reactions, organic extractions, electrochemistry, and enzyme reactions carried out at 60 °C [8]. Nevertheless, the synthetic components of DESs can be toxic, reducing their possible use for applications in food and pharmacology industries [9].

In 2011, Verpoorte and co-workers [10] coined the term "Natural Deep Eutectic Solvents" (NADES), for the mixtures formed by cellular constituents such as sugars, alcohols, amino acids, organic acids and choline derivates. NADES fully represent the Green Chemistry principles. They are considered as the third solvent in living cells, which explains their high solubilizing capacity for natural products. The different compositions of NADES result in a broad range of physical properties.

NADES are typically obtained by mixing a hydrogen-bond acceptor (HBA), with a hydrogen bond donor (HBD) molecule, leading to a significant depression of the melting point. Hydrogen bonding and Van der Walls interactions are the main driving force of this phenomenon. Alcohol, amine, aldehyde, ketone and carboxylic groups behave both as hydrogen-bond donor and acceptors. Taking into account the chemical nature of their components, NADES can be classified as follows: 1) Derivatives from organic acids, 2) Derivate from choline chloride, 3) Mixtures of sugars, 4) Others combinations [6].

Readily available components, simple preparation, biodegradability, safety, reusability and low cost are major advantages that are encouraging research on their analytical applications. Indeed, they show excellent physicochemical properties: negligible volatility, a wide range of liquid state, adjustable viscosity and polarity and a high solubilisation capacity [11,12]. Three methods are most commonly used for preparing NADES: a) heating and stirring: the mixture is placed in a bottle with a stirring bar and cap and heated with agitation till a clear liquid is formed (about 30–90 min) [8,13,14]; b) evaporating method: components are dissolved in water and evaporated with a rotatory evaporator. The liquid obtained is put in a desiccator with silica gel till they reach a constant weight [8]; c) freeze drying method: aqueous solutions of the individual counterparts are freezzed-dried [15].

When analyzing the publications concerning NADES applications (Fig. 1), Europe and Asia are the leading territories of this subject, while contributions from America (North and South) are beginning to walk. Taken together, NADES are designer solvents due to the numerous structural possibilities and the potential for tuning their physico-chemical properties for different purposes [13]. Unique interactions between the NADES with target analytes make it possible to selectively separate trace compounds from complex matrices.

Several interesting review reports concerning the features and applications of DES have been published recently. Bubalo et al. [16] presented an overview of different green approaches for the extraction of plant biologically active compounds, including supercritical fluid, subcritical water and NADES extractions. Their

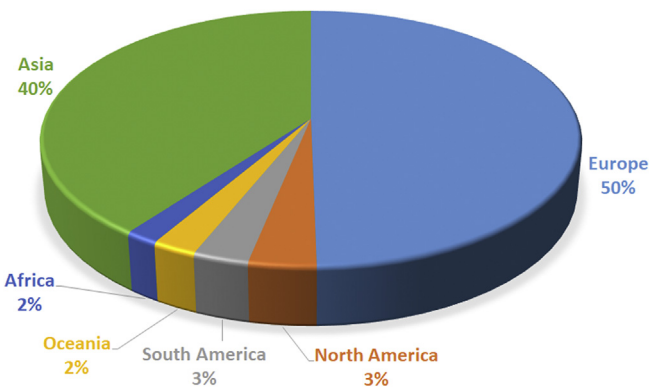


Fig. 1. World-wide geographical origin of the publications concerning NADES applications using the keywords natural deep eutectic solvents (source www.scopus.com; date of search: 07.19.18).

Please cite this article in press as: M.d.l.Á. Fernández, et al., Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments, Analytica Chimica Acta (2018), https://doi.org/10.1016/j.aca.2018.07.059

review evaluated contributions published until August 2017, with special emphasis on key experimental aspects and chemical interactions between analytes and supercritical, subcritical and eutectic solvents. Furthermore, the potential applications of green solvents for industry-scale are discussed. Zainal-Abidina et al. [17] reviewed the use of DES as potential extractants for various bioactive compounds, including phenolic acids, flavonoids, tanshinone, keratin, tocols, terpenoids, carrageenans, xanthones, isoflavones, α-mangostin, genistin and apigenin. Manuscripts published until December 2016 were covered. Besides, this work presents an overview of knowledge regarding the physicochemical properties of DESs, such as melting point, density, conductivity, and viscosity. Also, a comparison of DES, ILs, and conventional solvents used for the extraction of bioactive compounds is presented. Fernandes and co-workers [18] cover applications reported until the end of 2017 and their report is mainly focused on microextraction techniques (LPME, UAME and MAE) using DES and NADES as extracting solvents for food, biological and environmental samples and how these solvents could improve extraction efficiency for a variety of analytes. Pauli et al. [19] reviewed NADES properties (renewability, biodegradability, conductivity, viscosity, polarity, hydrophilicity, hydrophobicity, solubilizing, stabilizing abilities and biocompatibility) and applications in Natural Products research including their use as extraction and chromatographic media as well as their biomedical relevance. Their interesting study covers contribution published until November 2016. Taken together, these revisions are not focused on the objective evaluation of the greenness an analytical methodology. Thus, guided by the necessity of science aligned with the green chemistry principles, this review presents an overview of knowledge regarding use of NADES as extraction media, based on reported literature within the timeframe spanning from 2011 up to June 2018. The contributions were analyzed from a green perspective in terms of energy, time, sample and solvent consumption. Moreover, we include a critical analysis to clarify whether the use of NADES as extraction media is enough for greening an analytical methodology. On the other hand, strategies to make NADES-based extraction schemes even greener are also presented. Finally, recent trends and future perspectives on how NADES-based extraction approaches in combination with computational methodologies can contribute to the sustainability of analytical methodologies are presented.

2. NADES-mediated extraction methodologies

Since the appearance of NADES few years ago, most of the applications have been devoted to the extraction of biocompounds from natural sources. Table 1 lists the analytical characteristics of representative articles, grouped according to the extraction technique. Among the analytes evaluated, phenolic compounds continue to enjoy wide popularity whereas extraction of inorganic compounds is still poorly explored [20].

A great number of variables affect the extraction efficiency. Thus, several reports include optimizations tools for sample preparation step. Interestingly, most of the studies select multivariate approaches over the classical one-variable-at-a-time method, considering that it allows the evaluation of interacting effects between variables. The most commonly studied factors are sample/solvent ratio, time and temperature of extraction, NADES dilution and NADES composition [12,21–24]. One of the main drawbacks of NADES is their high viscosity, which leads to some practical problems, such as time-consuming solvent transfer operations and slow mass transfer in dissolutions or extractions. The high viscosity is attributed to the presence of an extensive hydrogen-bonding network between the compounds that restricts the mobility of the free species inside the NADES. Other interactions, such as van der Waals and electrostatic, may also contribute to NADES viscosity. The addition of water and the modification of their constituents are used to overcome this disadvantage [17].

Several authors have investigated the role of water addition in developing tailor-made NADES for specific applications. However, it is important to highlight that water can be added to the NADES during the preparation, as a component [11,20,25–28] or after this, as a diluents [9,21,22,29–38]. Dai et al. [13]studied the dilution effect on the supermolecular structures and physicochemical properties of NADES using two poorly water-soluble compounds (quercetin and carthamin). The eutectic mixture 1,2-propanediol–choline chloride– water (1:1:1; PCH) was diluted with deuterium oxide and was investigated with NMR. Results show that the supermolecular complex structures of PCH are preserved when the content of water is below 50%, though further dilution produces a solution of the free forms of the individual components in water. A similar phenomenon was also observed by Gutiérrez et al. [39] in urea-choline chloride mixture. To date, there are no reports that compare the supermolecular structure of NADES adding the same amount of water during the preparation step or after a dilution step.

Besides, the addition of water can be used to optimize NADES selectivity, adjusting their polarity. Moreover, NADES counterparts can be tailored to be target-specific. Thus, its composition should be selected based on the analyte and the sample chemical nature. Liu et al. [29] studied several NADES for the extraction of phenolics, terpenoids, phenolic acids and saponins in *Ginkgo biloba* and *Panax ginseng*. The highest yields were reached with malic acid-choline chloride (1:1) and glycerol-proline-sucrose (1:1:1) for G. biloba leaves, and malic acid-choline chloride (1:1) and malic acid-glucose (1:1) for P. ginseng leaves and stems. Ribeiro et al. [24] presented an interesting approach for the extraction of saponin and phenolic compounds from juá and sisal plant using NADES as adjuvants to aqueous and hydroalcoholic solutions. They found that the extraction efficiency and selectivity markedly increased by the addition of NADES. Liu et al. [40] used an ultrasonic-assisted liquid-liquid microextraction (UALLME) mediated by NADES for the determination of tert-butylhydroquinone (TBHQ) from oils. Also, the samples were analyzed by conventional liquid-liquid extraction using methanol as solvent. Some advantages to the UALLME method based on the NADESs compared with conventional extraction were lower sample and solvent consumption.

In addition to the features as solvents, the stabilization ability of NADES for biocompounds is a very important fact for their further applications. Dai et al. [14] studied the stabilization capacity of natural pigments from safflower. The studied polyphenols are more stable in sugar-based NADES than in water or 40% ethanol solution. Notably, the stabilization capacity of NADES can be adjusted by reducing water content with increasing viscosity. The strong stabilization ability is due to the formation of strong hydrogen bonding interactions between solutes and NADES molecules.

In the area of elemental analysis, Gupta and co-workers [20] proposed a green removal of lead (Pb II) from a contaminated soil. A NADES composed by choline chloride and glycerol mixed with the natural surfactant saponin obtained from soapnut fruit was used. The NADES and saponin showed a synergistic behaviour reducing the pH of the mixture and causing micellar solubilisation of Pb^{2+} from the soil. Indeed, the soil minerals did not undergo corrosion or mineralogical changes after soil washing. Their results are promising for the development of extraction techniques for other elemental species as well as soil decontamination applications.

NADES have also been used in Solid phase extraction (SPE). Gan et al. [41] designed a grafted material based on a choline chloride deep eutectic solvent onto an anion exchange resin for the neutral aromatic diterpenes. The performance properties of the proposed polymer were characterized by Fourier Transform Infrared

Please cite this article in press as: M.d.l.Á. Fernández, et al., Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments, Analytica Chimica Acta (2018), https://doi.org/10.1016/j.aca.2018.07.059

Table 1
Natural Deep Eutectic Solvents as extraction media.

NADES*	Sample	Extraction conditions*	Analytes	Separation-Detection technique[a]	Ref
Liquid- Liquid extraction					
Betaine monohydrate: glycerol (1:8) H&S: 50 °C, 90 min, 150 rpm	Palm oil	Sample: NADES (1:2) H&S: 120 min, 40 °C, 250 rpm Centrifugation:60 min	Palmitic acid	Titration method 2201 (IUPAC)	[43]
DL-Menthol: octanoic acid (1:1) H&S: 80 °C, 350 rpm, until a clear liquid was formed	Aqueous solutions	Sample: NADES (1:1) Stirring: 240 min, 25 °C Time stabilization: 1440 min Reused NADES	pesticides	UV–vis spectroscopy	[44]
Choline chloride: malonic acid (1:1)	Crude palm oil	NADES: methanol (1:10 v/v) Sample: hexane (1:10 w/v) NADES dil: Sample dil (1:1)	tocopherols	HPLC-DAD	[48]
H&S: 85 °C, until a clear liquid was formed		Stirring: 180 min, 200 rpm Time stabilization: 120 min Recovery of analytes from NADES extract: hexane	tocotrienols		
Lactic acid: glucose: water (6:1:6) H&S: 50 °C, 90 min	Extra virgin olive oils	Sample: hexane: NADES (1:1:5) Centrifugation: 10 min, 6000 rpm (supernatant 5 min, 9000 rpm)	Phenolic compounds	Spectrophotometry UV–Vis	[25]
Solid- liquid extraction mediated by Ultrasound					
Lactic acid- glucose- water (5:1:1) H&S: 80 °C, 60 min	Agro-food industrial by-products	Sample/NADES: 75 mg mL^{-1} UAE: 60 min, 40 °C Centrifugation: 30 min, 10000 rpm	phenolic compounds	HPLC-DAD	[11]
Malic acid: choline chloride (1:1), 20% water (w/w); Glycerol: proline: sucrose (1:1:1), 20% water (w/w)	*Ginkgo biloba*	Sample/NADES: 50 mg mL^{-1}	Ginkgolides phenolics acid	HPTLC	[29]
Malic acid: choline chloride (1:1), 20% water (w/w); Malic acid: glucose (1:1), 20% water (w/w)	*Panax ginseng*	Water bath: 40 °C, 60 min UAE: 30 min, 25 °C	ginkgolic acids		
H&S:50 °C, until a clear liquid was formed		Centrifugation: 20 min, 13.000 rpm Recovery of analytes from NADES extract: SPE, water (17 mL), ethanol (11 mL), methanol (1 mL)	ginsenosides		
Choline chloride: citric acid (1:1), 30% water (w/w) H&S: 70 °C, 600 rpm, until a clear liquid was formed (15–30 min)	Soy products	Sample: NADES (3:1) UAE: 60 min, 60 °C, 616 W Centrifugation: 5 min, 2000g NADES extract dilution: 300 μL of methanol, Centrifugation: 5 min, 6000 rpm	isoflavones	UHPLC-UV	[21]
Citric acid: D-(+)-maltose (4:1), 24% water (w/w) FD:1440 min.	Grape skin	Sample/NADES: 120 mg mL^{-1} UAE: 9 min, 25 °C	anthocyanins	UHPLC-Q-TOF–MS (contrast results with UV)	[22]
Betaine: glycerol: D-glucose, (4:20:1), 19% water (w/w) FD: −80 °C, 120 min	Green tea	Sample/NADES: 56 mg mL^{-1} UAE: 6.5 min, 25 °C	epigallocatechin-3-gallate	HPLC-UV	[47]
Cholinechloride: glycerol (1:1), 20% water (w/w) H&S: ≤100 °C, until a clear liquid was formed	Tartary buckwheat hull	Sample/NADES: 40 mg mL^{-1} UAE: 60 min, 40 °C, 200 W centrifugation: 30 min, 10000 rpm Reused NADES	rutin	HPLC-UV	[31]
Fructose:citric acid (1:1), 20% water (v/v) H&S: 50 °C, 90 min	Food samples	Sample/NADES: 25 mg mL^{-1} UAE: 15 min, 40% ultrasonic amplitude Centrifugation: 2600 g, 10 min	gluten	Inmunoaffinity	[32]
Choline chloride: fructose (1.9:1), 30% water H&S: 80 °C, until a clear liquid was formed (120–360 min)	Grape skin	Sample/NADES: 100 mg mL^{-1} UAE: 65 °C, 50 min Centrifugation: 5000 g, 15 min	total phenolic compounds total anthocyanins content	Spectrophotometric HPLC-UV Vis	[33]
Citric acid: glucose: water (1:1:2) H&S: 80 °C, 60 min	Onion	Sample/NADES: 50 mg mL^{-1} UAE: 30 min, 25 °C	quercetin	Electrochemical detection	[26]
L-proline: glycerol (2:5), 10% water	*Sophora japonica L.*	Sample/NADES: 50 mg mL^{-1} UAE: 45 min, 25 °C	quercetin kaempferolisorhamnetin	LC-DAD	[46]
FD: −80 °C, 90 min		Centrifugation: 12300 g, 30 min Recovery of analytes from NADES extract (SPE)	glycosides	UHPLC-Q-TOF-MS	
Choline chloride: lactic acid (1:2), 35% water H&S: 80 °C, until a clear liquid was formed	Medicinal herb	Sample/NADES: 20 mg mL^{-1} UAE: 60 °C, 21 min Centrifugation: 16200 g, 10 min. NADES extract diluted with water or methanol 1:10	alkaloid flavonoid anthraquinone saponin phenolic acid	HPLC -DAD	[23]
Choline chloride: malic acid, 35.4% water. H&S: 80 °C, 120–360 min (until a clear liquid was formed)	Wine lees	Sample/NADES: 0.1 g mL^{-1} UAE: 35 °C, 30.6 min, 341.5 W Centrifugation: 5000 g, 15 min	anthocyanins	Spectrophotometry UV–Vis HPLC-UV	[12]
Lactic acid: glycine: water (3:1:3) H&S: 40 min, 70 °C, 900 rpm	Folk plant	Sample/NADES: 0.01 g mL^{-1} UAE: 80 °C, 90 min Centrifugation: 15000 rpm, 10 min	phenolic compounds flavonoids	Spectrophotometry UV–Vis	[27]

Please cite this article in press as: M.d.l.Á. Fernández, et al., Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments, Analytica Chimica Acta (2018), https://doi.org/10.1016/j.aca.2018.07.059

Table 1 (*continued*)

Liquid- Liquid extraction					
NADES*	Sample	Extraction conditions*	Analytes	Separation-Detection technique[a]	Ref
		NADES extract diluted with water 1:20			
Choline chloride: ascorbic acid (2:1), 10% water.	Oil sample	Sample/NADES: 0.16 g mL^{-1}	tert-Butylhydroquinone	HPLC-UV	[40]
H&S: 85 °C, until a clear liquid was formed		Ultrasonic: 60°C, 30 min Centrifuged: 3000 rpm, 10 min			
Choline chloride: D-(+)-glucose (5:2)	*Mentha piperita* L.	Sample/NADES: 100 g mL^{-1}	volatile monoterpenes compounds	(HS-SPME)-GC-MS	[59]
FD: 80°C, 120 min		Centrifuged: 12300 rpm, 25 min	phenolic compounds	UHPLC-Q-TOF-MS	
Lactic acid- glucose- water (5:1:1)	*Larrea divaricata*	Sample/NADES: 75 mg mL^{-1}	Phenolic compounds and alkaloids	HPLC-DAD	[62]
H&S: 80°C, 60 min		Ultrasonic: 60°C, 40 min Centrifuged: 10000 rpm, 30 min Filtrated: 0.45 μm filter			
Solid- liquid extraction mediated by H&S					
Lactic acid: fructose (5:1), 25% water (v/v)	Vanilla pods	Sample/NADES: 50 mg mL^{-1} H&S: 50 °C, 60 min	vanillin	HPLC	[34]
H&S: 50 °C		Centrifugation: 30 min, 1300 rpm. NADES extract diluted with mobile phase 4:6			
Acetylcholine chloride: lactic acid (2:1), 30% water (v/v)	Fruits vegetables and spices	Sample/NADES: 330 mg mL^{-1} H&S:60 °C, 45 min, 1400 rpm	flavonoids	UHPLC-UV	[38]
UAE:30 W, 50 °C, 10–15 min (until a homogeneous liquid was formed)		Centrifugation: 2000g, 5 min NADES extract diluted with methanol 1:1(centrifugation: 2000 g, 5 min)		UHPLC-MS/MS	
Glucose: choline chloride, 90% water; sucrose: choline chloride, 25% water	*Carthamus tinctorius*	Sample/NADES: 17 mg mL^{-1}	Phenolic compounds	HPLC-DAD	[14]
H&S: 50 °C, 30–90 min		H&S: 40 °C, 30 min Centrifugation: 1300 rpm, 20 min			
Proline: malic acid (1:1), 25% water; Lactic acid: glucose (5:1)	*Carthamus tinctorius*	Sample/NADES: 30 mg mL^{-1} H&S: 40 °C, 60 min	Phenolic compounds	HPLC-DAD	[9]
H&S: 50 °C, 30–90 min		Centrifugation: 10968 g, 20 min Recovery of analytes from NADES extract: Diaion resin column, water (66.5 mL), ethanol (325 mL), methanol (1.5 mL)		UPLD-ESI-TOF-MS	
Lactic acid: glucose: water (5:1:3); Glucose: fructose: sucrose: water (1:1:1:11)	*Catharantus roseus*	Sample/NADES: 33 mg mL^{-1} H&S: 40 °C, 30 min	anthocyanins	UPLC-TOF-MS	[28]
H&S: 50 °C, 30–90 min		Centrifugation: 1300 rpm, 20 min. NADES extract diluted with water (formic acid 3%) 1:2			
Choline chloride: malonic acid (1:2); 50% water	*Ginkgo biloba*	Sample/NADES: 94.4 mg mL^{-1} H&S: 65 °C, 53 min, 250 rpm	Proanthocyanidin	Spectrophotometry UV–Vis	[56]
H&S: 80°C, until a homogeneous liquid was formed		Centrifugation: 10000 rpm, 10 min 0.5 mL of supernatant was diluted with water (1 mL) and mixed with 3 mL of 4-(dimethylamino) cinnamaldehyde) solution.			
Solid- liquid extraction mediated by Microwave					
Glycerol: xilitol: D(−) fructose (3:3:3), 20% water	*Ficus carica*	Sample/NADES: 50 mg mL^{-1}	phenolic compound	HPLC-UV	[35]
H&S: 80 °C, until a clear liquid was formed		MW: 10 min, 55 °C, 250 W Recovery of analytes from NADES extract: macroporous resin, water (250 mL), ethanol (250 mL)			
Choline chloride: maltose (1:2), 20% water	*Cajanus cajan*	Sample/NADES: 33 mg mL^{-1}	phenolic compounds	UPLC-MWD	[36]
H&S: 80 °C		MW: 60 °C, 12 min			
Choline chloride: lactic acid (1:2), 20% water	*Radix Scutellariae*	Sample/NADES: 67 mg mL^{-1}	flavonoids	HPLC-MWD	[49]
H&S: 85 °C		MW: 60 °C, 12 min, 500 W Recovery of analytes from NADES extract: macroporous resin, water (250 mL), ethanol (250 mL)			
Choline chloride: lactic acid (1:2), 32.19% water	*Lippia citriodora*	Sample/NADES: 100 mg mL^{-1} MW: 63.68 °C, 17.08 min, 500 W Centrifugation:13000 rpm, 15 min, 20°C	Phenolic compounds	HPLC-DAD-ESI-TOF-MS	[54]
H&S: 80 °C until a clear liquid was formed (between 30 min and 120 min		Filtered: 0.2 μm filter Diluted with water (10 mL).			
Solid phase extraction					
Choline chloride: glycerol (1:2) H&S: 80 °C, 120 min	*Phyllanthus flexuosus*	SPE: Anion excharge resin (200 mg) modified with NADES, methanol (1.1 mL), water (1.9 mL), acetonitrile (1.35 mL), acetic acid (0.15 mL)	diterpenoid	HPLC-UV	[41]
Other extractions					
Choline chloride: urea (0.69:1) heated until homogeneous colorless liquid formed	Pineapple leaf and kapok fiber	Sample/NADES/NaOH: 3 g sample, 96.8 g choline chloride, 60.1 g urea, 3.72 g NaOH. H&S: 1200 min, 90 °C.	ligocellulosoic fibers	not informed	[42]

(*continued on next page*)

Please cite this article in press as: M.d.l.Á. Fernández, et al., Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments, Analytica Chimica Acta (2018), https://doi.org/10.1016/j.aca.2018.07.059

Table 1 (*continued*)

Liquid- Liquid extraction					
NADES*	Sample	Extraction conditions*	Analytes	Separation-Detection technique[a]	Ref
		Cellulose Purification from NADES extract: water (1000 mL), H_2O_2 (20 mL), 0.2% cyanamide solution (180 mL), H&S: 50 °C, pH 10, 240 min.			
Choline chloride: fructose: water (5:2:5) H&S: 80 °C, 180 min, 350 rpm	Soil	Sample/NADES: 200 mg mL^{-1} Shaken 240 min Centrifugation	Pb	ICP-OES	[20]
Lactic acid: choline chloride (5:1), 5% water	Rice straw	Sample: NADES 1:10 H&S: 60 °C, 720 min, 100 rpm Centrifugation: 5000 rpm, 30 min	Lignin	Spectrophotometry UV–Vis	[37]
H&S: 60 °C, 15 min, 100 rpm		Lignin purification from NADES extract: water, 4 °C, 180 min, centrifugation 10000*g*, 10 min Reused NADES			
Choline chloride: proponic acid (2:1), 42% ethanol	*Agave sisalana*	Sample: NADES-ethanol 1:10	saponins	Spectrophotometry UV–Vis	[24]
Choline chloride: acetic acid, 19% water H&S: 100 °C, 60 min	*Ziziphus joazeiro*	H&S: 50 °C, 120 rpm, 90 min Sample: NADES-water: 1:20 H&S: 30 °C, 120 rpm, 90 min			
Choline chloride: glycerol (1:2)	sample solution of active pharmaceutical ingredients	Sample/NADES: 200 mg g^{-1}	ethanol isopropanol n-butanol acetone 1,4-dioxane, acetonitrile, tetrahydrofuran and methanol	SHS-GC/FID	[60]
H&S: 80 °C, until a clear liquid was formed		HS parameters were: vial pressure was 15.0 psi. The HS oven temperature was 140 °C. The vial equilibration time was 40 min.			

H&S: Heating and Stirring method; FD: Freeze-Drying method; UAE: Ultrasound Assisted Extraction; MW: Microwave method.

[a] HPTLC (High-Performance Thin-Layer Chromatography); ICP-OES (Inductively Coupled Plasma Optical Emission Spectrometry); UPLC-MWD (Ultra Performance Liquid Chromatography-Multiple Wavelength Detector); HPLC-MWD (High Performance Liquid Chromatography- Multiple Wavelength Detector); UPLC-TOF-MS (Ultra Performance Liquid Chromatography- Time of Flight Mass Spectrometry); UPLD-ESI-TOF-MS (Ultra Performance Liquid Chromatography- Electrospray Time of Flight Mass Spectrometry); HPLC-DAD (High Performance Liquid Chromatography- Diode Array Detector); UHPLC-MS/MS (Ultra Performance Liquid Chromatography-tandem mass spectrometry); HPLC-UV (High Performance Liquid Chromatography- Ultraviolet detector); UHPLC-Q-TOF–MS (Ultra Performance Liquid Chromatography- Quadrupole Time of Flight Mass Spectrometry); SHS-GC/FID (Static Headspace- Gas Chromatography with Flame Ionization Detector).

Spectrometry, Field Emission Scanning Electron Microscopy, and adsorption experiments. The extraction efficiency of the proposed NADES-based polymer was better than conventional materials (the resin alone and C18) for the extraction of cleistanthol from *P. flexuosus* extracts.

The compatibility of NADES with electrochemical detection was demonstrated by Gomez et al. [26]. They investigated the extraction of quercetin from onions using a NADES composed of Citric acid, Glucose and H_2O (CGH, 1:1:2). The portable electrochemical detection of quercetin was enhanced adding different amounts of NADES to the detection buffer achieving an improved signal up to 380%. Noteworthy, that the proposed methodology is entirely green from every point of view, since the extraction and the determination used only NADES as solvents.

Sustainable industrial processes using NADES have been developed with acceptable results. Kumar et al. [37] proposed a satisfactory biomass pretreatment process using NADES for lignin removal from lignocellulosic biomass residue (rice straw). Moreover, the precipitated lignin was separated from the NADES solution and the recovered green solvent was directly reused for a next cycle. Traditionally, the lignin removal from rice straw involves large amounts of organic solvents being NADES extraction an eco-friendly alternative. Another industrial application was proposed by Norzila Mohd and co-workers [42]. A green extraction of lignocellulosoic fibers from pineapple and kapok was performed for the acquisition of cellulose. Additionally, the use of NADES in the palm oil industry was investigated by Zahrina et al. [43]. Commonly, the deacidification process is performed by steam stripping which causes the loss of most of palm oil's natural antioxidants due to high temperature. The NADES selected showed satisfactory extraction efficiency and the amount of antioxidants can be preserved in the refined palm oil up to 99%, being the compounds stable during the extraction.

Until now, most of the NADES proposed for extraction have a hydrophilic character. Florindo et al. [44] developed hydrophobic NADES as extractants for the elimination of pesticides from aqueous solutions. DL-Menthol and tetrabutylammonium chloride salt were studied as hydrogen bond acceptors (HBAs) combined with acids with different alkyl chain lengths as hydrogen bond donors (HBDs). High extraction efficiencies of the pesticides evaluated were obtained using DL-Menthol and octanoic acid (1:1). Also, the reusability of the NADES was demonstrated, highlighting their relevant role as sustainable solvents in industrial applications.

2.1. NADES physicochemical properties affecting extraction parameters

It is important to highlight that a distinguished characteristic of NADES is that their physicochemical properties can be “tuned” for specific requirements. The latter opens unlimited possibilities for the design of extraction techniques. By selecting the proper chemical nature and composition of the components of NADES it is possible to design a specific system for target analytes.

NADES physicochemical studies available in the literature are still needed considering their importance in the extraction processes. The most relevant physicochemical properties that influence this process are pH, viscosity, solubility, polarity. NADES present a wide range of viscosity [8]. A decrease in viscosity leads to an increase in diffusivity, which can improve the extraction efficiency [31]. The viscosity of NADES differs significantly according to their composition, but in all cases it can be reduced by the addition of water [45]. A positive linear correlation of viscosity with temperature has been reported for NADES [19]. The conductivity of NADES increases when the viscosity decreases due to the dilution with water. Thus, the conductivity of NADES can be tailored by changing the water content [13].

Please cite this article in press as: M.d.l.Á. Fernández, et al., Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments, Analytica Chimica Acta (2018), https://doi.org/10.1016/j.aca.2018.07.059

Another physicochemical parameter that affects extraction is the solvent polarity. NADES with large amounts of water performed better for polar compounds while NADES with low water content are more appropriate for the extraction of weak polar compounds [8].

3. It is enough to use NADES to "green" an extraction process?

With growing concerns over the toxicity of organic solvents, NADES has emerged as a spark of light from nature bringing a new dimension to the analytical process. So far, water and conventional organic solvents are the most commonly-used solvents for the extraction of bioactive compounds from natural resources. However, water is only effective as extraction solvent for polar and hydrophilic bioactive compounds. Indeed, extraction squemes mediated by water are energy consuming. On the other hand, although the efficiency of organic solvents is unquestionable; their toxicity, environmental hazardous, high cost and low biodegradability extremely limit their applications.

As it has already stated, NADES have emerged as tunable green solvents that are safe for human consumption, a feature which promises great possibilities for pharmaceutical, cosmetic and food-related applications [33]. It is worth mentioning that NADES components are present at high concentrations in our daily diet.

A growing number of studies have compared the extraction efficiencies of NADES with traditional solvents [11,25,34,36]. Remarkably, NADES have demonstrated outstanding extractability for polar and weak polar compounds as well as elemental species when compared to conventional solvents such as water, methanol, ethanol, acetone, and ethyl acetate.

Interestingly, NADES extracts are compatible with the most popular separation techniques such as HPLC [11,21,22,46] and TLC [29]. Regarding their compatibility with instrumental detection systems, satisfactory results have been proven for immunoaffinity [32], mass spectrometry [22,28,46], ICP-OES [20], UV–Vis [21,36,44,47], and DAD [11,46]. Moreover, the addition of NADES to the electrolyte improves the electrochemical detection of phenolic compounds [26].

In view of the clear advantages of smart solvents over conventional extraction approaches, NADES are the "trendy" green solvents. Since the first approaches of NADES presented by Choi et al. [10] 6 years ago, the number of publications using them as extraction solvents has been exponentially growing, as shown in Fig. 2.

Although the contributing authors state that their NADES-mediated extractions are green, the following misalignments from Green Chem concept are evident: a) time and energy consuming techniques [20,27,29,44,48], b) dilution of NADES extracts with organic solvents before the injection [21,23,46], c) combination of NADES with hazardous solvents for the extraction [24,48], d) recovery of biocompounds from NADES extracts with resins and elution with methanol or ethanol [9,29,35,46,48,49].

The time has come to start thinking if NADES-mediated extraction are aligned with the principles of Green Analytical Chemistry [50]. Undoubtedly, the role of NADES in the area of green extraction techniques contribute to settle the statement of professor de la Guardia and co-workers [3] "from dream to green". However, to achieve this concept each step of the analytical process should be considered. In the near future, in order to quantify the greenness of an analytical methodology, green metrics such as NEMI pictogram [3], eco-scale [51], green certificate [3], should be applied [52].

3.1. Computational approach for greening analytical methodologies

The use of computational tools presents remarcable economic and environmental advantages for the selection of optimal system or process parameters in analytical methodologies, reducing the amounts of chemicals, energy and time consumption. Several experimental designs such as Box–Behnken or Composite Central combined with Response Surface Methodology (RSM) were used to optimize NADES extraction process (temperature, time and liquid/solid ratio) as well as the NADES synthesis conditions [11,53–56]. On the other hand, considering the large number of chemical combinations that can form NADES for a given application, it is impossible to study all of them experimentally. In silico methods are an interesting tool in the selection or design of suitable systems, as they provide a way to pre-screen system for a certain application before extensive experimental measurement. Jelinski and Cysewski [57] carried out a screening of 126 natural deep eutectic solvents (NADES), using the COSMO-RS (Conductor-like Screening Model for Real Solvents) methodology to identify those with the ability to strongly solvate rutin. The most effective was the system composed by proline- 2,3-diaminosuccinic acid, being the solubility of rutin in this solvent 130% greater than in the best reference system. COSMO-RS methodology was able to examine the interactions of rutin with a multicomponent NADES systems that has not been studied experimentally.

3.2. Other strategies to make NADES-mediated techniques even greener

In order to develop novel generations of extraction methods mediated by NADES, it is of utmost importance to design the cheapest, safest and most efficient solvent. In this sense, a smart strategy is to adapt the recent trends in microextraction techniques [58]. Recently, a deep eutectic solvent based liquid phase microextraction method (DES-LPME) for the extraction of rhodamine B prior to its micro-cuvette UV-VIS spectrophotometer determination. An excellent preconcentration factor was obtained using only microliter amounts of organic solvents, and much better extraction efficiency and sensitivity compared to traditional LPME approaches thanks to the formation of nano-sized and micro-sized cloudy DES droplets.

Interesting perspectives arise from the adaptation of microextraction techniques based on solid sorbents [59]. Solid phase microextraction is the most widely used one, combining extraction and preconcentration into a single step. The partition equilibrium of analytes between the stationary phase attached onto the fibre and the sample is modified by the presence of NADES as matrix medium. Also, Wang et al. [60] reported that Natural deep eutectic solvents provided high sensitivity for residual solvents detection in drug substances using static headspace gas chromatography (SHS-GC) method.

Another impressive possibility is the use of NADES as functionalizing agents for nanomaterials. Functionalization is a method that involves the addition of new functional groups by means of chemical or physical process. In 2015, deep eutectic solvents were used for the first time as functionalizing agents for graphene. The DES-graphene was characterized by FTIR, STA, Raman spectroscopy, XRD, SEM, and TEM. This new material can be used in many environmental and health-related applications, including drug delivery, wastewater treatment, and biosensors [61].

Very recently, a new microwave (MW) assisted preparation for NADES demanding only 20 s and negligible energy consumption was proposed [62]. A solid-liquid microextraction for alkaloids and phenolic compounds from *Larrea Divaricata* leaves was developed using the new MW-NADES and compared with traditionally prepared NADES.

Please cite this article in press as: M.d.l.Á. Fernández, et al., Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments, Analytica Chimica Acta (2018), https://doi.org/10.1016/j.aca.2018.07.059

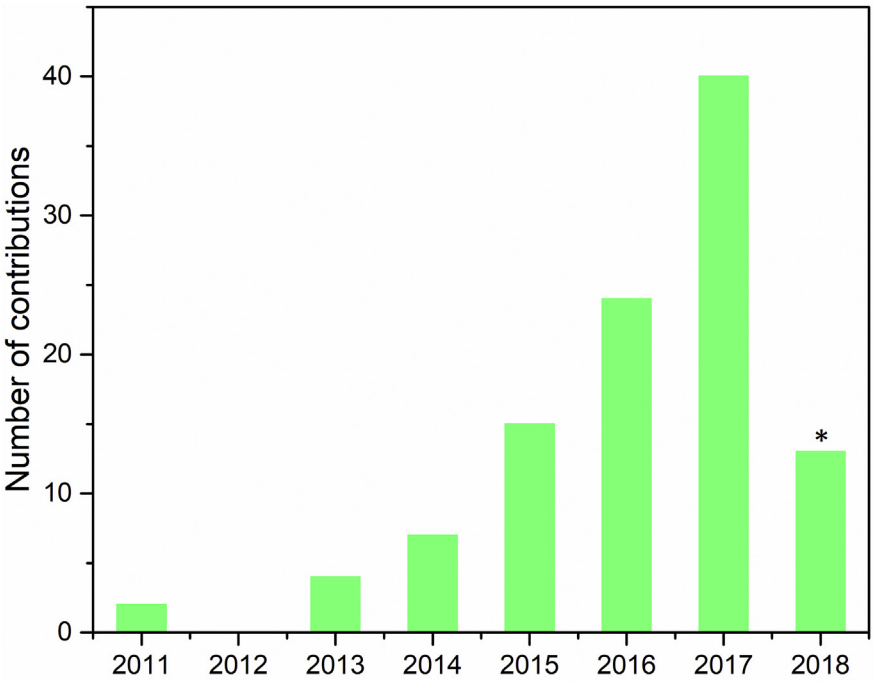


Fig. 2. Growing number of publications using NADES as extraction solvents. Keywords: "natural deep eutectic solvents" and then search within the results the keyword "extraction" (source www.scopus.com; date of search: 07.19.18).

4. Challenges and concluding remarks: "Green" nature of NADES in analytical sample preparation

Lately, there has been an awakening on the collective consciousness about how the human activity impacts on the environment. In this sense, chemists are encouraged to develop sustainable and green methodologies. In an analytical process the extraction is a crucial step, being the use of organic solvents the principal threat for health and environment. NADES have been introduced as a promising environmentally friendly solution, with excellent extraction properties, easy preparation and low cost. Although they are a great tool for extraction, as it has been deeply examined in this review, their use is often complemented with organic solvents and/or time and energy consuming processes. Analytical researchers devoted to the development of sustainable methodologies, are encouraged to focus not exclusively on the use of solvents. The capacity to understand chemistry and practice as a livelihood should be used wisely for the whole analytical process. In this sense, the application of micro techniques could enhance the greeness of the process. The main advantages of microextractions are related to the reduction of the solvent, extraction time and energy consumption.

In order to set up general trends for future work when developing a novel analytical method, the environmental and health impact must be considered as well as the selectivity and sensibility. Furthermore, green metrics have been developed specifically for analytical chemistry, thus every chemist should take the opportunity and apply them in order to evaluate the greenness of a method.

Acknowledgements

This work was supported by funding from the Facultad de Ciencias Agrarias, Universidad Nacional de Cuyo 06/P31-04 and Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) (PIP 11220130100185CO).

References

[1] M. Valcárcel, Analytical chemistry today and tomorrow, in: I.S. Krull (Ed.), Analytical Chemistry, InTech, London, 2012, pp. 93–114.
[2] P.T. Anastas, Green chemistry and the role of analytical methodology development, Crit. Rev. Anal. Chem. 29 (1999) 167–175.
[3] S. Armenta, S. Garrigues, M. de la Guardia, The role of green extraction techniques in Green Analytical Chemistry, Trac. Trends Anal. Chem. 71 (2015) 2–8.
[4] M. Vian, C. Breil, L. Vernes, E. Chaabani, F. Chemat, Green solvents for sample preparation in analytical chemistry, Current Opinion in Green and Sustainable Chemistry 5 (2017) 44–48.
[5] F. Pena-Pereira, A. Kloskowski, J. Namiesnik, Perspectives on the replacement of harmful organic solvents in analytical methodologies: a framework toward the implementation of a generation of eco-friendly alternatives, Green Chem. 17 (2015) 3687–3705.
[6] M. Espino, M. de los Ángeles Fernández, F.J.V. Gomez, M.F. Silva, Natural designer solvents for greening analytical chemistry, Trac. Trends Anal. Chem. 76 (2016) 126–136.
[7] A.P. Abbott, G. Capper, D.L. Davies, R.K. Rasheed, V. Tambyrajah, Novel solvent properties of choline chloride/urea mixtures, Chem. Commun. 9 (2003) 70–71.
[8] 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.
[9] Y. Dai, G.J. Witkamp, R. Verpoorte, Y.H. Choi, Natural deep eutectic solvents as a new extraction media for phenolic metabolites in carthamus tinctorius L, Anal. Chem. 85 (2013) 6272–6278.
[10] 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.
[11] M.D.L.Á. Fernández, M. Espino, F.J.V. Gomez, M.F. Silva, Novel approaches mediated by tailor-made green solvents for the extraction of phenolic compounds from agro-food industrial by-products, Food Chem. 239 (2018) 671–678.
[12] T. Bosiljkov, F. Dujmić, M. Cvjetko Bubalo, J. Hribar, R. Vidrih, M. Brnčić, E. Zlatic, I. Radojčić Redovniković, S. Jokić, Natural deep eutectic solvents and ultrasound-assisted extraction: green approaches for extraction of wine lees anthocyanins, Food Bioprod. Process. 102 (2017) 195–203.
[13] Y. Dai, G.J. Witkamp, R. Verpoorte, Y.H. Choi, Tailoring properties of natural deep eutectic solvents with water to facilitate their applications, Food Chem. 187 (2015) 14–19.
[14] Y. Dai, R. Verpoorte, Y.H. Choi, Natural deep eutectic solvents providing enhanced stability of natural colorants from safflower (Carthamus tinctorius), Food Chem. 159 (2014) 116–121.
[15] M.C. Gutiérrez, M.L. Ferrer, C.R. Mateo, F.D. Monte, Freeze-drying of aqueous solutions of deep eutectic solvents: a suitable approach to deep eutectic

suspensions of self-assembled structures, Langmuir 25 (2009) 5509–5515.
[16] M. Cvjetko Bubalo, S. Vidović, I. Radojčić Redovniković, S. Jokić, New perspective in extraction of plant biologically active compounds by green solvents, Food Bioprod. Process. 109 (2018) 52–73.
[17] M.H. Zainal-Abidin, M. Hayyan, A. Hayyan, N.S. Jayakumar, New horizons in the extraction of bioactive compounds using deep eutectic solvents: a review, Anal. Chim. Acta 979 (2017) 1–23.
[18] S.C. Cunha, J.O. Fernandes, Extraction techniques with deep eutectic solvents, Trac. Trends Anal. Chem. 105 (2018) 225–239.
[19] Y. Liu, J.B. Friesen, J.B. McAlpine, D.C. Lankin, S.N. Chen, G.F. Pauli, Natural deep eutectic solvents: properties, applications, and perspectives, J. Nat. Prod. 81 (2018) 679–690.
[20] S. Mukhopadhyay, S. Mukherjee, N.F. Adnan, A. Hayyan, M. Hayyan, M.A. Hashim, B. Sen Gupta, Ammonium-based deep eutectic solvents as novel soil washing agent for lead removal, Chem. Eng. J. 294 (2016) 316–322.
[21] S. Bajkacz, J. Adamek, Evaluation of new natural deep eutectic solvents for the extraction of isoflavones from soy products, Talanta 168 (2017) 329–335.
[22] K.M. Jeong, J. Zhao, Y. Jin, S.R. Heo, S.Y. Han, D.E. Yoo, J. Lee, Highly efficient extraction of anthocyanins from grape skin using deep eutectic solvents as green and tunable media, Arch Pharm. Res. (Seoul) 38 (2015) 2143–2152.
[23] L. Duan, L.L. Dou, L. Guo, P. Li, E.H. Liu, Comprehensive evaluation of deep eutectic solvents in extraction of bioactive natural products, ACS Sustain. Chem. Eng. 4 (2016) 2405–2411.
[24] B.D. Ribeiro, M.A.Z. Coelho, I.M. Marrucho, Extraction of saponins from sisal (Agave sisalana) and juá (Ziziphus joazeiro) with cholinium-based ionic liquids and deep eutectic solvents, Eur. Food Res. Technol. 237 (2013) 965–975.
[25] 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.
[26] F.J.V. Gomez, M. Espino, M. de los Angeles Fernandez, J. Raba, M.F. Silva, Enhanced electrochemical detection of quercetin by natural deep eutectic solvents, Anal. Chim. Acta 936 (2016) 91–96.
[27] C. Bakirtzi, K. Triantafyllidou, D.P. Makris, Novel lactic acid-based natural deep eutectic solvents: efficiency in the ultrasound-assisted extraction of antioxidant polyphenols from common native Greek medicinal plants, Journal of Applied Research on Medicinal and Aromatic Plants 3 (2016) 120–127.
[28] Y. Dai, E. Rozema, R. Verpoorte, Y.H. Choi, Application of natural deep eutectic solvents to the extraction of anthocyanins from Catharanthus roseus with high extractability and stability replacing conventional organic solvents, J. Chromatogr. A 1434 (2016) 50–56.
[29] X. Liu, S. Ahlgren, H.A.A.J. Korthout, L.F. Salomé-Abarca, L.M. Bayona, R. Verpoorte, Y.H. Choi, Broad range chemical profiling of natural deep eutectic solvent extracts using a high performance thin layer chromatography–based method, J. Chromatogr. A 1532 (2018) 198–207.
[30] W. Liu, K. Zhang, Y. Qin, J. Yu, A simple and green ultrasonic-assisted liquid-liquid microextraction technique based on deep eutectic solvents for the HPLC analysis of sesamol in sesame oils, Analytical Methods 9 (2017) 4184–4189.
[31] Y. Huang, F. Feng, J. Jiang, Y. Qiao, T. Wu, J. Voglmeir, Z.G. Chen, Green and efficient extraction of rutin from tartary buckwheat hull by using natural deep eutectic solvents, Food Chem. 221 (2017) 1400–1405.
[32] H. Lores, V. Romero, I. Costas, C. Bendicho, I. Lavilla, Natural deep eutectic solvents in combination with ultrasonic energy as a green approach for solubilisation of proteins: application to gluten determination by immunoassay, Talanta 162 (2017) 453–459.
[33] K. Radošević, N. Ćurko, V. Gaurina Srček, M. Cvjetko Bubalo, M. Tomašević, K. Kovačević Ganić, I. Radojčić Redovniković, Natural deep eutectic solvents as beneficial extractants for enhancement of plant extracts bioactivity, LWT - Food Sci. Technol. (Lebensmittel-Wissenschaft -Technol.) 73 (2016) 45–51.
[34] C.G. González, N.R. Mustafa, E.G. Wilson, R. Verpoorte, Y.H. Choi, Application of natural deep eutectic solvents for the "green"extraction of vanillin from vanilla pods, Flavour Fragrance J. 33 (2018) 91–96.
[35] T. Wang, J. Jiao, Q.-Y. Gai, P. Wang, N. Guo, L.-L. Niu, Y.-J. Fu, Enhanced and green extraction polyphenols and furanocoumarins from Fig (Ficus carica L.) leaves using deep eutectic solvents, J. Pharmaceut. Biomed. Anal. 145 (2017) 339–345.
[36] 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, Separ. Purif. Technol. 149 (2015) 237–244.
[37] A.K. Kumar, B.S. Parikh, M. Pravakar, Natural deep eutectic solvent mediated pretreatment of rice straw: bioanalytical characterization of lignin extract and enzymatic hydrolysis of pretreated biomass residue, Environ. Sci. Pollut. Control Ser. 23 (10) (2015) 9265–9275.
[38] S. Bajkacz, J. Adamek, Development of a method based on natural deep eutectic solvents for extraction of flavonoids from food samples, Food Analytical Methods 11 (5) (2017) 1330–1344.
[39] M.C. Gutiérrez, M.L. Ferrer, C.R. Mateo, F. del Monte, Freeze-drying of aqueous solutions of deep eutectic solvents: a suitable approach to deep eutectic suspensions of self-assembled structures, Langmuir 25 (2009) 5509–5515.
[40] W. Liu, K. Zhang, J. Chen, J. Yu, Ascorbic acid and choline chloride: a new natural deep eutectic solvent for extracting tert-butylhydroquinone antioxidant, J. Mol. Liq. 260 (2018) 173–179.
[41] K. Gan, W. Tang, T. Zhu, W. Li, H. Wang, X. Liu, Enhanced extraction of cleistanthol from Phyllanthus flexuosus by deep eutectic solvent-modified anion-exchange resin, J. Liq. Chromatogr. Relat. Technol. 39 (2016) 882–888.
[42] S.F.S. Draman, R. Daik, N. Mohd, Eco-friendly extraction and characterization of cellulose from Lignocellulosoic fiber, ARPN Journal of Engineering and Applied Sciences 11 (2016) 9591–9595.
[43] I. Zahrina, M. Nasikin, E. Krisanti, K. Mulia, Deacidification of palm oil using betaine monohydrate-based natural deep eutectic solvents, Food Chem. 240 (2018) 490–495.
[44] C. Florindo, L.C. Branco, I.M. Marrucho, Development of hydrophobic deep eutectic solvents for extraction of pesticides from aqueous environments, Fluid Phase Equil. 448 (2017) 135–142.
[45] K. Kumar, R. Pathak, Phytochemical analysis and assessment of in vitro antibacterial activity of non-polar solvent based Camelina seed extracts, Indian J. Plant Physiol. 21 (2016) 255–262.
[46] M.W. Nam, J. Zhao, M.S. Lee, J.H. Jeong, J. Lee, Enhanced extraction of bioactive natural products using tailor-made deep eutectic solvents: application to flavonoid extraction from Flos sophorae, Green Chem. 17 (2015) 1718–1727.
[47] K.M. Jeong, J. Ko, J. Zhao, Y. Jin, D.E. Yoo, S.Y. Han, J. Lee, Multi-functioning deep eutectic solvents as extraction and storage media for bioactive natural products that are readily applicable to cosmetic products, J. Clean. Prod. 151 (2017) 87–95.
[48] N. Abdul Hadi, M.H. Ng, Y.M. Choo, M.A. Hashim, N.S. Jayakumar, Performance of choline-based deep eutectic solvents in the extraction of tocols from crude palm oil, JAOCS, Journal of the American Oil Chemists' Society 92 (2015) 1709–1716.
[49] Z.-F. Wei, X.-Q. Wang, X. Peng, W. Wang, C.-J. Zhao, Y.-G. Zu, Y.-J. Fu, Fast and green extraction and separation of main bioactive flavonoids from Radix Scutellariae, Ind. Crop. Prod. 63 (2015) 175–181.
[50] P. Anastas, N. Eghbali, Green chemistry: principles and practice, Chem. Soc. Rev. 39 (2010) 301–312.
[51] A. Gałuszka, Z.M. Migaszewski, P. Konieczka, J. Namieśnik, Analytical Eco-Scale for assessing the greenness of analytical procedures, Trac. Trends Anal. Chem. 37 (2012) 61–72.
[52] M. Tobiszewski, Metrics for green analytical chemistry, Analytical Methods 8 (2016) 2993–2999.
[53] X. Peng, M.H. Duan, X.H. Yao, Y.H. Zhang, C.J. Zhao, Y.G. Zu, Y.J. Fu, Green extraction of five target phenolic acids from Lonicerae japonicae Flos with deep eutectic solvent, Separ. Purif. Technol. 157 (2016) 249–257.
[54] M. Ivanović, M.E. Alañón, D. Arráez-Román, A. Segura-Carretero, Enhanced and green extraction of bioactive compounds from Lippia citriodora by tailor-made natural deep eutectic solvents, Food Res. Int. 111 (2018) 67–76.
[55] Y.-J. Zeng, P. Xu, H.-R. Yang, M.-H. Zong, W.-Y. Lou, Purification of anthocyanins from saskatoon berries and their microencapsulation in deep eutectic solvents, LWT (Lebensm.-Wiss. & Technol.) 95 (2018) 316–325.
[56] J. Cao, L. Chen, M. Li, F. Cao, L. Zhao, E. Su, Efficient extraction of proanthocyanidin from Ginkgo biloba leaves employing rationally designed deep eutectic solvent-water mixture and evaluation of the antioxidant activity, J. Pharmaceut. Biomed. Anal. 158 (2018) 317–326.
[57] T. Jeliński, P. Cysewski, Application of a Computational Model of Natural Deep Eutectic Solvents Utilizing the COSMO-rs Approach for Screening of Solvents with High Solubility of Rutin, 2018.
[58] J. Płotka-Wasylka, K. Owczarek, J. Namieśnik, Modern solutions in the field of microextraction using liquid as a medium of extraction, Trac. Trends Anal. Chem. 85 (2016) 46–64.
[59] K.M. Jeong, Y. Jin, D.E. Yoo, S.Y. Han, E.M. Kim, J. Lee, One-step sample preparation for convenient examination of volatile monoterpenes and phenolic compounds in peppermint leaves using deep eutectic solvents, Food Chemistry 251 (2018) 69–76.
[60] M. Wang, S. Fang, X. Liang, Natural deep eutectic solvents as eco-friendly and sustainable dilution medium for the determination of residual organic solvents in pharmaceuticals with static headspace-gas chromatography, J. Pharmaceut. Biomed. Anal. 158 (2018) 262–268.
[61] M. Hayyan, A. Abo-Hamad, M.A. AlSaadi, M.A. Hashim, Functionalization of graphene using deep eutectic solvents, Nanoscale research letters 10 (2015) 324.
[62] F.J. Gomez, M. Espino, M.A. Fernández, M.F. Silva, A greener approach to prepare natural deep eutectic solvents, Chemistry 3 (2018) 6122–6125.

María de los Angeles Fernández graduated from National University of Cuyo as a BS in Bromatology. Then she made her PhD in the group of Dr. Maria Fernanda Silva at the Institute of Agricultural Biology (Green Analytical Chemistry Lab) from the National Council for Research (CONICET). She has published 10 papers in the fields of Analytical Chemistry and Food Chemistry. Currently, she is an assistant researcher (UNCuyo). Her interests are extractions mediated by green solvents and the revalorization of agro food industrial wastes.

Please cite this article in press as: M.d.l.Á. Fernández, et al., Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments, Analytica Chimica Acta (2018), https://doi.org/10.1016/j.aca.2018.07.059

Joana Boiteux graduated from National University of Cuyo as a BS in Bromatology. Then she made her PhD in the group of Dr. Gabriela Lucero at the Institute of Agricultural Biology (Phytopathology Lab) from the National Council for Research (CONICET). Actually, she is carrying out her postdoctoral research in the group of Dr. Maria Fernanda Silva at the Institute of Agricultural Biology (Green Analytical Chemistry Lab). She has published 5 papers in the fields of Analytical Chemistry and Phytopathology. Her interests are green methodologies based on plant extracts for postharvest diseases.

Magdalena Espino graduated from National University of San Luis as BS in Pharmacy. Currently, she is carrying out her doctoral research in the group of Dr. Maria Fernanda Silva at the Institute of Agricultural Biology (Green Analytical Chemistry Lab). She has published 3 papers in the fields of Analytical Chemistry. Her interests are green solvents for the extraction of bioactive compounds from medicinal plants.

Dr. Federico J. V. Gomez graduated from National University of San Luis as a BS in Chemistry. Then he made his PhD in the group of Dr. Maria Fernanda Silva at the Institute of Agricultural Biology (Green Analytical Chemistry Lab) from the National Council for Research (CONICET). He has published 13 papers in the fields of Analytical Chemistry. Currently, he is an assistant researcher (CONICET). His interests are the development and characterization of disposable, sustainable and portable electrochemical sensors for food-related compounds.

María Fernanda Silva is a Professor at the National University of Cuyo and the group leader of the Green Analytical Chemistry Lab at the Institute of Agricultural Biology from the National Council for Research (CONICET). Her group is focused on the study of the biological role of plant secondary metabolites and the development of methodologies aligned with the principles Green Analytical Chemistry for the extraction and determination of analytes of food and pharmaceutical interest. The outcomes of the research activities have been presented and recognized at national and international scientific meetings and are regularly published in peer-refereed journals. She has published 70 papers in the fields of Analytical Chemistry. Her research has received support from the National Council for Research (CONICET), National Agency for Science and Technology (ANPCyT), and National University of Cuyo.

Please cite this article in press as: M.d.l.Á. Fernández, et al., Natural deep eutectic solvents-mediated extractions: The way forward for sustainable analytical developments, Analytica Chimica Acta (2018), https://doi.org/10.1016/j.aca.2018.07.059