



HAL
open science

Alternative and sustainable solvents for green analytical chemistry

Ombéline Claux, Cyrille Santerre, Maryline Abert-Vian, David Touboul,
Nadine Vallet, Farid Chemat

► **To cite this version:**

Ombéline Claux, Cyrille Santerre, Maryline Abert-Vian, David Touboul, Nadine Vallet, et al.. Alternative and sustainable solvents for green analytical chemistry. *Current opinion in green and sustainable chemistry*, 2021, 31, pp.100510. 10.1016/j.cogsc.2021.100510 . hal-03378099

HAL Id: hal-03378099

<https://hal.science/hal-03378099v1>

Submitted on 14 Oct 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

Alternative and Sustainable Solvents for Green Analytical Chemistry

Ombéline Claux^{1,2}, Cyrille Santerre^{3,4}, Maryline Abert-Vian¹, David Touboul⁴,

Nadine Vallet³, Farid Chemat^{1,*}

¹ Avignon University, INRAE, UMR 408, GREEN Extraction Team, F-84000 Avignon, France

² Pennakem Europa, 224 avenue de la Dordogne, F-59944 Dunkerque, France

³ Institut Supérieur International Parfum Cosmétique Arômes, Plateforme scientifique, 34-36 rue du parc de Clagny, 78000 Versailles, France

⁴ Université Paris-Saclay, CNRS, Institut de Chimie des Substances Naturelles, UPR 2301, 91198, Gif-sur-Yvette, France

* Corresponding author: farid.chemat@univ-avignon.fr

Abstract

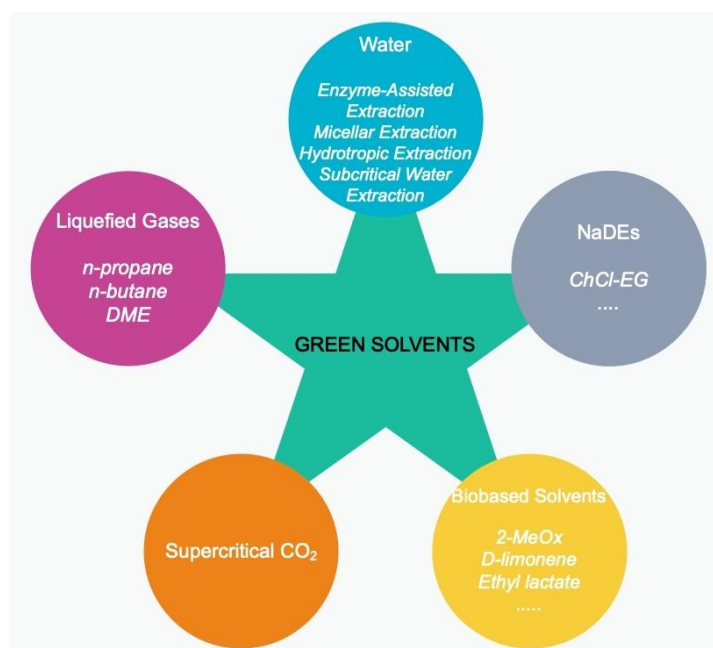
Analytical chemistry relies massively on solvents, which are generally petroleum-based and have hazardous effects. The ideal alternative solvents suitable for analysis should have high selectivity, solvency, low toxicity and low environmental impacts, be easily biodegradable and recyclable and obtained from renewable resources at a reasonable price. Obviously, finding the ideal solvent that meets all the aforementioned requirements is a big challenge. Therefore, the selection of the optimum solvent will always be a compromise depending on the extraction procedure, the analytical method, the matrix and the target molecules. In this current opinion we provide an instantaneous picture of current knowledge on alternative and sustainable solvents used in analytical laboratories either for sample preparation or analysis in terms of innovation and development of safe products and procedures.

Keywords

Alternative solvent, green extraction, green analysis, NADES, bio-based solvents, supercritical solvent, liquefied gases

28 Introduction

29 The greenest and most sustainable solvent that could be used in analytical chemistry is
 30 undoubtedly no solvent. However, both sample preparation and analytical methods require
 31 solvent, to have samples in liquid form and enable convenient separation of molecules of
 32 interest. Common solvents are principally volatile organic compounds (VOCs) obtained from
 33 non-renewable petrochemical resources and suspected to be harmful to both human health and
 34 the environment. Due to the new emphasis on environmental and safety protections and the
 35 development of green chemistry, finding alternative solvents to petroleum-derived solvents has
 36 become a major concern for analytical chemists. Therefore, sustainable alternatives are getting
 37 more and more numerous and the suitable solvent needs to be chosen wisely. This current
 38 opinion is aimed to give an instantaneous picture of current knowledge on alternative and
 39 sustainable solvents (Figure 1) used in analytical laboratories either for sample preparation or
 40 analysis.



41

42

Figure 1. Alternative and sustainable solvents

43 Alternative solvents for sample preparation

44 *Overview of alternative solvents for sample preparation*

45 The common belief is generally that water is the greenest and safest solvent, partly because it
 46 is the most abundant molecule on the Earth's surface. Water also presents the advantages of
 47 having a low economical cost, being environmentally harmless and non-toxic. The simplest and
 48 most conventional way to perform extraction using water as a solvent is maceration [1]. The

49 procedure can be optimized regarding soaking time, temperature and the repetition of several
50 extraction steps to exhaust the matrix. The properties of water can be slightly modified by using
51 specific additives. For example, the addition of enzymes can greatly improve the selectivity or
52 the efficiency of the extraction [2]. A wide range of enzymes are available with specific
53 properties, mode of action and operational conditions. Micellar and hydrotropic extractions also
54 rely on water and an additional compound, respectively a surfactant and a hydrotrope. Those
55 amphiphilic molecules can improve the solubility of hydrophobic compounds in the aqueous
56 media by respectively forming micelles and aggregates [3,4]. The main difference between the
57 two techniques is that micellar extraction resembles a two-liquid-phase extraction method
58 (above a temperature called “cloud point” micelles become instable and two phases are formed)
59 while hydrotropic extraction only involves a continuous liquid phase. Subcritical water
60 extraction (SWE) can be used to extract non-polar compounds with water as well. SWE takes
61 place at temperatures between the boiling and critical points of water, *i.e.* 100°C at 1 bar and
62 374.1°C at 221 bar, at pressures high enough to keep water in the liquid state. The polarity of
63 subcritical water is measured by the value of its dielectric constant ϵ , which decreases as
64 temperature increases. Therefore, by tuning water temperature at high pressure, its polarity can
65 be modulated to become similar to those of organic solvents in order to target specific molecules
66 of interest [5].

67 Natural Deep Eutectic Solvents (NADESs) are mixtures of natural solids (common primary
68 metabolites such as sugars, organic acids, amino acids, alcohols and choline chloride [6–8])
69 that have melting points far below those of any of their individual components. This specificity
70 is mainly due to the generation of intermolecular hydrogen bonds between hydrogen bond
71 acceptors and hydrogen bond donors. NADESs are environmentally friendly and readily
72 biodegradable as they are considered the third solvent in living cells [9]. This feature explains
73 their high solubilizing capacity for natural products. The large number of combinations that can
74 be made, their simple preparation and low cost are also major advantages that are encouraging
75 research on their extraction applications.

76 The term “bio-based solvents” gathers a lot of biomolecules that can be sorted into three
77 categories based on the agro-sector they are produced from: cereal/sugar, oleo-proteaginous
78 and wood. Bio-solvents obtained from cereal or sugar sources are mainly obtained by
79 fermentation of sweet juices and valorization of lignocellulose residues derived from cereal
80 production wastes. In this category we can find for example ethanol [10], ethyl acetate [11],
81 esters of lactic acid [12], derivatives of succinic acid, or furfural and its derivatives such as 2-

82 methyl-tetrahydrofuran also known as 2-methyloxolane (2-MeOx) [13] or cyclopentyl methyl
83 ether (CPME) [14]. The oleo-proteaginous bio-based solvents are produced from oilseeds
84 (sunflower, soybean, rapeseed). It is typically the case of fatty acid esters and glycerol
85 derivatives. The wood sector offers the possibility to produce terpene hydrocarbons such as d-
86 limonene, p-cymene or α - and β -pinene from conifers or fruit peels. Overall, a wide range of
87 bio-based solvents are currently available and each one has its own specificities and properties.
88 The selection of a particular solvent makes it possible to target specific molecules to extract
89 and analyze such as polyphenols, carotenoids, aromas or lipids.

90 Liquefied gases are gases that can be liquefied under their own vapor pressure inside a
91 pressurized container and under moderate pressure (1 to 100 bar). They offer the advantages
92 of dissolving natural substances at relatively low temperatures avoiding deterioration of
93 sensitive components and being easy to remove from the extracts due to their volatility. More
94 and more studies report the use of liquefied gases as green solvents for extraction such as *n*-
95 propane [15], *n*-butane [16] and dimethyl ether (DME) [17].

96 Supercritical fluids (SFs) are substances at conditions of temperature and pressure above their
97 critical point. Under these conditions, the fluid phase possesses characteristics between those
98 of gas and liquid phases. The main advantage of a SF is that its density (and hence its solvating
99 power) can be tuned by changing its pressure and/or temperature, permitting selective
100 extraction of target analytes. On top of that, SFs exhibit almost no surface tension making them
101 able to penetrate microporous materials and leave almost no solvent residue in the final extract.
102 Carbon dioxide (CO₂) is the most commonly used SF thanks to its moderate critical temperature
103 and pressure, *i.e.* 31°C and 74 bar. Moreover, this fluid is inert, inexpensive, non-flammable,
104 environmentally sustainable odorless and tasteless. A lot of studies report the use of
105 supercritical CO₂ for the extraction of various analytes such as essential oils, carotenoids or
106 vegetable oils [18].

107 Table 1. Examples of application of alternative solvents for sample preparation^a

Technique	Matrix	Analytes	Conditions	Analysis	Reference
Water					
Conventional maceration	Apple pomace	Polyphenols	100°C, 1 h, pH 2.5, SLR 1:5 (w/v), repeated 4 times	UHPLC-DAD, UHPLC-MS	[1]
Enzyme-assisted extraction	Tomato waste	Lycopene	40°C, 5 h, ESR 0.2 (v/w)	HPLC-DAD	[2]
Surfactant-assisted extraction	Orange peel	Pectin	7 min, 400 W, pH 1.2, LSR 21.5 (v/w), 8 g/L surfactant	FTIR	[3]
Hydrotrope extraction	Rosemary leaves	Carnosic acid	RT, 24 h, pH 2, SLR 1:10 (w/v), 30%w amphiphile solution	HPLC-UV	[4]
Subcritical water extraction	Defatted orange peels	Flavanones	150°C, 10 MPa, 10 mL/min	HPLC-UV	[5]
NADESS					
ChCl-MA molar ratio 1:1	<i>Ginkgo biloba</i> leaves <i>Panax ginseng</i> leaves	Phenolic acids Saponins	40°C, 1 h, SLR 1:20 (w/v)	HPTLC	[7]
ChCl-EG molar ratio 1:4, 10%w water	Orange peels	Polyphenols	60°C, 100 min, SLR 1:10 (w/v)	HPLC-UV	[8]
ChCl-Gly molar ratio 1:1	<i>Byrsonima intermedia</i> leaves	Polyphenols	45°C, 25 min, SLR 1:15 (w/v)	HPLC-DAD, UHPLC-MS	[6]
Bio-based solvents					
EtOH	Bilberry	Polyphenols	UAE, 24 kHz, 30 min, SLR 1:10 (w/v)	HPTLC	[10]
Ethyl acetate	Blackcurrant pomace	Polyphenols	Maceration, RT, SLR 1:100 (w/v), repeated 3 times	HPLC-DAD	[11]
Ethyl lactate	Turmeric	Curcuminoids	Maceration, RT, 30 min, SLR 1:1000 (w/v)	HPLC-DAD	[12]
2-MeOx	Lentisk fruits	Oil	Soxhlet, 45-60°C, 8 h, SLR 1:4 (w/v)	HPTLC, GC-FID	[13]
CPME	<i>Litsea cubeba</i> kernels	Oil	Reflux, BP, 3 h, SLR 1:20 (w/v)	GC-FID, GC-MS, HPLC-UV	[14]
Liquefied gases					
<i>n</i> -butane	Flaxseed	Oil	54°C, 0.5 MPa, 1 h, SLR 1:20 (w/v)	GC-FID	[16]
<i>n</i> -propane	Cashew nuts	Oil	60°C, 8 MPa, 1 h, 6%w EtOH	GC-FID, GC-MS, HPLC-MS	[15]
DME	<i>Chaetoceros gracilis</i> <i>Pleurochrysis carterae</i>	Lipids	25°C, 0.59 MPa, 45 min	GC-MS	[17]
Supercritical fluid extraction					
CO ₂	Apple seeds	Oil Phenolic compounds	40°C, 24 MPa, 140 min, flow rate 1 L/h	GC-FID, HPLC-MS	[18]

108 ^aChCl, choline chloride; MA, malic acid; EG, ethylene glycol; Gly, glycerol; MeOH, methanol; EtOH, ethanol; DMC, dimethyl
109 carbonate; 2-MeOx, 2-methyloxolane; CPME, cyclopentyl methyl ether; DME, dimethyl ether; SLR, solid:liquid ratio; LSR,
110 liquid:solid ratio; ESR, enzyme:substrate ratio; RT, room temperature; BP, boiling point; PLE, pressurized liquid extraction;
111 UAE, ultrasound-assisted extraction; UHPLC, ultra-high-performance liquid chromatography; HPLC, high-performance liquid
112 chromatography; FTIR, Fourier transform infrared spectroscopy; HPTLC, high-performance thin layer chromatography; GC,
113 gas chromatography; DAD, diode array detector; UV, ultra-violet detector; MS, mass spectrometer

114 ***Success story***

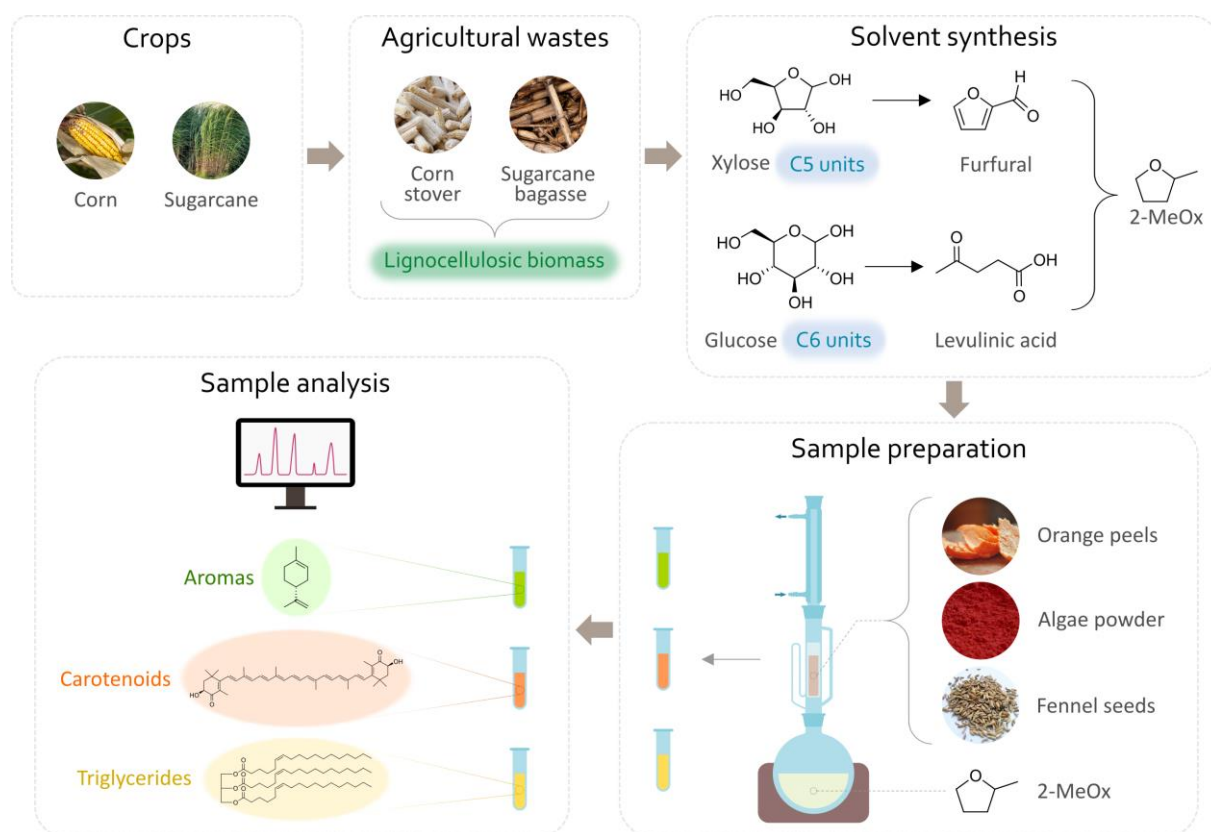
115 2-methyloxolane (2-MeOx), also known as 2-methyltetrahydrofuran, is a cyclic ether issued
116 from carbohydrates obtained from lignocellulosic biomass. 2-MeOx is produced at industrial
117 scale from agricultural wastes as corn stover or sugarcane bagasse. Its production involves three
118 steps: (i) a harsh acidic treatment of the material for deconstructing lignocellulose and release
119 pentose and hexose sugar units; (ii) a biorefining process for the conversion of C5 and C6 sugar
120 units into furfural and levulinic acid respectively; (iii) several hydrogenation reactions from
121 furfural and levulinic acid to finally obtained 2-MeOx [19].

122 Recently, the potential of 2-MeOx to extract aromas from different matrices was investigated.
123 In 2019, Ozturk *et al.* used 2-MeOx among other bio-based solvents to perform the extraction
124 of limonene from orange peel residues and compared the results to those obtained with hexane
125 [20]. At optimum conditions, it was found that 2-MeOx outperformed hexane by increasing
126 limonene extraction yield by 40%. The following year, its ability to extract volatile compounds
127 from hop cones was also demonstrated [21]. This time again the aroma yield obtained with 2-
128 MeOx (20.2%) was higher than what was obtained with *n*-hexane (17.9%) and both extracts
129 had similar compositions and olfactory profiles.

130 2-MeOx appears to be an efficient bio-based solution for preparation of color samples as well,
131 particularly in the case of carotenoids. Its efficiency was lately evaluated to recover astaxanthin
132 from *Haematococcus pluvialis* cultures [22]. 2-MeOx enabled more than 80% of carotenoid
133 recovery in only 30 min and was hence one of the most effective bio-based solvent tested in
134 this study.

135 More and more studies report the efficiency of 2-MeOx for lipid extraction, either from plant
136 seeds, fruits, microalgae, microorganisms, or even animals such as larvae. As illustrations, the
137 studies of Bettaieb Rebey *et al.* on fennel and anise oils [23], and Ravi *et al.* on black soldier
138 fly larvae lipids [24] can be cited. Briefly, the papers describe that 2-MeOx enables a higher
139 crude oil yield than the benchmark *n*-hexane and that the extracts have similar fatty acid
140 profiles. 2-MeOx also provides extracts with higher phospholipids and total phenolic contents
141 than the conventional ones.

142 Overall, the results of recent studies on the possible use of 2-MeOx for extraction purposes
143 indicate that this bio-based solvent is suitable for eco-extraction of different analytes. Therefore,
144 it could replace hazardous petrochemical solvents as *n*-hexane, chloroform, dichloromethane
145 etc. in sample preparation stages for analysis of aromas, colors or lipids.



146

147 Figure 2. 2-MeOx as a bio-based alternative solvent for sample preparation in analytical
 148 chemistry

149 **Alternative solvents for analysis**

150 *Overview of alternative solvents for analysis*

151 The most widely used chromatography technique in the literature is currently reverse phase
 152 chromatography (RPLC) using C18 columns and binary water/acetonitrile mixtures.
 153 Acetonitrile is a toxic solvent obtained as a by-product of the production of acrylonitrile, the
 154 manufacture and use of which has a high environmental cost. One of the simplest alternatives
 155 is the use of alcohol, particularly ethanol, as a substitute for acetonitrile. Dogan *et al.* [25]
 156 demonstrated in 2020 the separation of pharmaceutical compounds such as famotidine,
 157 paracetamol and thiocolchicoside with water + phosphate buffer / ethanol gradients with similar
 158 sensitivity than methods based on water/acetonitrile mixtures. Another option is to eliminate
 159 the use of acetonitrile by drastically modifying the chromatographic conditions while keeping
 160 C18 stationary phase. For example, Ali *et al.* [26] proposed the separation of terephthalic acid
 161 (TPA) contaminants (mono-, di-, and tri-carboxylic aromatic acids) by saturating the stationary
 162 phase with Tween 20 (polyoxyethylene(20)sorbitan monolaurate) and eluting the compounds
 163 under isocratic conditions with a mobile phase composed of acidified water (pH 2) by a
 164 sulphuric acid solution. Finally, the water can also be employed as a subcritical fluid. The

165 dielectric constant of water together with the surface tension and viscosity are decreasing when
166 increasing temperature from 25°C to 250°C, meaning that subcritical water at 250°C has lower
167 polarity than pure methanol or acetonitrile. Therefore, Doctor and Yang [27] described the use
168 of subcritical water with phosphate buffer at pH between 3.4 and 3.85 for the separation and
169 analysis of aspirin and metformin HCl on C18 column.

170 It is also possible to eliminate the use of water and acetonitrile in micellar liquid
171 chromatography to achieve chromatographic analysis still on C18 column. Ramezani and
172 Absalan [28] published in 2019 the monitoring of melanin concentration in milk by micellar
173 liquid chromatography using a mobile phase containing a mixture of sodium dodecyl sulphate
174 (SDS) and a mixture of choline chloride-ethylene glycol-based natural deep eutectic solvent
175 (NADES), butanol, and glacial acetic acid. NADESs were firstly introduced by Choi *et al.*
176 (2011) [29] as a third class of liquids, unlike water and lipid phase, existing in living cells, and
177 playing a crucial role as an alternative medium for biosynthesis, transport and storage of
178 compounds with intermediate polarity. Due to their liquid stability within a wide temperature
179 range, very low volatility, chemical and thermal stability, non-flammability, and nontoxic
180 constituents, NADESs are considered as green solvents. The same methodology was then used
181 for the efficient analysis of four crucial cardiovascular drugs, optimizing in both cases the
182 composition of the mobile phase using chemometric tools [30]. Thus, Raj [31] carried out a
183 screening of NADESs as alternative solvents in thin layer chromatography (TLC) in 2020. The
184 most successful mobile phase, which enabled separation of all the tested alkaloids, was the
185 equimolar mixture of menthol and phenol with a 35% addition of methanol, avoiding the
186 classical use of acetone, chloroform or diethyl ether.

187 Beyond the elimination of acetonitrile or even water as a chromatographic solvent,
188 enantioselective or normal phase liquid chromatography (NPLC) are based on non-polar and/or
189 chlorinated organic solvents from petrochemistry for elution. The most popular approach in the
190 literature to overcome these solvents, in particular alkanes such as hexane, is the use of CO₂ as
191 a supercritical fluid. Finally, agro-solvents such as limonene or 2-methyloxolane also play an
192 important role in the substitution of apolar or intermediate polarity solvents in chromatography
193 even if their report in the literature is still scarce [32].

194 ***Success story***

195 Supercritical CO₂ has a low viscosity with liquid-like densities and high solubilizing power.
196 Thus, the low viscosity and high diffusion allow separations and extractions 3 to 10 times faster
197 than in liquid chromatography with equivalent particle size, moreover reducing health and
198 environmental risks, and costs over long term. Supercritical CO₂ is miscible with alcohols, in
199 particular ethanol, allowing a green approach in analytical and preparative chromatography. In
200 the latter case, the purified samples are finally solubilized in alcohol, which requires little
201 energy to evaporate, while the CO₂ can be recycled up to 98% per cycle. Supercritical Fluid
202 Chromatography (SFC) is particularly suitable for the analysis of lipids, soluble in organic
203 solvents and in the initial chromatographic conditions. In particular, the work of the groups of
204 T. Bamba [33], M. Holcapeck [34] or D. Touboul [35] have demonstrated the capacity of SFC
205 to efficiently separate complex lipid mixtures (phospholipids, sphingolipids, glycolipids ...) by
206 subclasses with analytical retention times of about fifteen minutes, compared to about 45
207 minutes for classical NPLC methods using ternary mixtures of organic solvents (acetone,
208 hexane, ethyl acetate ...). Chollet *et al.* [35] illustrated this approach by the analysis of
209 *Nannochloropsis* extracts, considered as a promising alga for green industries due to its ability
210 to accumulate polyunsaturated fatty acids at a high level. These methods can be quantitative
211 within the limit of availability of pure standards for each lipid subclass. Beyond apolar analytes,
212 Ventura [36] has established that SFC is also efficient for the separation of crude therapeutic
213 peptides and peptide libraries when combining supercritical CO₂ elution with methanol and
214 additives such as trifluoroacetic acid and ammonia. In the field of large-scale compound
215 purification, supercritical CO₂ can be used as an eluent in flash chromatography [37], while the
216 use of liquid CO₂ in centrifugal tubes to conduct TLC has been established [38].

217 Table 2. Example of applications of alternative solvents for analysis^a

Solvent	Polarity	Proton donor	Technology	Target	Reference
Ethanol					
Ethanol/water	Polar	Yes	HPLC	Pharmaceutical drugs (famotidine, paracetamol, thiocolchicoside), Alkaloid (caffeine)	[25]
Water					
Liquid water	Polar	Yes	Micellar and sub-micellar liquid chromatography	TPA contaminants (mono-, di-, and tricarboxylic aromatic acids)	[26]
Subcritical water	Polar	Yes	SBWC	Pharmaceutical drugs (aspirin, metformin)	[27]
Eutectic solvents					
ChCl and EG	Polar	Yes	Modified micellar chromatography	Nitrogen aromatic compound (melamine)	[28]
				Pharmaceutical drugs (aspirin, atorvastatin, metformin, metoprolol)	[29]
Phenolics and terpenes	Polar and non polar	/	TLC	Alkaloids (sanguinarine, coptisine, chelerythrine, chelidonine, berberine)	[31]
Agro-solvents					
Limonene	Non polar	No	HPLC	Lipids (cholesteryl ester, phospholipids)	[32]
2-MeOx	Mid polar	No			
Carbon dioxide					
Supercritical CO ₂	Non polar	No	SFC	Lipids (fatty acids, phospholipids, MGDG, DGDG)	[33]
					[34]
				Peptides	[35]
Liquid CO ₂	Non polar	No	Flash chromatography	Fatty acid (sorbic acid), benzoic acid (4-hydroxybenzoic acid), Vitamin (niacinamide), Pharmaceutical drugs (antipyrene, ketoprofen, ibuprofen), Nitrogen compounds (N-Benzylbenzamide, 4-dimethylamino pyridine), Alkaloids (noscipin, caffeine)	[36]
			TLC	PAH (chamazulene)	[37]
					[38]

218 ^aChCl, choline chloride; EG, ethylene glycol; 2-MeOx, 2-methyloxolane; HPLC, high-performance liquid chromatography;
 219 SBWC, subcritical water chromatography; TLC, thin-layer chromatography; SFC, supercritical fluid chromatography; TPA,
 220 terephthalic acid; MGDG, monogalactosyldiacylglycerol; DGDG digalactosyldiacylglycerol; PAH, polycyclic aromatic
 221 hydrocarbon.

222 Future trends

223 The selection of the ideal solvent for analytical chemistry is a compromise between the
 224 efficiency of extraction procedure, the analytical method, the matrix specificities and the target
 225 molecules. Sustainable alternatives to common petrochemical and hazardous solvents for
 226 sample preparation and analysis have been discussed in this review. Two recent success stories,
 227 2-MeOx, for sample preparation, and supercritical carbon dioxide, for analytical separation
 228 have been particularly emphasized. However, the panorama depicted in this paper reminds us
 229 that in front of the complexity of target molecules in natural products, there is no universal
 230 solvent for analytical chemistry.

231 **References**

- 232 [1] P.A.R. Fernandes, C. Le Bourvellec, C.M.G.C. Renard, F.M. Nunes, R. Bastos, E. Coelho,
 233 D.F. Wessel, M.A. Coimbra, S.M. Cardoso, Revisiting the chemistry of apple pomace
 234 polyphenols, *Food Chem.* 294 (2019) 9–18.
 235 <https://doi.org/10.1016/j.foodchem.2019.05.006>.
- 236 [2] G. Catalkaya, D. Kahveci, Optimization of enzyme assisted extraction of lycopene from
 237 industrial tomato waste, *Sep. Purif. Technol.* 219 (2019) 55–63.
 238 <https://doi.org/10.1016/j.seppur.2019.03.006>.
- 239 [3] D.-L. Su, P.-J. Li, S.Y. Quek, Z.-Q. Huang, Y.-J. Yuan, G.-Y. Li, Y. Shan, Efficient
 240 extraction and characterization of pectin from orange peel by a combined surfactant and
 241 microwave assisted process, *Food Chem.* 286 (2019) 1–7.
 242 <https://doi.org/10.1016/j.foodchem.2019.01.200>.
- 243 [4] A. Mazaud, R. Lebeuf, M. Laguerre, V. Nardello-Rataj, Hydrotropic Extraction of
 244 Carnosic Acid from Rosemary with Short-Chain Alkyl Polyethylene Glycol Ethers, *ACS*
 245 *Sustain. Chem. Eng.* 8 (2020) 15268–15277.
 246 <https://doi.org/10.1021/acssuschemeng.0c05078>.
- 247 [5] D. Lachos-Perez, A.M. Baseggio, P.C. Mayanga-Torres, M.R. Maróstica, M.A. Rostagno,
 248 J. Martínez, T. Forster-Carneiro, Subcritical water extraction of flavanones from defatted
 249 orange peel, *J. Supercrit. Fluids.* 138 (2018) 7–16.
 250 <https://doi.org/10.1016/j.supflu.2018.03.015>.
- 251 [6] K. Fraige, R.D. Arrua, A.T. Sutton, C.S. Funari, A.J. Cavalheiro, E.F. Hilder, V. da S.
 252 Bolzani, Using natural deep eutectic solvents for the extraction of metabolites in
 253 *Byrsonima intermedia* leaves, *J. Sep. Sci.* 42 (2019) 591–597.
 254 <https://doi.org/10.1002/jssc.201800905>.
- 255 *[7] X. Liu, S. Ahlgren, H.A.A.J. Korthout, L.F. Salomé-Abarca, L.M. Bayona, R. Verpoorte,
 256 Y.H. Choi, Broad range chemical profiling of natural deep eutectic solvent extracts using
 257 a high performance thin layer chromatography–based method, *J. Chromatogr. A.* 1532
 258 (2018) 198–207. <https://doi.org/10.1016/j.chroma.2017.12.009>.
- 259 This reference is of special interest. The authors relate the development of a new analytical
 260 method for the qualitative and quantitative analysis of NADES extracts from natural
 261 products. This HPTLC-based method is then implemented to investigate the application
 262 of various NADESs with the extraction of different groups of active compounds.
- 263 [8] B. Ozturk, C. Parkinson, M. Gonzalez-Miquel, Extraction of polyphenolic antioxidants
 264 from orange peel waste using deep eutectic solvents, *Sep. Purif. Technol.* 206 (2018) 1–
 265 13. <https://doi.org/10.1016/j.seppur.2018.05.052>.
- 266 **[9] H. Vanda, Y. Dai, E.G. Wilson, R. Verpoorte, Y.H. Choi, Green solvents from ionic
 267 liquids and deep eutectic solvents to natural deep eutectic solvents, *Comptes Rendus*
 268 *Chim.* 21 (2018) 628–638. <https://doi.org/10.1016/j.crci.2018.04.002>.
- 269 This reference is of outstanding interest and considered as a key review on NADESs. It
 270 includes historical point, overview of current applications including extraction and new
 271 perspectives.
- 272 [10] H.K. Ravi, C. Breil, M.A. Vian, F. Chemat, P.R. Venskutonis, Biorefining of Bilberry
 273 (*Vaccinium myrtillus* L.) Pomace Using Microwave Hydrodiffusion and Gravity,
 274 Ultrasound-Assisted, and Bead-Milling Extraction, *ACS Sustain. Chem. Eng.* 6 (2018)
 275 4185–4193. <https://doi.org/10.1021/acssuschemeng.7b04592>.

- 276 [11] S. Farooque, P.M. Rose, M. Benohoud, R.S. Blackburn, C.M. Rayner, Enhancing the
277 Potential Exploitation of Food Waste: Extraction, Purification, and Characterization of
278 Renewable Specialty Chemicals from Blackcurrants (*Ribes nigrum* L.), *J. Agric. Food*
279 *Chem.* 66 (2018) 12265–12273. <https://doi.org/10.1021/acs.jafc.8b04373>.
- 280 [12] A.A. D'Archivio, M.A. Maggi, F. Ruggieri, Extraction of curcuminoids by using ethyl
281 lactate and its optimisation by response surface methodology, *J. Pharm. Biomed. Anal.*
282 149 (2018) 89–95. <https://doi.org/10.1016/j.jpba.2017.10.042>.
- 283 [13] E. Chaabani, M. Abert Vian, S. Dakhlaoui, S. Bourgou, F. Chemat, R. Ksouri, Pistacia
284 lentiscus L. edible oil: green extraction with bio-based solvents, metabolite profiling and
285 in vitro anti-inflammatory activity, *Oilseeds Fats Crops Lipids.* 26 (2019) 25.
286 <https://doi.org/10.1051/ocl/2019024>.
- 287 [14] X. Zhuang, Z. Zhang, Y. Wang, Y. Li, The effect of alternative solvents to n-hexane on
288 the green extraction of Litsea cubeba kernel oils as new oil sources, *Ind. Crops Prod.* 126
289 (2018) 340–346. <https://doi.org/10.1016/j.indcrop.2018.10.004>.
- 290 [15] A.B. Zanqui, C.M. da Silva, J.B. Ressutte, D.R. de Moraes, J.M. Santos, M.N. Eberlin, L.
291 Cardozo-Filho, E.A. da Silva, S.T.M. Gomes, M. Matsushita, Extraction and assessment
292 of oil and bioactive compounds from cashew nut (*Anacardium occidentale*) using
293 pressurized n-propane and ethanol as cosolvent, *J. Supercrit. Fluids.* 157 (2020) 104686.
294 <https://doi.org/10.1016/j.supflu.2019.104686>.
- 295 [16] S. Wang, Z. Zhang, T. Zhang, X. Wang, Extraction and Characterization of Flaxseed Oil
296 Obtained with Subcritical n-Butane, *J. Oleo Sci.* 69 (2020) 1011–1020.
297 <https://doi.org/10.5650/jos.ess20051>.
- 298 [17] H. Kanda, R. Hoshino, K. Murakami, Wahyudiono, Q. Zheng, M. Goto, Lipid extraction
299 from microalgae covered with biomineralized cell walls using liquefied dimethyl ether,
300 *Fuel.* 262 (2020) 116590. <https://doi.org/10.1016/j.fuel.2019.116590>.
- 301 [18] G. Ferrentino, S. Giampiccolo, K. Morozova, N. Haman, S. Spilimbergo, M. Scampicchio,
302 Supercritical fluid extraction of oils from apple seeds: Process optimization, chemical
303 characterization and comparison with a conventional solvent extraction, *Innov. Food Sci.*
304 *Emerg. Technol.* 64 (2020) 102428. <https://doi.org/10.1016/j.ifset.2020.102428>.
- 305 [19] V. Rapinel, O. Claux, M. Abert-Vian, C. McAlinden, M. Bartier, N. Patouillard, L.
306 Jacques, F. Chemat, 2-Methyloxolane (2-MeOx) as Sustainable Lipophilic Solvent to
307 Substitute Hexane for Green Extraction of Natural Products. Properties, Applications, and
308 Perspectives, *Molecules.* 25 (2020) 3417. <https://doi.org/10.3390/molecules25153417>.
- 309 [20] B. Ozturk, J. Winterburn, M. Gonzalez-Miquel, Orange peel waste valorisation through
310 limonene extraction using bio-based solvents, *Biochem. Eng. J.* 151 (2019) 107298.
311 <https://doi.org/10.1016/j.bej.2019.107298>.
- 312 [21] V. Rapinel, A. Chemat, C. Santerre, J. Belay, F. Hanaei, N. Vallet, L. Jacques, A.-S.
313 Fabiano-Tixier, 2-Methyloxolane as a Bio-Based Solvent for Green Extraction of Aromas
314 from Hops (*Humulus lupulus* L.), *Molecules.* 25 (2020) 1727.
315 <https://doi.org/10.3390/molecules25071727>.
- 316 [22] C. Samorì, L. Pezzolesi, P. Galletti, M. Semeraro, E. Tagliavini, Extraction and milking
317 of astaxanthin from *Haematococcus pluvialis* cultures, *Green Chem.* 21 (2019) 3621–
318 3628. <https://doi.org/10.1039/c9gc01273g>.
- 319 [23] I. Bettaieb Rebey, S. Bourgou, P. Detry, W.A. Wannes, T. Kenny, R. Ksouri, I.H. Sellami,
320 M.-L. Fauconnier, Green Extraction of Fennel and Anise Edible Oils Using Bio-Based

- 321 Solvent and Supercritical Fluid: Assessment of Chemical Composition, Antioxidant
322 Property, and Oxidative Stability, *Food Bioprocess Technol.* 12 (2019) 1798–1807.
323 <https://doi.org/10.1007/s11947-019-02341-8>.
- 324 [24] H.K. Ravi, M.A. Vian, Y. Tao, A. Degrou, J. Costil, C. Trespeuch, F. Chemat, Alternative
325 solvents for lipid extraction and their effect on protein quality in black soldier fly
326 (*Hermetia illucens*) larvae, *J. Clean. Prod.* 238 (2019) 117861.
327 <https://doi.org/10.1016/j.jclepro.2019.117861>.
- 328 *[25] A. Dogan, C.C. Eylem, N.E.B. Akduman, Application of green methodology to
329 pharmaceutical analysis using eco-friendly ethanol-water mobile phases, *Microchem. J.*
330 157 (2020) 104895. <https://doi.org/10.1016/j.microc.2020.104895>.
- 331 This reference is of special interest. The results of the study indicate that eco-friendly
332 ethanol and water based mobile phase can apply in pharmaceutical analysis. It also
333 reminds that the greenness of an analytical method should be evaluated from sampling to
334 detection.
- 335 [26] A. al-K.F. Ali, N.D. Danielson, Micellar and sub-micellar liquid chromatography of
336 terephthalic acid contaminants using a C18 column coated with Tween 20, *Anal. Chim.*
337 *Acta.* 1105 (2020) 214–223. <https://doi.org/10.1016/j.aca.2020.01.036>.
- 338 [27] N. Doctor, Y. Yang, Separation and Analysis of Aspirin and Metformin HCl Using Green
339 Subcritical Water Chromatography, *Molecules.* 23 (2018).
340 <https://doi.org/10.3390/molecules23092258>.
- 341 [28] A.M. Ramezani, G. Absalan, Employment of a natural deep eutectic solvent as a
342 sustainable mobile phase additive for improving the isolation of four crucial
343 cardiovascular drugs by micellar liquid chromatography, *J. Pharm. Biomed. Anal.* 186
344 (2020) 113259. <https://doi.org/10.1016/j.jpba.2020.113259>.
- 345 [29] Y.H. Choi, J. van Spronsen, Y. Dai, M. Verberne, F. Hollmann, I.W.C.E. Arends, G.-J.
346 Witkamp, R. Verpoorte, Are Natural Deep Eutectic Solvents the Missing Link in
347 Understanding Cellular Metabolism and Physiology?, *Plant Physiol.* 156 (2011) 1701–
348 1705. <https://doi.org/10.1104/pp.111.178426>.
- 349 [30] A.M. Ramezani, R. Ahmadi, G. Absalan, Designing a sustainable mobile phase
350 composition for melamine monitoring in milk samples based on micellar liquid
351 chromatography and natural deep eutectic solvent, *J. Chromatogr. A.* 1610 (2020) 460563.
352 <https://doi.org/10.1016/j.chroma.2019.460563>.
- 353 *[31] D. Raj, Thin-layer chromatography with eutectic mobile phases—preliminary results, *J.*
354 *Chromatogr. A.* 1621 (2020) 461044. <https://doi.org/10.1016/j.chroma.2020.461044>.
- 355 This reference is of special interest. This is the first study to report the successful use of
356 eutectic mobile phases for thin-layer chromatography.
- 357 [32] N. Prache, S. Abreu, P. Sassiati, D. Thiébaud, P. Chaminade, Alternative solvents for
358 improving the greenness of normal phase liquid chromatography of lipid classes, *J.*
359 *Chromatogr. A.* 1464 (2016) 55–63. <https://doi.org/10.1016/j.chroma.2016.07.083>.
- 360 [33] T. Yamada, T. Uchikata, S. Sakamoto, Y. Yokoi, S. Nishiumi, M. Yoshida, E. Fukusaki,
361 T. Bamba, Supercritical fluid chromatography/Orbitrap mass spectrometry based
362 lipidomics platform coupled with automated lipid identification software for accurate lipid
363 profiling, *J. Chromatogr. A.* 1301 (2013) 237–242.
364 <https://doi.org/10.1016/j.chroma.2013.05.057>.

- 365 [34] M. Lída, M. Holčapek, High-Throughput and Comprehensive Lipidomic Analysis Using
366 Ultrahigh-Performance Supercritical Fluid Chromatography–Mass Spectrometry, *Anal.*
367 *Chem.* 87 (2015) 7187–7195. <https://doi.org/10.1021/acs.analchem.5b01054>.
- 368 **[35] C. Chollet, S. Boutet-Mercey, L. Laboureur, C. Rincon, M. Méjean, J. Jouhet, F.
369 Fenaille, B. Colsch, D. Touboul, Supercritical fluid chromatography coupled to mass
370 spectrometry for lipidomics, *J. Mass Spectrom.* 54 (2019) 791–801.
371 <https://doi.org/10.1002/jms.4445>.
- 372 This reference is of outstanding interest. The authors provide discussion about
373 supercritical fluid chromatography including history, principles, particular focus on
374 application in the field of lipidomics and future developments.
- 375 [36] M. Ventura, Advantageous use of SFC for separation of crude therapeutic peptides and
376 peptide libraries, *J. Pharm. Biomed. Anal.* 185 (2020) 113227.
377 <https://doi.org/10.1016/j.jpba.2020.113227>.
- 378 *[37] R. McClain, V. Rada, A. Nomland, M. Przybyciel, D. Kohler, R. Schlake, P. Nantermet,
379 C.J. Welch, Greening Flash Chromatography, *ACS Sustain. Chem. Eng.* 4 (2016) 4905–
380 4912. <https://doi.org/10.1021/acssuschemeng.6b01219>.
- 381 This reference is of special interest. The authors provide a proof of principle for the use of
382 liquid carbon dioxide as a mobile phase for flash chromatography.
- 383 [38] B.W. Baldwin, T.S. Kuntzleman, Liquid CO₂ in Centrifuge Tubes: Separation of
384 Chamazulene from Blue Tansy (*Tanacetum annuum*) Oil via Extraction and Thin-Layer
385 Chromatography, *J. Chem. Educ.* 95 (2018) 620–624.
386 <https://doi.org/10.1021/acs.jchemed.7b00610>.
- 387