Received: 22 July 2020 | Revised: 28 September 2020 | Accepted: 29 September 2020

DOI: 10.1002/ansa.202000089

ANALYTICAL SCIENCE ADVANCES

WILEY-VCH

REVIEW

Extraction and derivatization for perfluorocarboxylic acids in liquid and solid matrices: A review

Monika Stróżyńska[1,2,3,4] | **Katrin Schuhen**[1,3]

[1] Wasser 3.0 gGmbH, Karlsruhe, Germany

[2] Institute for Environmental Sciences Landau, University of Koblenz–Landau, Landau in der Pfalz, Germany

[3] ABCR GmbH, Karlsruhe, Germany

[4] SAS hagmann GmbH & Co. KG, Horb am Neckar, Germany

Correspondence
Katrin Schuhen, Wasser 3.0 gGmbH, Neufeldstr. 17a-19a, 76187 Karlsruhe, Germany.
Email: schuhen@wasserdreinull.de

Funding information
German Federal Ministry for Economic Affairs; Central Innovation Program for SME

Abstract

Perfluorocarboxylic acids (PFCAs) are anthropogenic organic compounds with very unique and useful properties, for example, surfactant properties and immense stability. These substances are nowadays widely used in many industrial and consumer products. Their presence in human, biological, and environmental samples throughout the world has been described in numerous research articles. Unfortunately, PFCAs have also been found to be toxic, persistent, and bioaccumulative. Therefore, there is a great need for a constant and reliable detection of PFCAs in various matrices. Nowadays, the analysis based on liquid chromatography coupled to mass spectrometry (LC-MS and LC-MS/MS) is considered to be the method of choice. Determination of PFCAs by gas chromatography (GC) is not so well established as the LC methods. Nevertheless, GC can be considered as a complementary method, which can help to gain more reliable results and to crosscheck the LC analysis. The sample preparation is crucial, but also a time- and cost-consuming part of the PFCAs analysis. This article reviews the two most important sample preparation steps for the analysis of PFCAs: extraction and derivatization. It discusses the possible enrichment of PFCA using various extraction techniques used both for LC and GC. The derivatizing agents used prior to the GC analysis are described. The sample pretreatment as well as the most relevant problems and the sensitivity of the methods are presented. Moreover, advantages and disadvantages of LC and GC analysis are discussed.

KEYWORDS
derivatization, extraction, gas chromatography-mass spectrometry, Perfluorocarboxylic acids, PFOA, SPE

1 | INTRODUCTION

In the past years, a growing presence of the designation "PFOA-free" on cookware and outdoor clothing can be observed worldwide. Perfluorooctanoic acid (PFOA), used in the production of water-repellent non-stick coatings, is the best known and most common representative of a whole group of harmful compounds, perfluorocarboxylic acids (PFCAs). PFCAs do not occur in nature but have an anthropogenic origin. These compounds consist of a carboxyl group and a carbon chain, in which all possible binding sites are completely occupied by fluorine atoms. The most common PFCAs have a chain length of 4-14 carbon atoms. The chain length can influence their

properties, such as volatility or solubility in water.[1] The carbon-fluorine bonds are very strong (approximately C-F 460 kJ/mol),[2] which leads to the PFCA being extremely stable.[3] These compounds have several useful properties, for example, dirt, grease, oil, and water repellent. As a result, they have found many industrial as well as everyday applications. Both hydrophilic and fluorinated hydrophobic groups are present in the structure, which can cause a reduction of the surface tension. This improves the efficiency of these compounds compared to classic surfactants. Therefore, the PFCA are often referred as "super surfactants."[2]

Despite such excellent properties, the production of PFOA is forbidden in the European Union. In 2017, the EU added PFOA, its salts and certain related substances as a new entry to Annex XVII of REACH.[4] This means that from 2020 both PFOA and its salts can no longer be manufactured, used, or imported in the European Union. The ban also applies its precursor compounds. The reasons for this are their widely described negative effects on human health. PFOA and other PFCAs bind to proteins in the blood, liver, and kidneys and have a long residence time in the human body.[5] Neurotoxicity, reproductive, and developmental toxicity of PFOA have been proven.[6] Environmental Chemicals Agency (ECHA) has classified PFOA as toxic after repeated exposure, carcinogenic, and toxic for reproduction.[7] PFCAs have been detected in blood and serum samples worldwide.[8–10] Everyone can come into contact with PFCAs because these compounds are found in many everyday products. PFCAs have been detected in leather, outdoor textiles, baking paper,[11] upholstery, dental floss,[12] impregnation agents, fire extinguishing foams, and pesticide solutions.[13] PFCAs have also been detected in vegetables, fish, meat, dairy products, and cereals.[14–17]

Like all human-made substances, PFCAs also end up in the environment. One of the main sources of PFCAs pollution is the manufacture of fluoropolymers. Usually, the concentrations of PFCAs for industrial applications are in the range of 100 and 5000 ppm.[18] Further sources of PFCAs in the environment are the PFCAs precursors. It has been proven that fluorotelomer alcohols (FTOH) are degraded to perflurocarboxylic acids.[19,20] The concentration of PFCAs in surface soils was examined worldwide and quantifiable amounts of PFCAs were observed in all samples.[21] Many studies have shown the presence of PFCAs in various waters, for example in river,[22] sea,[23] and drinking water.[24]

Therefore, it is crucial to apply reliable analytical methods for detection and quantitative determination of PFCAs in both environmental samples and everyday products. Sample preparation is very important, but often also the most time-consuming step for correct PFCAs analysis. It can greatly affect the reliability and accuracy of the result. This includes clean-up, filtration, drying, derivatization, and various extraction procedures. This review focuses on two most applied processes: extraction (with simultaneous enrichment) of the analytes from the matrix and the derivatization, which is indispensable for gas chromatographic determination. Figure 1 shows general workflow for the analysis of samples containing PFCAs. It presents a simplified schema, which can be expanded and modified depending of the matrix complexity and concentration of the analytes.

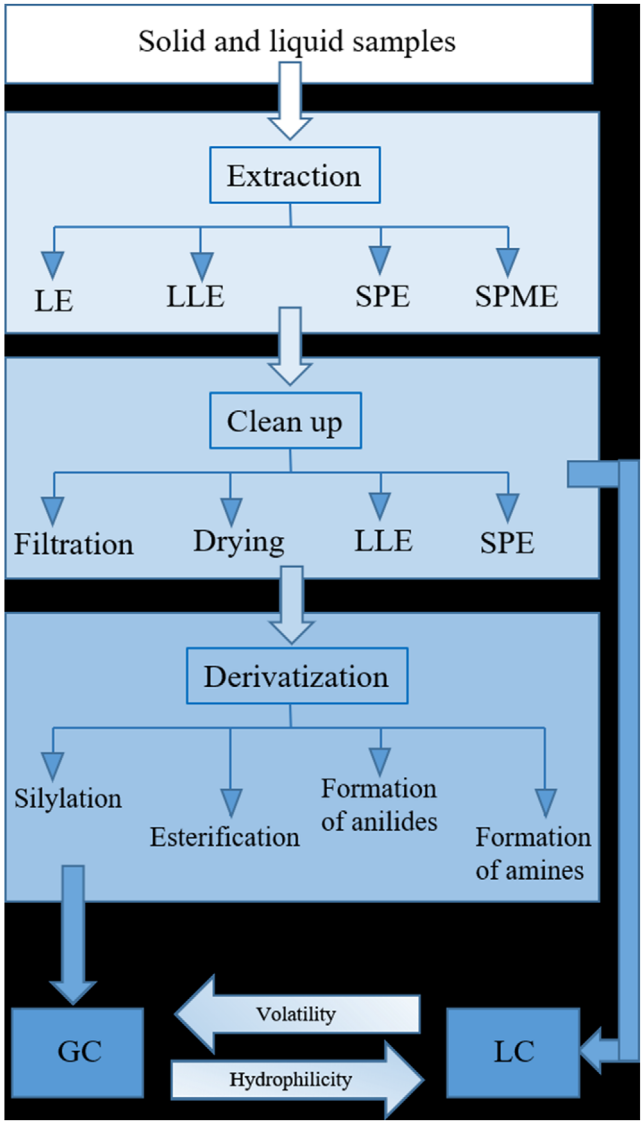

FIGURE 1 General workflow for the analysis of PFCAs in solid and liquid samples

2 | LIQUID CHROMATOGRAPHY AND GAS CHROMATOGRAPHY ANALYSIS OF PFCAS

Nowadays, liquid chromatography coupled with mass spectrometry (LC-MS) is the method of choice for the analysis of PFCAs. Numerous articles have been written on PFCAs detection in various matrices using LC-MS. These include biological samples such as serum,[25] blood, plasma,[10] animal tissue,[26] and plants.[27] In addition, aqueous samples were analyzed in many studies. LC-MS systems were helpful for the determination of PFCAs in water from the ocean[28] and in the analysis of river water,[22] drinking water,[24] as well as for more complex matrices, like effluent from sewage treatment plants.[29] The detection limits are usually in the range of microgram per liters and nanograms per liter.[30] In general, LC-MS and LC-MS/MS are effective and well established methods for PFCAs analysis. Moreover, a standard method (DIN) for the determination of selected polyfluorinated compounds (including

PFCAs) in water, wastewater, and sludge is available online. However, there are some drawbacks of LC-MS. First of all, there is no commercial, standardized mass spectra library for LC-MS.[31] Therefore, empirical libraries are usually used for the results interpretation. For this reason, the LC-MS is used more for target analyses and not for the non-target screening. A well-known problem in electrospray ionization (ESI), as is commonly used in LC-MS, is the ion suppression [131]. The background contamination during LC-MS analysis of PFCAs must also be taken into account. It has been found that internal LC parts and the Teflon® Septa built into the device can cause additional PFCAs signals. Shimadzu presented an application note, where a precolumn was installed between the mixer and the sample injector, so that the PFOA contaminants were eluted from the sample after PFOA analyte.[32] Yamashita et al successfully modified the LC-MS system to achieve detection limits in the range of parts per quadrillion.[28] Teflon HPLC tubing was replaced with stainless steel and polyetheretherketone (PEEK) tubing. Moreover, degasser and solvent-selection valves were isolated from the HPLC system. The autosampler vials with Teflon-lined cap were also replaced and only polyethylene caps were used. Despite the application of LC-MS, Ahrens et al also reported no instrumental blank contaminations. They used Teflon-free SPE-manifold as well as valves and tubes made of polypropylene.[33] Moreover, to eliminate instrumental blank contamination, the HPLC system was modified in the same way, as proposed by Yamashita et al.[28] The GC-MS analysis of PFCAs is also not always free of background signals. For example, Stróżyńska and Schuhen presented a GC-MS method for the detection of PFCAs and described the presence of background signals from the water purification systems.[30] Before the analysis, all potential sources of contamination must be identified and eliminated.[28]

The most important advantage of gas chromatography over LC is its resolution power. Therefore, it can be very useful for the identification of PFCAs branched isomers, which can probably not be separated using a common LC-MS system. Perfluorinated acids are manufactured mostly in two industrial synthetic routes: electrochemical fluorination (ECF) and telomerization.[34] The ECF process usually results in a mixture of structural isomers. Therefore, the PFCAs isomers are widely distributed in the environment and a GC-MS analysis could provide important information about the source of contamination.

However, the GC determination of PFCAs has also some drawbacks such as high detection limits, a small range of analytes, and long analysis time.[35] Moreover, the necessary derivatization step can cause loss of analytes and additional contamination. For the GC-MS analysis, the samples should be water-free. The presence of water causes strong deterioration in detector sensitivity. Therefore, the samples must be extracted into an organic solvent.

3 | EXTRACTION OF WATER SAMPLES

An analysis of the polar organic trace substances such as PFCAs is challenging, because these compounds often cannot be easily separated from the aqueous matrix. The recovery rates of many polar analytes using LLE are low, because they have a relatively high partial solubility in water.[36] For this reason, adequate sample preparation is one of the most important and sometimes the most complex part in the analysis of environmental samples.[37] Commonly used extraction methods include: liquid-liquid extraction (LLE), solid-phase extraction (SPE), and solid-phase micro extraction (SPME) in various versions and combinations.

LLE is one of the oldest extraction methods, which is based on the different solubility of the substances in these two liquid phases. The often used organic solvents include hexane, dichloromethane, or toluene, but other extraction agents such as ionic liquids can also be used.[38] As early as 1980, Belisle and Hagen used a hexane/ether mixture as an extracting agent for serum and plasma to detect PFOA.[39]

When extracting perfluorocarboxylic acids from water, the use of ion pair solutions is very effective (ion pair extraction, IPE). Quaternary ammonium compounds, such as tetrabutylammonium salts, can be used to form an ion pair with PFCAs and to transport them into the organic phase.[40–43] IPE method was originally developed by Ylinen et al.[42] Motas Guzmann et al applied tetrabutylammonium hydrogen sulfate (TBAHS) for the extraction of PFCAs and derivatized the sample with isobutyl chloroformiate. The limits of quantification (LOQ) for the analyzed breast milk samples were relatively high: 10 ng/μL for PFOA and PFNA, 12 ng/μL PFDA and 15 ng/μL for PFUnDA and PFDoDA, respectively.[41] Orata, Quinete, and Wilken[43] used tetrabutylammonium hydroxide as a counter ion for the reaction of PFCAs with benzyl bromide. The LOQ of their GC-MS method did not have the sensitivity to study potential human exposure but was applicable to contaminated environmental samples (0.2 μg/L PFOA). Developed by González-Barreiro et al, LLE method for perfluoroalkyl substances in the effluent from the sewage treatment plant was compared with SPE at two different pH values. The LLE method gave the best results for PFCAs with chain lengths less than seven carbon atoms, while the SPE method in the experiments was best suited for perfluorocarboxylates with >10 carbon atoms in the chain. The detection limit for both methods was in the same range (0.2-0.6 ng/L).[44]

Modern LLE applications are mostly micro-extraction techniques. Goh *et al* developed a hollow fiber LPME (HF-LPME) for the analysis of PFCAs in water. Detection was carried out using a UHPLC-MS/MS system and the presented linearity range was between 5 and 10 000 ng/L.[45] This method could be rapid and efficient possibility for real-time monitoring of contaminants in environmental waters. Hu et al used dispersive LLME (DLLME) for the analysis of PFCAs in river and lake waters.[46] The aim of the authors was to develop rapid, efficient, and eco-friendly method for the analysis of PFCAs in aqueous matrices. However, the limits of quantification in the range of 2.7−9.0 ng/mL are relatively high compared to the typical concentrations of PFCAs in the environment. Liu et al presented the determination of PFCAs in water using DLLME with tetrabutylammonium hydrogen sulfate as ion pair reagent.[47] Detection limits were achieved at the level of 37-51 pg/mL. This procedure is relatively simple, but has some limitations, such as differences in the efficiency of extracting compounds with different chain lengths. However, the further development of this method for micro-extraction can reduce the consumption of environmentally harmful solvents.

A further frequently applied extraction technique for PFCAs is SPE. This technique enables the analytes to be enriched and isolated from the matrix at the same time. It can be also used as a clean-up step for complex matrices.[48] The SPE process usually starts with conditioning followed by passing the aqueous sample through the solid sorbent. After adsorption, the phase is washed and the elution with a suitable solvent is carried out. The SPE phases are available in the form of cartridges, 96-well microplates, SPE disks or as a Micro Extraction by Packed Sorbent (MEPS) in the syringe. Choosing the sorbent and elution solvent is a crucial step for the successful SPE process. The interactions between sorbents and analytes are nonpolar (Van der Waals forces or dispersion forces), polar (hydrogen bonds, dipole-dipole, and induced dipole-dipole), ion exchange (ionic), and covalent interactions.[49] Reverse phases, normal phases, ion exchange, or so-called mixed mode materials are available on the market.

One of the most commonly used solid phases for water analysis is a chemically modified silica gel with octadecyl groups (C18 phase).[48] Polymer-based materials (styrene/divivinylbenzene)[50] and ion exchanger are also frequently used. The detection limits using SPE are usually in the low nanogram per liter range.[51,52] Extremely low detection limits of 0.01 ng/L could be obtained for large volumes of drinking water (20-40 L).[53] For the ion-exchange SPE, the sorbents with weak and strong cation and anion functional groups can be applied. Among them, weak anion exchangers are usually used for the adsorption of perfluorocarboxylic acids. Three examples of commonly used for this purpose commercial phases are: Strata-X-AW (Phenomenex), Oasis WAX (Waters), and Chromabond HR-XAW (Macherey-Nagel).[54] Usually, the PFCAs are eluted after the adsorption with 0.1% NH_4OH solution in methanol. Sample preparation according to DIN for the analysis of PFCAs in water using HPLC-MS/MS is carried out in the same way.[55] SPE was used to extract PFCAs from various samples, such as serum,[25] effluent from the sewage treatment plant,[33] ice samples,[56] drinking water, and surface water.[1] Moody and Fields used SPE in 1999 to detect PFOA in groundwater. The detection limit was 18 µg/L.[57] They used Empore™ strong anion exchange disks to extract PFCAs from groundwater collected from fire-training facilities. The use of SAX,[76] WAX,[54] and C18[78] as SPE phases for PFCA has been described in the literature.

SPE can be also carried out without SPE cartridges. Strozynska and Schuhen modified the classic ion exchange solid phase extraction for PFCAs (DIN 38407-42) and adapted it for the newly developed derivatization method. Instead of SPE cartridges, Strozynska and Schuhen used the common weak-ion-exchange SPE phase and carried out a dispersive SPE (d-SPE) direct in the water sample. The method was successfully applied for relatively clean matrix like effluent from a wastewater treatment plant. However, more complex matrices with a high amount of solid particles require additional clean-up. The QuEChERS (quick, easy, cheap, effective, rugged, and safe) sample preparation method also uses d-SPE. However, in the classic QuEChERS, d-SPE is only used as a clean-up step. The homogenized sample is driven into an organic solvent by the partitioning power of a blend of salts. However, there is an example of the extraction of PFCAs with this method. Li *et al* used a modified QuEChERS procedure to the extraction and concentration of perfluorinated compounds as well as for removal of interferences.[58]

A further technique, which is applicable for the extraction of PFCAs, is SPME. This simple, powerful, and innovative extraction method was invented by Prof. Janusz Pawliszyn in the early 1990s.[59] With this technique, the analytes are adsorbed on a coated quartz fiber, which enables them to be separated from the matrix and simultaneously enriched. The fiber is coated with a sorption material that is adapted for target analytes. The coatings that are most commonly used include polydimethylsiloxane (PDMS), carboxen, and polyacrylate (PA). After adsorption, the SPME fiber is placed in the injection port. Due to the high temperature of the injector (GC) or solvent (LC), the analytes desorb and can be measured.[60] A simple method using ion-pair SPME[61] has been developed for perfluoroalkyl acids. The sample was derivatized in the injector and measured by GC-MS-NCI. The achieved quantification limits ranged from 0.05 µg/L (perfluorodecanoic acid) to 2.5 µg/L (perfluoroheptanoic acid). Montelone et al[62] have developed a headspace-SPME method for aqueous samples. Applying CAR/PDMS fiber and derivatization with chloroformiates, they achieved good detection limits of 0.17-14.3 ng/L. However, no PFCAs were found in any of the six examined river water samples.

As described Alzaga and Bayona, the PDMS fiber does not present drawbacks of PFCA contamination as in SPE. Unfortunately, the SPME methods have some disadvantages. Because the manual injection is very laborious, the GC-system should be equipped with special SPME-auto sampler, if the analysis is carried out routinely. Moreover, the SPME-fibers are relatively expensive - the prices are usually in the range of few hundred dollars. The fibers can also be very brittle and there is a limited number of extractions, which can be carried out with one fiber.

4 | EXTRACTION OF SOLID SAMPLES

The extraction technique used for solid samples depends on the matrix. The easiest way to extract PFCAs from a solid sample is solid-liquid extraction. This process can be supported by pressure (PLE), heating, or sonication. Alternatively, a headspace-SPME can also be used to extract the PFCAs. In the solid-liquid extraction process, the soluble components are separated from a solid sample. The sample is shaken out with an organic solvent (methanol, MTBE) and/or heated in order to transport the analytes to the liquid phase as quickly as possible.

In an extensive study of 116 articles for EPA, Guo et al[12] extracted all solid samples in methanol for 24 h. Rat tissue,[63,64] soil, sediment, and plants were also prepared using this method.[65,66] Methanol was also used for the extraction of suspended matter in an ultrasonic bath.[67] Kotthoff et al analyzed 115 everyday products, including textiles, carpets, baking paper, and ski waxes. Depending on the matrix, they used sequential extraction, SPE with weak anion exchangers, and ion pair extraction.[11] As solvent, acetone, hexane or methyl *tert*-butyl ether were used. Herzke et al,[15] Vestergren et al,[14] and Fujii et al. used the ion pair extraction to extract PFCAs from vegetables and other foods. The detection of PFCA with chain length from six to fourteen described

by Vestergren *et al.*[14] employed not only IPE but also subsequent solid phase extraction clean-up on Florisil and graphitized carbon. In the method described by Fuji *et al.*[68] the extracts were only centrifuged and no further clean-up was conducted. Henderson *et al.* applied tetrabutylammonium hydrogen sulphate as ion pair reagent in the analysis of mouse serum and liver homogenates. Quantification limits in this research were below 50 ng/mL for perfluorooctanoic acid and perfluorononanoic acid.[40] The advantage of this method is the simultaneous determination of derivatized PFCAs with fluorotelomer alcohols. However, the measurements were carried out in single ion measurement (SIM) mode. Therefore, the method cannot be applied for nontarget screening. Moreover, diazomethane, which was used in this research as a derivatizing agent, should be avoided because of its toxicity. The ion pair liquid extraction was also used for liver samples from polar cod and ice gulls. In this experiment, the measurements were carried out with HPLC and therefore no derivatization was needed. The method detection limits (MDL) for PFCA ranged from 0.22 (PFHxDA) to >15 ng/g wet weight.[26] Pressurized liquid extraction (PLE) was used for packaging materials.[69,70]

The headspace-SPME can be also applied for the extraction of PFCAs. In contrast to the classic SPME method, the fiber in HS-SPME is not in direct contact with the sample. The sample is placed in a tightly closed glass and heated. The analytes are evaporated and transferred to the gas phase. The SPME fiber is placed in the same vessel so that the analytes from the gas phase can be adsorbed on the fiber. Subsequently, a thermal desorption takes place in the GC injector. HS-SPME was used, for example, for sediment samples in combination with PLE.[71] In this research, the SPME was carried out on polydimethylsiloxane (PDMS) fiber. First, a freeze-dried, homogenized sediment was extracted with organic solvent mixture. Then, the extracts were dried (rotary evaporation and N_2 stream) and a metallic clip, working as a magnetic stirrer, was added to the sample. Once the sample was sealed, a negative pressure was applied into the vial and the boron trifluoride derivatizing reagent was added. After the derivatization reaction took place, water saturated with NaCl was added and a headspace-SPME was carried out. Achieved LOQ for PFOA and PFDA in sediments were 2.3 and 1.6 ng/g, respectively.

A more complex method, an extraction with supercritical fluids, the HS-SPME (SFE-HS-SPME) was developed by Liu et al.[72] This method has been successfully used to analyze PFCAs in sediments from rivers and beaches near industrial areas. The use of SPME enables the detection of PFCAs in the nanogram per liter range.

5 | DERIVATIZATION OF PFCAS PRIOR TO GC-MS ANALYSIS

GC-MS can be an alternative and/or supplement to the LC systems. There are numerous publications on PFCAs analysis using GC-MS.[35,51,53,62,68,69,73] Although the boiling points of PFCAs are approx. 40-50°C lower than those of the corresponding carboxylic acids with an equivalent number of carbon atoms, they cannot be analyzed directly by GC.[35] Due to the low volatility of perfluorocarboxylic acids, the samples must be derivatized. This will convert the COOH group into a less polar derivative. Alkyl and silyl ester derivatives are most frequently formed, but the formation of benzyl esters and thioesters have also been described in the literature. The derivatization reactions and their use are summarized in Table 1.

For the formation of methyl esters, mostly diazomethane, methyl iodide and a mixture of BF_3/methanol are used. Chloroformates, a group of esters of chloroformic acid, are also used as derivatizing agents in combination with the corresponding alcohols. Perfluorocarboxylic acids form propyl, isopropyl, butyl and isobutyl esters in the reaction with these compounds. Motas Guzmann et al[41] applied relatively simple derivatization with isobutyl chloroformiates. Briefly, the extracts were evaporated to dryness and dissolved in acetonitrile. Then, pyridine, isobutyl alcohol, and isobutyl chloroformiate were added to the sample. After stirring in an ultrasonic bath and subsequent extraction with hexane, the samples were analyzed. This is a typical procedure for the derivatization of PFCAs with chloroformiates, which was adopted from the method described by Dufková et al.[52,74] The detection limits reported by Dufková were in the range of micrograms per liter for GC-EI-MS[74] and nanograms per liter for GC-NCI-MS.[52] Currently, there are no published, optimized methods for ethyl ester derivatives. A comparison between the reagent mixtures ethyl chloroformate/ethanol and propyl chloroformate/propanol was described. The reaction with propyl chloroformate/propanol achieved significantly higher signals for all analytes.[62] Figure 2 shows the derivatization reactions with propyl chloroformiate and benzyl bromide.

N, *N*′-dicyclohexylcarbodiimide (DCC) is frequently applied as a catalyst, for example, by derivatization with 2,4 difluoroaniline. The products of this reaction are 2,4-difluoroanilides of PFCAs. This reaction takes place in the presence of a catalyst. This method consists of several sample preparation steps: pH adjustment, shaking, phase separation and washing the organic phase with HCl, $NaHCO_3$, and NaCl solution. The phase is then passed through a filter with Na_2SO_4 and evaporated to dryness. The residues are dissolved in a hexane-diethyl ether mixture. A further cleaning is then carried out on the silica gel column. After elution with hexane, the sample is evaporated and analyzed.[53,75] The aim of the research of Li and Sun was cost-effective detection of PFCAs using GC-MS. They applied solid phase extraction and anilide derivatization for surface water samples.[76] However, the method is not simple. The presented derivatization procedure is similar to this described above: pH adjustments, addition of NaCl and ethyl acetate, re-extraction, washing, drying with Na_2SO_4, and evaporation under nitrogen.

The formation of benzyl ester consists of two steps: First, an ion pair of tetrabutylammonium cation and acid residue anion is formed, followed by alkylation with benzyl bromide (80°C, 15 min). The organic phase is evaporated and dissolved in dichloromethane.[42] Ylinen et al applied this method only for PFOA detection, achieving detection limits of 1 µg/mL in plasma and 0.1 µg/mL in urine.[42] This was one of very early methods of the PFOA analysis (1985). The continuation of this research was presented in 2009, achieving LOQ of 0.3 µg/g and 0.2 µg/L for PFOA in fish muscles and water samples, respectively.[43] However, the fish muscles sample preparation was very laborious.

TABLE 1 Derivatization reactions and extraction techniques used for the analysis of PFCAs

Derivatizing agent	Sample	Extraction	Analysis	Source
Formation of methyl esters				
BF3/Methanol	Sediment	HS-SPME	GC-MS NCI	71
Diazomethane	Rats tissue	LE	GC-ECD	63
Diazomethane	Plasma, urine and liver tissue	LE	GC-ECD	39
Diazomethane	Serum, liver tissue	IP-LE	GC-MS EI	40
Diazomethane	Soil, sediment, plants	LE	GC-MS NCI	66
Methyl iodide	Groundwater	SPE	GC-MS EI, GC-MS NCI	57
Formation of propyl esters				
Propyl chloroformate	Surface water	HS-SPME	GC-MS/MS NCI	62
Formation of isopropyl esters				
Isopropanol	–	–	GC-MS NCI	73
Formation of butyl esters				
Tetrabutylammonium	WWTP (Waste water treatment plants) Effluent, Sea water	SPME	GC-MS NCI	61
Tetrabutylammonium	Surface water	DLLME	GC-MS/MS NCI	47
Butanol	Sediment	HS-SPME	GC-MS/MS NCI	72
Formation of isobutyl esters				
Isobutyl chloroformate	Breast milk	IP-LLE	GC-MS EI	41
Isobutyl chloroformate	WWTP effluent and influent	SPE	GC-MS EI	51
Isobutyl chloroformate	Urine	SPE	GC-MS EI	81
Isobutyl chloroformate	Surface water	–	GC-MS EI, GC-ECD	74
Isobutyl chloroformate	Surface water	SPE	GC-MS NCI	52
Isobutyl chloroformate	River and lake water	DLLME	GC-MS EI	46
Formation of benzyl esters				
Benzyl bromide	Plasma, Urine	IP-LLE	GC-MS EI, GC-FID	42
Benzyl bromide	Rats tissue und serum	LE	GC-MS NCI	64
Benzyl bromide	Surface water, fish	IP-LLE	GC-MS EI	43
Benzyl bromide	Food	IP-LLE	GC-MS NCI	68
Formation of silyl esters				
BSTFA	Packaging, textiles	PLE	GC-MS EI	69
BSTFA	Soil	LE	GC-MS EI	65
TESiOH	WWTP effluent	SPE	GC-MS-EI	30
Formation of difluoroanilides				
2,4-Difluoroaniline	Water	LE	GC-MS EI, GC-FID	82
2,4-Difluoroaniline	Serum	IP-LLE	GC-MS NCI	9
2,4-Difluoroaniline	Bear liver	IP-LLE	GC-MS EI	75
2,4-Difluoroaniline	Surface water, sediment	SPE	GC-MS EI	53
2,4-Difluoroaniline	Surface water, biological samples	IP-LLE	GC-MS NCI	34
Formation of amines				
DMF-DMA	Dental floss, sediment	LE	GC-MS-EI	77

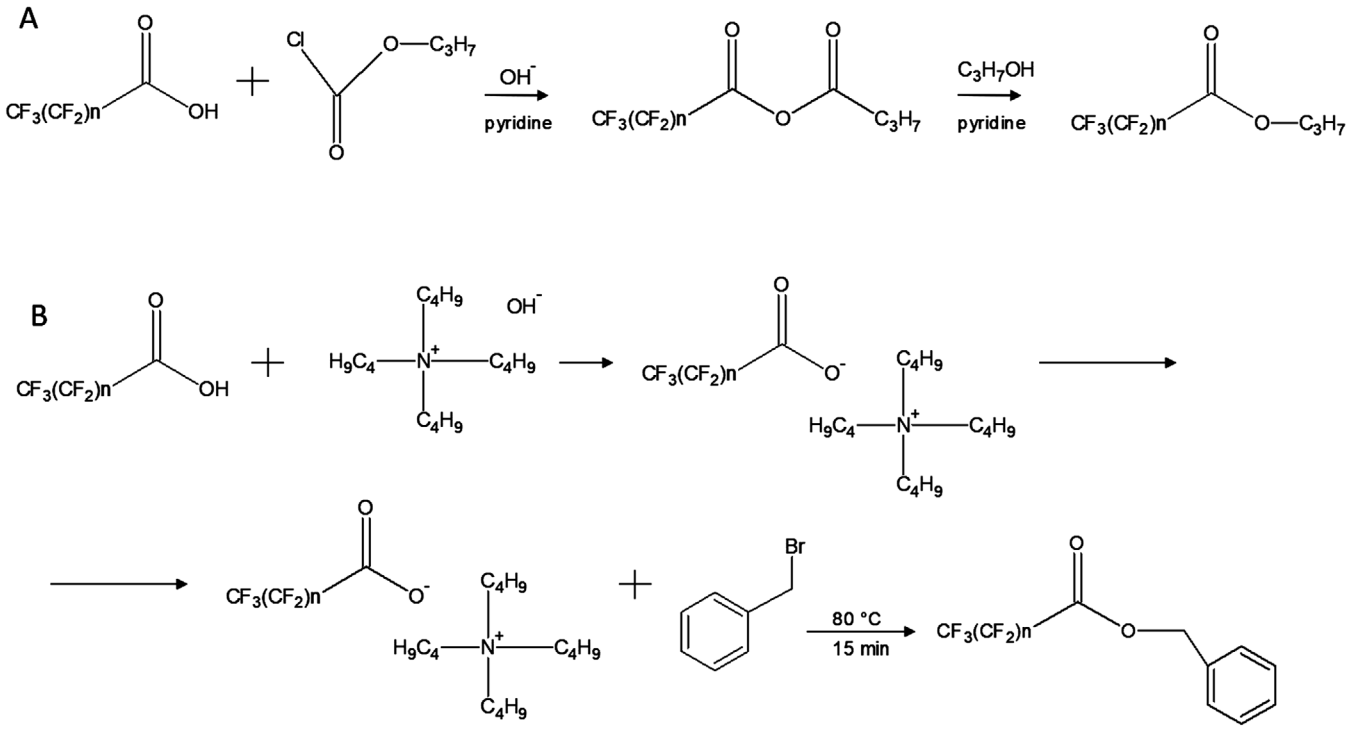

FIGURE 2 Reactions of PFCA with propyl chloroformiate (A) and benzyl bromide (B)

After homogenization of the muscles, the sample was dissolved in tetrabutylammonium solution (adjusted to pH 10) and carbonate buffer. The next steps were the three-stage extraction with MTBE, enrichment, addition of methylene chloride, and clean-up. Sample extracts were cleaned up using activated silica and eluted with acetone. The acetone fraction was evaporated to dryness at room temperature under a stream of nitrogen. The residue was dissolved in acetone and benzyl bromide solution. After 15 min at 80°C, the sample was evaporated to dryness and dissolved in methylene chloride for GC analysis. Fujii et al[68] modified this method and applied it successfully in 2014 for the analysis of dietary samples. There was no sample clean-up with silica, and the reaction was carried out for 1 h at 60°C. The method had a low detection limit (0.3-10 pg/g) for PFCAs with eight to 14 carbon atoms.

A silylation reaction for PFCAs using BSTFA was successfully applied for packaging materials, textiles,[69] and soil samples.[65] BSTFA was added to the extract and the reaction was carried out at 40°C in a water bath for 60 min. After cooling, the sample was dissolved in dichloromethane. However, the temperature program must be carefully optimized for the analysis of PFCA. It was shown that, in the HP5 column, the peak of PFOA-TMS derivative can have the same retention time as the BSTFA and it can make the analysis impossible.[77] Moreover, the sample must be absolutely water-free, because the moisture decomposes BSTFA. There is also another silylation method, which is not moisture sensitive. Strozynska and Schuhen developed a new silylation reaction for perfluorocarboxylic acids (PFCAs, C3-C12), which takes place directly in water.[30] The method is based on an acid-catalyzed esterification of PFCAs with triethylsilanol. During the reaction, a triethylsilyl ester is formed that can be easily analyzed by GC-MS. The method was applied for effluent from wastewater treatment plant with LOQ 4-48 ng/L depending on the actual PFCA. This reaction was also carried out with other acids, which are not fully fluorinated.[78] The analytes examined included PFOA, octanoic acid, and polyfluorinated carboxylic acids. It could be shown that for a successful TESiOH reaction, the alpha-C atom of carboxylic acid must be linked to strongly electronegative substituents. The compounds in which the COOH group is directly connected to a CF_2 group react completely and form triethylsilyl esters. The compounds that contain a CH_2 group instead of a CF_2 group react only partially, so that the unreacted acid is visible on the chromatogram.[78]

Another new interesting reaction of PFCAs is derivatization with dimethylformamide dimethyl acetal (DMF-DMA).[77] The method was developed for the analysis of PFCAs in solid samples by GC-MS and is very simple. After extraction with MTBE, the samples were mixed with derivatizing agent and injected into GC. The method provides separation of nine PFCAs (C4–C12) in 15 min and is characterized by good precision (max. RSD = 6.21%), linearity and detection limits in the range of 0.15-0.38 ng/mL. The derivatization reaction takes place in hot GC injector forming corresponding *N,N,N′,N′*-tetramethyl diamines. A structure of perfluorocarboxylic acid derivatives formed in this reaction with *N,N*-dimethylformamide dialkylacetals was extensively explained using several techniques of mass spectrometry.[79] In contrast to carboxylic acids, perfluorocarboxylic acids are not able to form alkyl esters as the main product in this reaction. Perfluorooctanoic acid forms a salt with *N,N*-dimethylformamide dialkylacetals. This salt undergoes a further reaction inside the injection block of

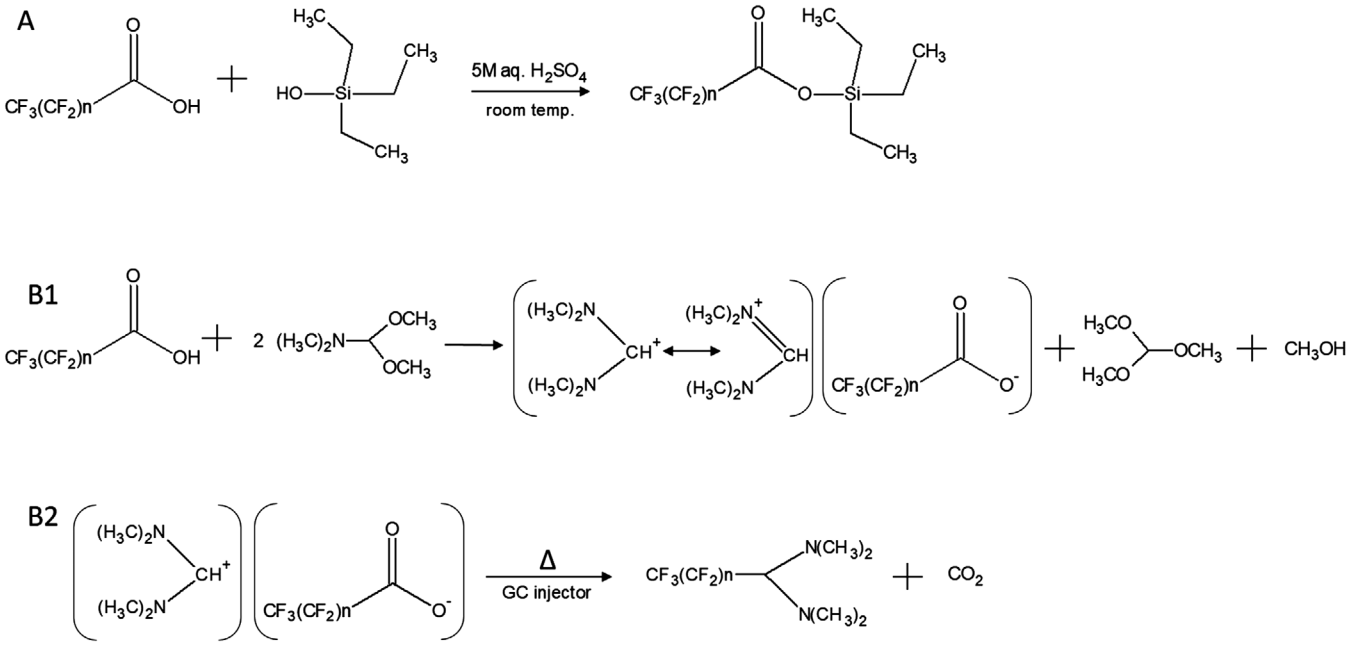

FIGURE 3 Reactions of PFCA with triethylsilanol (A) and DMF-DMA (B)

a GC by loss of CO_2 and then forms 1,1-perfluorooctane-(*N,N,N,N*-tetramethyl)-diamine. This method was successfully applied for dental floss extracts and sediment. Figure 3 shows the derivatization reactions with triethylsilanol and DMF-DMA.

6 | SUMMARY AND OUTLOOK

The continuous development of the analytical devices results in more rapid, robust, and sensitive analytical measurements. However, the progress in sample preparation techniques is much slower than the progress in GC and LC manufactures. The extraction of the analytes follows the same laws of physics and chemistry as a hundred years ago. For the extraction and derivatization, mostly the same or only slightly modified methods have been used in publications for 20-30 years. The achievement of better resolution and sensitivity is mostly caused by using more complex, expensive but also more sensitive analytical devices. Nowadays, most articles about method development describe the application of the newest, high-end devices with immense sensitivity. The research based on low-cost, commonly available devices does not arouse such interest, because the detection limits are higher than the LOD achieved with more complex and expensive devices. However, if the derivatization works and is used for the analysis with simple, single-quad GC-EI-MS, it is also applicable for more complex and sensitive devices. Therefore, the detection limits can be easily improved and such research should get more attention.

The high resolution of GC systems can be very useful for the analysis of the PFCAs isomers. However, there are only a few publications about detection of PFCAs isomers by GC-MS. Stróżyńska and Schuhen presented the separation of perfluorononanoic acid and its branched isomer after derivatization with triethylsilanol.[30] De Silva et al[75] used 2,4-difluoroaniline for the separation of PFOA isomers, which took place between 87 and 99 minutes on the GC-chromatogram. Naile et al showed a method to detect PFCAs isomers, but the retention time of the last analyte (perfluorododecanoic acid) was 340 min.[66] Nowadays, this separation can be also achieved with LC-MS systems. For instance, Pellizzaro *et al*. presented the separation of PFOA and its isomer in less than four minutes using UHPLC system.[80]

There is a great need for further improvement in extraction, enrichment and derivatization. A significant trend to minimize the amount of solvent and other chemicals used in the analytical chemistry can be observed. The microextraction techniques will certainly be further developed to meet the requirements of green chemistry and minimize the costs of the analysis. The extraction devices are nowadays smaller and more compact. There is no place for liquid extraction with a few litres of solvent in modern analytical chemistry. On the other hand, very complex derivatization reactions with many sample preparation steps and toxic reagents are still applied in laboratories worldwide. The simplification of these methods is crucial to reducing the cost of the analysis and to making GC an equivalent alternative to LC-MS systems in the analysis of PFCAs.

ACKNOWLEDGMENTS

The research projects of Wasser 3.0 (www.wasserdreinull.de) were conducted by means of the financial support by the German Federal Ministry for Economic Affairs and Energy through the provision of ZIM (Central Innovation Program for SME) project funds. We highly appreciate technical and research support from the SAS Hagmann GmbH (Horb, Germany).

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICAL APPROVAL

This article does not contain any studies with human participants performed by any of the authors.

ORCID

Katrin Schuhen https://orcid.org/0000-0002-8509-6544

REFERENCES

1. Janda J, Nödler K, Brauch H-J, Zwiener C, Lange FT. Robust trace analysis of polar (C2-C8) perfluorinated carboxylic acids by liquid chromatography-tandem mass spectrometry: method development and application to surface water, groundwater and drinking water. *Environ Sci Pollut Res*. 2019;26:7326-7336.
2. Kissa E *Fluorinated Surfactants. Synthesis, Properties, Applications*. New York, NY: Dekker 1994.
3. Wang P, Wang T, Giesy JP, Lu Y. Perfluorinated compounds in soils from Liaodong Bay with concentrated fluorine industry parks in China. *Chemosphere*. 2013;91(6):751-757.
4. European Chemicals Agency (ECHA). REACH Annex XVII: REACH Restricted Substance List 2018. http://www.chemsafetypro.com/Topics/EU/REACH_annex_xvii_REACH_restricted_substance_list.html Accessed July 21, 2020.
5. Umweltbundesamt. Besorgniserregende Eigenschaften von PFC. https://www.umweltbundesamt.de/themen/chemikalien/chemikalien-reach/stoffe-ihre-eigenschaften/stoffgruppen/per-polyfluorierte-chemikalien-pfc/besorgniserregende-eigenschaften-von-pfc Accessed May 26, 2020.
6. Stahl T, Mattern D, Brunn H. Toxicology of perfluorinated compounds. *Environ Sci Eur*. 2011;23(38):1-52.
7. European Chemicals Agency (ECHA). RAC adopts 13 scientific opinions on the harmonised classification and labelling of industrial chemicals and pesticide active substances 2011. https://echa.europa.eu/en/web/guest/view-article/-/journal_content/4709c09f-6dde-4aab-8d8c-4991b7622f45 Accessed July 21, 2020.
8. Yeung LWY, So MK, Jiang G, et al. Perfluorooctanesulfonate and related fluorochemicals in human blood samples from China. *Environ Sci Technol*. 2006;40(3):715-720.
9. Silva AOde, Mabury SA. Isomer distribution of perfluorocarboxylates in human blood: potential correlation to source. *Environ Sci Technol*. 2006;40(9):2903-2909.
10. Kannan K, Corsolini S, Falandysz J, et al. Perfluorooctanesulfonate and related fluorochemicals in human blood from several countries. *Environ Sci Technol*. 2004;38(17):4489-4495.
11. Kotthoff M, Müller J, Jürling H, Schlummer M, Fiedler D. Perfluoroalkyl and polyfluoroalkyl substances in consumer products. *Environ Sci Pollut Res Int*. 2015;22(19):14546-14559.
12. Guo Z, Liu X, Krebs KA, et al. US EPA's Perfluorocarboxylic Acid Content in 116 Articles of Commerce 2009. https://www.oecd.org/env/48125746.pdf Accessed July 21, 2020.
13. Fiedler S, Pfister G, Schramm K-W. Poly- and perfluorinated compounds in household consumer products. *Toxicol Environ Chem*. 2010;92(10):1801-1811.
14. Vestergren R, Berger U, Glynn A, Cousins IT. Dietary exposure to perfluoroalkyl acids for the Swedish population in 1999, 2005 and 2010. *Environ Int*. 2012;49:120-127.
15. Herzke D, Huber S, Bervoets L, et al. Perfluorinated alkylated substances in vegetables collected in four European countries; occurrence and human exposure estimations. *Environ Sci Pollut Res*. 2013;20(11):7930-7939.
16. D'Hollander W, Herzke D, Huber S, et al. Occurrence of perfluorinated alkylated substances in cereals, salt, sweets and fruit items collected in four European countries. *Chemosphere*. 2015;129:179-185.
17. Heo J-J, Lee J-W, Kim S-K, Oh JE. Foodstuff analyses show that seafood and water are major perfluoroalkyl acids (PFAAs) sources to humans in Korea. *J Hazard Mater*. 2014;279:402-409.
18. Prevedouros K, Cousins IT, Buck RC, Korzeniowski SH. Sources, fate and transport of perfluorocarboxylates. *Environ. Sci. Technol*. 2006;40(1):32-44.
19. Wallington TJ, Hurley MD, Xia J, et al. Formation of C 7 F 15 COOH (PFOA) and other perfluorocarboxylic acids during the atmospheric oxidation of 8:2 fluorotelomer alcohol. *Environ Sci Technol*. 2006;40(3):924-930.
20. Ellis DA, Martin JW, Silva AOde, et al. Degradation of fluorotelomer alcohols: a likely atmospheric source of perfluorinated carboxylic acids. *Environ Sci Technol*. 2004;38(12):3316-3321.
21. Rankin K, Mabury SA, Jenkins TM, Washington JW. A North American and global survey of perfluoroalkyl substances in surface soils: distribution patterns and mode of occurrence. *Chemosphere*. 2016;161:333-341.
22. So MK, Miyake Y, Yeung WY, et al. Perfluorinated compounds in the Pearl River and Yangtze River of China. *Chemosphere*. 2007;68(11):2085-2095.
23. Ahrens L, Xie Z, Ebinghaus R. Distribution of perfluoroalkyl compounds in seawater from northern Europe, Atlantic Ocean, and Southern Ocean. *Chemosphere*. 2010;78(8):1011-1016.
24. Post GB, Louis JB, Cooper KR, Boros-Russo BJ, Lippincott RL. Occurrence and potential significance of perfluorooctanoic acid (PFOA) detected in New Jersey public drinking water systems. *Environ Sci Technol*. 2009;43(12):4547-4554.
25. Beesoon S, Webster GM, Shoeib M, Harner T, Benskin JP, Martin JW. isomer profiles of perfluorochemicals in matched maternal, cord, and house dust samples: manufacturing sources and transplacental transfer. *Environ Health Perspect*. 2011;119(11):1659-1664.
26. Berger U, Haukås M Validation of a screening method based on liquid chromatography coupled to high-resolution mass spectrometry for analysis of perfluoroalkylated substances in biota. *Journal of Chromatography A*. 2005;1081(2):210-217.
27. Lechner M, Knapp H Carryover of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) from soil to plant and distribution to the different plant compartments studied in cultures of carrots (Daucus carota ssp. Sativus), potatoes (Solanum tuberosum), and cucumbers (Cucumis Sativus). *J Agric Food Chem*. 2011;59(20):11011-11018.
28. Yamashita N, Kannan K, Taniyasu S, et al. Analysis of perfluorinated acids at parts-per-quadrillion levels in seawater using liquid chromatography-tandem mass spectrometry. *Environ Sci Technol*. 2004;38(21):5522-5528.
29. Loganathan BG, Sajwan KS, Sinclair E, Senthil Kumar K, Kannan K. Perfluoroalkyl sulfonates and perfluorocarboxylates in two wastewater treatment facilities in Kentucky and Georgia. *Wat Res*. 2007;41(20):4611-4620.
30. Stróżyńska M, Schuhen K Dispersive solid-phase extraction followed by triethylsilyl derivatization and gas chromatography mass spectrometry for perfluorocarboxylic acids determination in water samples. *J Chromatogr A*. 2019;1597:1-8.
31. Díaz R, Ibáñez M, Sancho JV, Hernández F. Target and non-target screening strategies for organic contaminants, residues and illicit substances in food, environmental and human biological samples by UHPLC-QTOF-MS. *Anal Methods*. 2012;4(1):196-209.
32. Dolman S, Pelzing M An optimized method for the determination of perfluorooctanoic acid, perfluorooctane sulfonate and other perfluorochemicals in different matrices using liquid chromatography/ion-trap mass spectrometry. *J Chromatogr B*. 2011;879(22):2043-2050.
33. Ahrens L, Felizeter S, Sturm R, Xie Z, Ebinghaus R. Polyfluorinated compounds in waste water treatment plant effluents and surface waters along the River Elbe, Germany. *Mar Pollut Bull*. 2009;58(9):1326-1333.

34. Silva AOde, Muir DCG. Distribution of perfluorocarboxylate isomers in select samples from the North American environment. *Environ Toxicol Chem*. 2009;28(9):1801-1814.
35. Shafique U, Schulze S, Slawik C, Kunz S, Paschke A, Schüürmann G. Gas chromatographic determination of perfluorocarboxylic acids in aqueous samples - A tutorial review. *Anal Chim Acta*. 2017;949:8-22.
36. Pichon V Solid-phase extraction for multiresidue analysis of organic contaminants in water. *J Chromatogr A*. 2000;885(1-2):195-215.
37. Ribeiro C, Ribeiro AR, Maia AS, Gonçalves VM, Tiritan ME. New trends in sample preparation techniques for environmental analysis. *Crit Rev Anal Chem*. 2014;44(2):142-185.
38. Yao C, Li T, Twu P, Pitner WR, Anderson JL. Selective extraction of emerging contaminants from water samples by dispersive liquid-liquid microextraction using functionalized ionic liquids. *J Chromatogr A*. 2011;1218(12):1556-1566.
39. Belisle JU, Hagen DF. A method for the determination of perfluorooctanoic acid in blood and other biological samples. *Anal Biochem*. 1980;101:369-376.
40. Henderson WM, Weber EJ, Duirk SE, Washington JW, Smith MA. Quantification of fluorotelomer-based chemicals in mammalian matrices by monitoring perfluoroalkyl chain fragments with GC/MS. *J Chromatogr B*. 2007;846(1-2):155-161.
41. Motas Guzmàn M, Clementini C, Pérez-Cárceles MD, et al. Perfluorinated carboxylic acids in human breast milk from Spain and estimation of infant's daily intake. *Sci Total Environ*. 2016;544:595-600.
42. Ylinen M, Hanhijrvi H, Peura P, Rämö O. Quantitative gas chromatographic determination of perfluorooctanoic acid as the benzyl ester in plasma and urine. *Arch Environ Contam Toxicol*. 1985;14(6):713-717.
43. Orata F, Quinete N, Wilken R-D. Long chain perfluorinated alkyl acids derivatisation and identification in biota and abiota matrices using gas chromatography. *Bull Environ Contam Toxicol*. 2009;83(5):630-635.
44. González-Barreiro C, Martínez-Carballo E, Sitka A, Scharf S, Gans O. Method optimization for determination of selected perfluorinated alkylated substances in water samples. *Anal Bioanal Chem*. 2006;386(7-8):2123-2132.
45. Goh SXL, Lee HK Automated bundled hollow fiber array-liquid-phase microextraction with liquid chromatography tandem mass spectrometric analysis of perfluorinated compounds in aqueous media. *Anal Chim Acta*. 2018;1019:74-83.
46. Hu Z, Li Q, Xu L, Zhang W, Zhang Y. Determination of perfluoroalkyl carboxylic acids in environmental water samples by dispersive liquid–liquid microextraction with GC-MS analysis. *J Liq Chromatogr Relat Technol*. 2020;43(7-8):282-290.
47. Liu W-L, Ko Y-C, Hwang B-H, Li ZG, Yang TC, Lee MR. Determination of perfluorocarboxylic acids in water by ion-pair dispersive liquid-liquid microextraction and gas chromatography-tandem mass spectrometry with injection port derivatization. *Anal Chim Acta*. 2012;726:28-34.
48. Ferrer I Validation of new solid-phase extraction materials for the selective enrichment of organic contaminants from environmental samples. *Trends Anal Chem*. 1999;18(3):180-192.
49. Cazes J, ed. *Encyclopedia of Chromatography*. 3rd ed. 2009.
50. Ferenc A, Biziuk M. Solid phase extraction technique – trends, opportunities and applications. *Pol J Environ Stud*. 2006;15(5):677-690.
51. Jurado-Sánchez B, Ballesteros E, Gallego M. Semiautomated solid-phase extraction followed by derivatisation and gas chromatography–mass spectrometry for determination of perfluoroalkyl acids in water. *J Chromatogr A*. 2013;1318:65-71.
52. Dufková V, Čabala R, Ševčík V. Determination of C(5)-C(12) perfluoroalkyl carboxylic acids in river water samples in the Czech Republic by GC-MS after SPE preconcentration. *Chemosphere*. 2012;87(5):463-469.
53. Scott BF, Moody CA, Spencer C, Small JM, Muir DC, Mabury SA. Analysis for perfluorocarboxylic acids/anions in surface waters and precipitation using GC—MS and analysis of PFOA from large-volume samples. *Environ Sci Technol*. 2006;40(20):6405-6410.
54. DIN. Validierungsdokument zu DIN 38407-42: Bestimmung ausgewählter polyfluorierter Verbindungen in Wasser – Verfahren mittels Hochleistungs-Flüssigkeitschromatographie und massenspektrometrischer Detektion (HPLC-MS/MS) nach Fest-Flüssig-Extraktion (F42) 2011. https://www.wasserchemische-gesellschaft.de/dev/validierungsdokumente?download=33:f42-din-38407-42-2011-03&lang=de. Accessed October 9, 2020.
55. DIN 38407-42:2011-03. German standard methods for the examination of water, waste water and sludge - Jointly determinable substances (group F) - Part 42: Determination of selected polyfluorinated compounds (PFC) in water - Method using high performance liquid chromatography and mass spectrometric detection (HPLC/MS-MS) after solid-liquid extraction (F 42).
56. Young CJ, Furdui VI, Franklin J, Koerner RM, Muir DC, Mabury SA. Perfluorinated acids in arctic snow: new evidence for atmospheric formation. *Environ Sci Technol*. 2007;41(10):3455-3461.
57. Moody CA, Field JA Determination of perfluorocarboxylates in groundwater impacted by fire-fighting activity. *Environ Sci Technol*. 1999;33:2800-2806.
58. Li J, Cui Y, Xie S, et al. Determination of perfluorocarboxylic acids and perfluorosulfonic acids in aquatic products by quick, easy, cheap, effective, rugged, and safe sample preparation with liquid chromatography-tandem mass spectrometry. *Food Anal Methods*. 2018;11(6):1627-1635.
59. Pawliszyn J Theory of solid-phase microextraction. *J Chromatogr Sci*. 2000;38(7):270-278.
60. Stróżyńska M, Schuhen K, GIT Laborbuch: Festphasenmikroextraktion (SPME): Teil 2 der Laborbuchreihe: Methoden der Probenvorbereitung 2018. https://www.git-labor.de/forschung/umwelt/git-laborbuch-festphasenmikroextraktion-spme Accessed July 21, 2020.
61. Alzaga R, Bayona JM Determination of perfluorocarboxylic acids in aqueous matrices by ion-pair solid-phase microextraction–in-port derivatization–gas chromatography–negative ion chemical ionization mass spectrometry. *J Chromatogr A*. 2004;1042(1-2):155-162.
62. Monteleone M, Naccarato A, Sindona G, Tagarelli A. A rapid and sensitive assay of perfluorocarboxylic acids in aqueous matrices by headspace solid phase microextraction-gas chromatography-triple quadrupole mass spectrometry. *J Chromatogr A*. 2012;1251:160-168.
63. Kudo N, Bandai N, Kawashima Y. Determination of perfluorocarboxylic acids by gas-liquid chromatography in rat tissues. *Toxicol Lett*. 1998;99(3):183-190.
64. Ylinen M, Auriola S Tissue distribution and elimination of perfluorodecanoic acid in the rat after single intraperitoneal administration. *Pharmacol Toxicol*. 1990;66(1):45-48.
65. Yi LB, Chai LY, Xie Y, Peng QJ, Peng QZ. Isolation, identification, and degradation performance of a PFOA-degrading strain. *Genet Mol Res*. 2016;15(2).
66. Naile JE, Garrison AW, Avants JK, Washington JW. Isomers/enantiomers of perfluorocarboxylic acids: method development and detection in environmental samples. *Chemosphere*. 2016;144:1722-1728.
67. Ahrens L, Plassmann M, Xie Z, Ebinghaus R. Determination of polyfluoroalkyl compounds in water and suspended particulate matter in the river Elbe and North Sea, Germany. *Front Environ Sci Eng China*. 2009;3(2):152-170.
68. Fujii Y, Harada KH, Koizumi A. Analysis of perfluoroalkyl carboxylic acids in composite dietary samples by gas chromatography/mass spectrometry with electron capture negative ionization. *Environ Sci Technol*. 2012;46:11235-11242.
69. Lv G, Wang L, Liu S, Li S. Determination of perfluorinated compounds in packaging materials and textiles using pressurized liquid extraction with gas chromatography-mass spectrometry. *Anal Sci*. 2009;25(3):425-429.
70. Zafeiraki E, Costopoulou D, Vassiliadou I, Bakeas E, Leondiadis L. Determination of perfluorinated compounds (PFCs) in various

foodstuff packaging materials used in the Greek market. *Chemosphere*. 2014;94:169-176.
71. Alzaga R, Salgado-Petinal C, Jover E, Bayona JM. Development of a procedure for the determination of perfluorocarboxylic acids in sediments by pressurised fluid extraction, headspace solid-phase microextraction followed by gas chromatographic–mass spectrometric determination. *J Chromatogr A*. 2005;1083(1-2):1-6.
72. Liu W-L, Hwang B-H, Li Z-G, Jen JF, Lee MR. Headspace solid phase microextraction in-situ supercritical fluid extraction coupled to gas chromatography-tandem mass spectrometry for simultaneous determination of perfluorocarboxylic acids in sediments. *J Chromatogr A*. 2011;1218(43):7857-7863.
73. Langlois I, Berger U, Zencak Z, Oehme M. Mass spectral studies of perfluorooctane sulfonate derivatives separated by high-resolution gas chromatography. *Rapid Commun Mass Spectrom*. 2007;21(22):3547-3553.
74. Dufková V, Cabala R, Maradová D, Stícha M. A fast derivatization procedure for gas chromatographic analysis of perfluorinated organic acids. *J Chromatogr A*. 2009;1216(49):8659-8664.
75. Silva AOde, Mabury SA. Isolating isomers of perfluorocarboxylates in polar bears (Ursus maritimus) from two geographical locations. *Environ Sci Technol*. 2004;38(24):6538-6545.
76. Li Z, Sun H Cost-effective detection of perfluoroalkyl carboxylic acids with gas chromatography: optimization of derivatization approaches and method validation. *Int J Environ Res Public Health*. 2019;17(1). https://doi.org/10.3390/ijerph17010100.
77. Stróżyńska M, Schuhen K Derivatization of perfluorocarboxylic acids with N,N-dimethylformamide dimethylacetal prior to GC–MS analysis. *Chromatographia*. 2020;83(3):477-482.
78. Stróżyńska M. Entwicklung neuer Derivatisierungsmethoden für die GC-MS Analyse von Perfluorcarbonsäuren in variablen Probenmatrices. 2020. (Unpublished doctoral dissertation). University of Koblenz-Landau, Landau, Germany.
79. Stróżyńska M, Gross JH, Schuhen K. Structural investigation of perfluorocarboxylic acid derivatives formed in the reaction with N,N-dimethylformamide dialkylacetals. *Eur J Mass Spectrom*. 2019;30:146906671988054.
80. Pellizzaro A, Zaggia A, Fant M, Conte L, Falletti L. Identification and quantification of linear and branched isomers of perfluorooctanoic and perfluorooctane sulfonic acids in contaminated groundwater in the veneto region. *J Chromatogr A*. 2018;1533:143-154.
81. Jurado-Sánchez B, Ballesteros E, Gallego M. Analytical method for biomonitoring of perfluoroalkyl acids in human urine. *Talanta*. 2014;128:141-146.
82. Gołębiowski M, Siedlecka E, Paszkiewicz M, Brzozowski K, Stepnowski P. Perfluorocarboxylic acids in cell growth media and technologically treated waters: determination with GC and GC-MS. *J Pharm Biomed Anal*. 2011;54(3):577-581.

How to cite this article: Stróżyńska M, Schuhen K. Extraction and derivatization for perfluorocarboxylic acids in liquid and solid matrices: a review. *Anal Sci Adv*. 2021;2:343–353. https://doi.org/10.1002/ansa.202000089