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Hydrolysis of FTOH precursors, a simple method to account for some of the unknown PFAS

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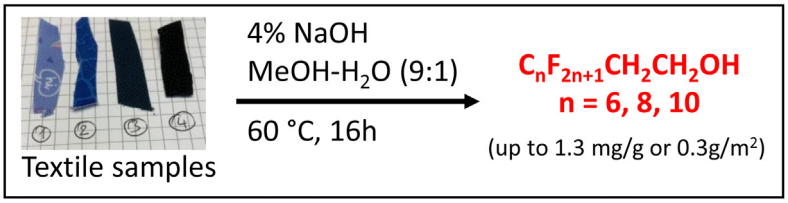
HIGHLIGHTS

- Hydrolysis of FTOH precursors - simple method to account for unknown PFAS
- 4% NaOH, MeOH–H2O (9:1), 60 °C, 16h
- FTOH content in textile samples up to 500–1300 times higher after hydrolysis

GRAPHICAL ABSTRACT



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ABSTRACT

There is a growing concern over a suspected presense of unknown perfluoroaliphatic substances (PFAS) in consumer goods and in the environment. Such unknown substances, possibly with high molecular weight, might be precursors of hazardous or controlled known PFAS. Recent studies confirmed that total organic fluorine (TOF) content often can not be explained by the measured target PFAS. One of the suspected classes of such unknowns are polymers with fluorotelomer alcohol (FTOH) residues in a side chain. In this report we suggest hydrolysis of precursors, as a complementary method to account for the unknown PFAS. It was shown here that hydrolysis allows to preserve structural information on the perlfuorinated parts of the precursors, which can be an advantage for the purpose of accurate risk assessment or source identification. A convenient procedure for hydrolysis with 4% sodium hydroxide in water-methanol mixture (1:9) at 60 °C for 16 h was shown to convert model substances - FTOH acrylate, methacrylate and isobutyrate esters as well as FTOH phenylcarbamate to free FTOHs. Analysis of extracts of textile samples with preliminary hydrolysis and without it showed up to 1300-fold higher level of "hidden" FTOHs.

1. Introduction

1.1. Hidden PFAS precursors

There are a growing concern and scientific evidence that per- and polyfluoroalkyl substances (PFAS) included in monitoring programs are just a small part of the total PFAS burden (OECD 2019; Borg et al., 2017; Casson et al., 2018; Robel et al., 2017). Majority of known PFAS contain a perfluoroalkyl radical, from $-C_3F_7$ to $-C_{17}F_{35}$ (OECD, 2019). It was shown that fluorotelomer alcohols of general formula $C_NF_{2N+1}C_MH_{2M}OH$ (N:M FTOH) are often present in consumer products like textiles (Herzke et al., 2012). More recently it was shown that identifiable PFAS represent only minor part of the total organic fluorine in textile: volatile PFAS, ionic PFASs and known precursors accounted for 0–2.2%, 0–0.41%, and 0.021–14%, respectively, of the total fluorine determined by particle-induced gamma ray emission spectroscopy (PIGE). After extraction, textiles retained 110 ± 30% of the original fluorine as determined by PIGE, indicating that most of the fluorine remains associated with

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the papers and textiles (Robel et al., 2017). Reliable methods are required for analysis of potential precursors of specific PFAS to evaluate not only immediate, but potential or long-term impact and risk as well.

Two methods are available at present for detection of "hidden PFAS" – Total Organic Fluorine, **TOF** and its modification, Extractable Organic Fluorine, **EOF** (Akhdhara et al., 2019; Dubocq et al., 2019; Loi et al., 2011; Lu et al., 2019; Musijowski et al., 2007; Schellenberger et al., 2019; Schultes et al., 2019; Taniyasu et al., 2015; Tokranov et al., 2019; Yeung et al., 2008, 2009a, 2009b, 2013) and Total Oxidizable Precursors, **TOP** (Casson et al., 2018; Mumtaz et al., 2019; Houtz et al., 2016; Houtz and Sedlak, 2012; Wang et al., 2020; Zhang et al., 2019).

TOF is based on combustion of the whole sample including all fluorine-containing components with formation of a single fluorine-containing moiety - fluoride anion, with subsequent analysis for the latter by a variety of technics (Schultes et al., 2019). The method has a good potential for quantitative determination of fluorine. However, it results in a complete loss of information on the structure of precursors. Consequently, a contribution of other sources of fluorine like fluoride itself or non-polyfluorinated organic substances with isolated fluorine atoms (Bassetto et al., 2015; Filler and Saha, 2009; Wang et al., 2014), organic substances with S–F or P–F bonds, fluoroaromatic substances, or natural fluoroorganic compounds (Bartholomé et al., 2017; Carvalho and Oliveira, 2017; Key et al., 1997; Murphy et al., 2001; O'Hagan et al., 2002; Shuman et al., 1970) might be significant (Fig. 1).

EOF is a modification of TOF (Yeung et al., 2009a,b; Yeung et al., 2013). In EOF a sample is first extracted with organic solvent followed by TOF analysis of the extract. It has a potential of reflecting only organic fluorine, but the completeness of extraction is always under question. Use of stable isotope labeled internal standards is not possible.

TOP is based on mild oxidation of non-fluorinated parts of precursors with conversion to perfluorocarboxylic or perfluorosulfonic acids, with subsequent analysis of those by target PFAS methods (Casson and Chiang, 2018; Mumtaz et al., 2019; Houtz et al., 2016; Houtz and Sedlak, 2012; Wang et al., 2020; Zhang et al., 2019).

TOP allows for semi-quantitative use of labeled standards and preserves structural information in part. The risk of false positive results is largely eliminated as well. The method was recently expanded to ultra-short PFAS like trifluoroacetic acid (Janda et al., 2019). However, it is difficult to achieve reproducible extent of conversion. With a limited amount of oxidant, other substances present in a sample might consume most or all the oxidant and prevent oxidation of target compounds, thus affecting identification of precursors and accurate quantitation of hidden PFAS (Fig. 2).

Hydrolysis, as pre-treatment method for hidden PFAS. Browsing the available databases shows that large part of patented organofluorine compounds are derivatives of simple PFAS containing an oxygen link, like, for example polymers with fluorotelomer side-chains. C–O bonds in esters are known to be susceptible to hydrolysis. Therefore, hydrolysis, followed by target PFAS analysis can be an alternative or complementary method for assessing hidden PFAS. In our opinion, the method would have the following potential advantages:

- Potential completeness: an excess of the hydrolysis agent can be used.
- Retention of structural information: only certain chemical bonds can be hydrolyzed. Unlike the two methods described above, hydrolysis would allow to differentiate between, for example FTOH, PFCA and PFSA derivatives. Original length of a perfluorinated chain would remain.
- No risk of false positives.
- Good compatibility with labeled standards.

Therefore, the here proposed method, which can be called "Total Hydrolyzable Precursors", **THP,** offers certain advantages, especially better information on the nature of organofluorine content of a sample.

No information was available in the literature on hydrolysis rates of PFAS precursors. However, hydrolysis was used for preparative transformation of certain PFAS derivatives into others. There exists enough evidence that hydrolysis occurs in relatively mild conditions (Agouridas et al., 2009; Eames and Khanom, 2004; Klein et al., 2010; Mori et al., 2001; Ou et al., 2014; Winter et al., 2006; You et al., 2014; Zell et al., 2014). There is a number of reports on conversion of FTOH esters to free FTOHs. The methods included use of enzymes (Mori et al., 2001), reductive cleavage of ester group with lithium triethylborohydride in THF at room temperature (Eames and Khanom, 2004) or with lithium aluminiumhydride (Agouridas et al., 2009), reaction with sodium methoxylate in methanol at room temperature for 1 h (Winter and

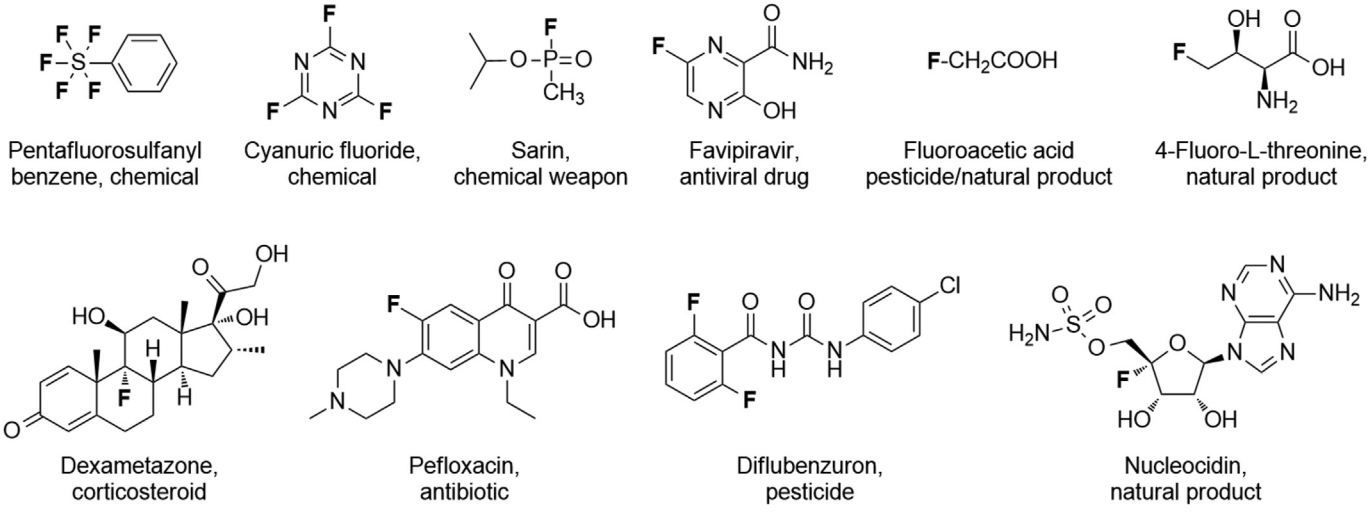

Fig. 1. Examples of common Fluorine-containing substances, which are not PFAS.

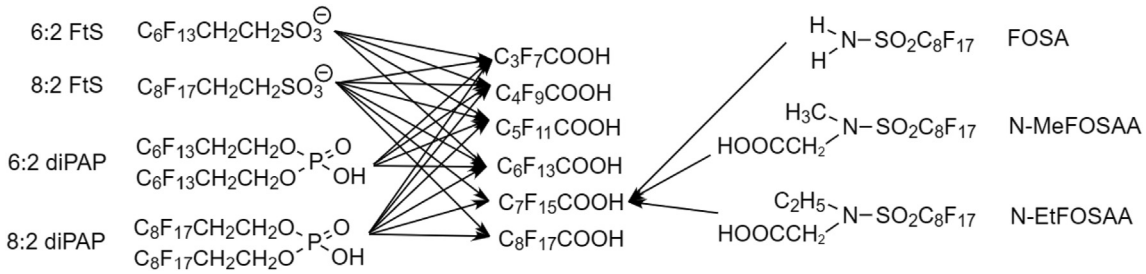

Fig. 2. Entanglement of structural information with TOP method: formation of different oxidation products from the same precursor and formation of the same products from different precursors. Data from (Houtz and Sedlak (2012)).

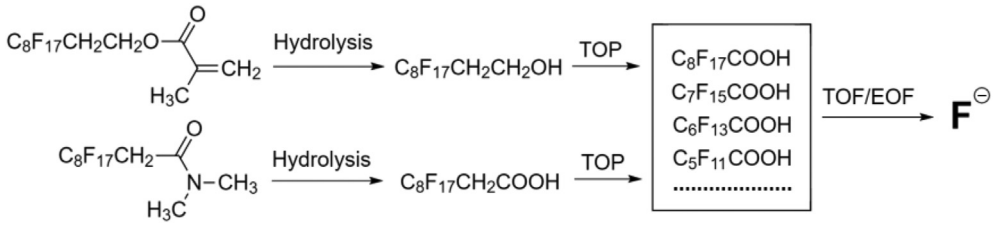

Fig. 3. Example of expected preservation and loss of structural information upon hydrolysis, TOP and TOF/EOF analysis: good preservation with THP, entanglement with TOP, complete loss with TOF/EOF (theoretical analysis).

Gard, 2006), reaction with lithium hydroxide in methanol at room temperature for 3 h (Klein et al., 2010), hydrogenolysis of FTOH trifluoroacetates with hydrogen at 40 °C and 25 bar in dioxane in presense of sodium methoxylate (Zell et al., 2014), basic hydrolysis with potassium hydroxide in aqueous methanol for 10 h at room temperature (Ou et al., 2014), or just with potassium hydroxide in water (You et al., 2014). FTOHs were detected among by-products in DABCO-catalyzed condensation of FTOH acrylates with aldehydes (Le Lamer et al., 2006).

The purpose of the present work was development of a simple practical method for hydrolysis of FTOH derivatives and testing the method on textile samples.

2. Materials and methods

2.1. Test substances

Polymers with fluorotelomer side-chain have been identified as an important class of hidden PFAS precursors (Herzke et al., 2012). No sample of such polymer was available for research, only a limited number of model substances: 6:2 FTOH Acrylate and Methacrylate – the respective monomers, 6:2 FTOH Isobutyrate – closer analog of polymers with ester group at a saturated carbon atom, a series of branched FTOH Methacrylates with different fluorinated chain lengths, and a methacrylate ester of somewhat more complex FTOH with an additional free HO-group – hydroxy iso-9:3 FTOH Methacrylate and Phenylcarbamate ester of 10:2 FTOH (Table S1). Acrylic and methacrylic esters of FTOHs are derivatives of FTOHs with the highest number of literature references and the highest number of reported commercial sources (Fig. S1, S2).

Chemicals and consumables. Neat FTOH esters were purchased from Aldrich, USA (10:2 FTOH Phenylcarbamate, CAS 305849-13-2, Cat. No. CPR588423), from Apollo Scientific, UK (6:2 FTOH iso-Butyrate, CAS 242812-05-1, cat. No. PC2526, lot AS477447) and from Fluorochem, UK (6:2 FTOH Acrylate, CAS 17527-29-6, cat. No. 019154, lot FCB015726; 6:2 FTOH Methacrylate, CAS 2144-53-8, cat. No. 007141, lot FCB029094; Iso-5:2 FTOH Methacrylate, CAS 65195-44-0, cat. No. 010617, lot M34202401; Iso-7:2 FTOH Mehtacrylate, CAS 50836-66-3, cat. No. 010619, lot M36207101; Iso-9:2 FTOH Methacrylate, CAS 88752-37-8, cat. No. 010620, lot FCB044944; Hydroxy iso-9:3 FTOH Methacrylate, CAS 17527-29-6, cat. No. 007108, lot 38366201) and were used as received. Common chemicals and solvents were of trace analysis grade.

Clear glass vials, screw top with solid green Thermoset cap with PTFE liner (Supelco, USA), volume 4, 7, 15, 22 or 40 mL (cat nos. 27138, 27150-U, 27161, 27172-U, 27181, respectively) were used for preparation of standard solutions, reagents and for carrying hydrolysis experiments.

REACTI-THERM III #TS-18823 heating/stirring module (Thermo Scientific, USA) was used as heating block/thermostat for hydrolysis experiments.

2.2. Selection of textile samples

Four polyester samples were selected for the study (Fig. S3). In the previous screening two of them (no. 1 and no. 2) were shown to contain FTOHs, while samples 3 and 4 have been found FTOH free.

2.3. Selection of hydrolysis method

This brief analysis of the literature confirmed that basic hydrolysis of FTOH esters occurs at relatively mild conditions. On the basis of convenience 1 N Sodium hydroxide in 90% methanol was selected as hydrolysis medium. Preliminary tests have shown that elevated temperature is required and one or two hours may not be suffcient for complete (>99%) conversion. Full conversion was achieved upon overnight (16 h) heating at 60 °C in closed screw-cap vials in a heating block, without stirring.

Different compositions of methanol-water mixtures would likely work just as well or even better. It is likely that other common solvents like ethanol, isopropanol, dioxane, DMSO, sulfolane, their mixtures and mixtures with water can be used as long as they dissolve alkali, are stable at reaction conditions and allow convenient work-up of the mixture after hydrolysis. Aprotic polar solvents like DMSO or sulfolane might allow reaction without heating.

Solvents with higher boiling point would allow reaction at higher temperature and shorter hydrolysis times.

2.4. Identification and quantification of hydrolysis products

6:2, 8:2 and 10:2 FTOHs were identified and quantified in the hydrolysis products using standard GC-MS method in PCI mode. Branched FTOHs and hydroxy-FTOH were identified by their mass-spectra (EI and PCI, similar to those of available FTOHs) and by retention times. Reaction mixtures were also analyzed on GC Q Exactive with mass resolution 120000. No unexpected PFAS were detected. No attempt was made, however, to identify or quantify non-fluorinated reaction products.

Typical hydrolysis experiment, model substances. To 0.2 mL of 1 M solution of sodium hydroxide (prepared from 1 g of NaOH, 2.5 mL of water and 22.5 mL of methanol) in a 7 mL glass vial a solution of model substances and internal standards was added at once. The vial was closed, shaken, and transferred to a heater/thermostat kept at 60 °C and left overnight. After 16 h at 60 °C the heater was stopped, and the vials were allowed to cool to room temperature. A 0.6 mL portion of a 1:1 mixture of *tert*-butyl methyl ether and n-hexane were added, followed by 2 mL of water. After 30 min on a shaker, the layers were allowed to separate, and ca 0.3 mL of upper layer was transferred to a plastic Eppendorf vial with 50 mg of anhydrous sodium sulfate and the extracts were left drying for 1 h with occasional shaking. A 0.1 mL portion was transferred to a GC vial for instrumental analysis. Blanks were executed with each batch of samples.

Hydrolysis of textile samples. Experiments were carried out in the same manner, but with different quantities of components. To 0.5 mL of 1 M solution of sodium hydroxide (prepared from 1 g of NaOH, 2.5 mL of water and 22.5 mL of methanol) in a 7 mL glass vial a ca 30 mg of textile sample was added as 3–4 small pieces, followed by internal standards. The vial was closed, shaken, and transferred to a heater/thermostat kept at 60 °C and left overnight. After 16 h at 60 °C the heater was stopped, and the vials were allowed to cool to room temperature. After precipitation of sediment (presumably, degradation products of textile) 0.2 mL of clear solution was transferred to another vial. A 0.6 mL portion of a mixture of *tert*-butyl methyl ether and n-hexane were added, followed by 2 mL of water. Samples were shaken for 30 min. In case of textile samples, the organic layer remained an emulsion. Therefore, the bulk of aqueous layer was removed by a pipette and discarded. Anhydrous sodium sulfate was added in portions until the organic layer was clear after shaking. A 0.3 mL of the clear extract was transferred to a plastic Eppendorf vial with 50 mg of anhydrous Sodium Sulfate and the extracts were left drying for 1 h with occasional shaking. A 0.1 mL portion was transferred to a GC vial for instrumental analysis. Blanks were executed with each batch of samples.

2.5. Instrumental analysis

Quantitative determination of FTOHs and precursors by GC-MS in PCI mode. FTOHs were analyzed by gas chromatography mass-spectrometry (GC–MS) using selected ion monitoring (SIM). An Agilent 7890A GC with split/splitless injector coupled to a 5975C MSD (Agilent, Böblingen, Germany) was used with helium carrier gas flow rate of 0.8 mL min^{-1}, and methane as reagent gas in positive chemical ionization (PCI) mode. Injection volume was 1 μL, constant injector temperature was set to 200 °C in splitless mode, the GC temperature program has been previously described (Barber et al., 2007). Transfer line temperature was set to 250 °C with the ion source temperature of 250 °C. The column was Supelcowax 10 fused silica capillary column, 60 m × 0.25 mm x 0.25 mm film thickness (Supelco, USA). Quantification of FTOHs was done using the internal standard method with ^{13}C and/or ^{2}H isotope-labeled 4:2, 6:2, 8:2 and 10:2 FTOHs. Quantification of FTOH esters was done using the internal standard method with native or ^{2}H isotope-labeled diisopropylbenzenes. Full-scan PCI mass-spectra of esters were recorded (Fig. S4–S15).

Analysis of model substances and reaction mixtures by HRAM mass-spectrometry. All model substances were characterized by their high-resolution (120000) mass-spectra in EI mode (Fig. S16–S26) on Orbitrap GC-MS (GC Q Exactive, Thermo Scientific, USA) with Trace 1310 gas chromatograph. The column used was Rtx-200MS, 30 m × 0.25 mm x 1 mm film thickness (stationary phase - crossbond trifluoropropylmethyl polysiloxane).

3. Results and discussion

3.1. Hydrolysis of model substances

A ca 1 M solution of NaOH in 90% aqueous methanol was selected as hydrolytic agent. Such mixture would provide high concentration of hydroxide ions, would be able to dissolve model substances and, at least to some extent, suspected polymers. If required, the mixture would allow for moderate heating to further accelerate hydrolysis.

A series of tests was carried out and all model substances were found to hydrolyze easily. Conversion was 90%–100% upon standing overnight at ambient temperature or upon short heating at 60 °C. The only detected volatile product in all cases was corresponding FTOH.

All model substances were simple esters, easily soluble in common organic solvents. In contrast, FTOH-based polymers might be not as soluble, which could reduce the rate of hydrolysis. Moreover, ester groups within a polymer chain will be more sterically hindered and this could lead to further reduction of hydrolysis rate. Therefore, to assure proper hydrolysis of unknown FTOH precursors in real samples, a longer heating period (16 h) was selected. Under these conditions, conversion of all model substances was complete, no traces of starting materials were detected (Fig. S27). The yield of 6:2 FTOH from 6:2 FTOH acrylate, methacrylate and isobutyrate (average of 6 parallel runs) was measured quantitatively using standard analysis for FTOHs and was found to be 101 ± 15%.

3.2. PCI Mass-spectra of FTOH esters and branched FTOHs (Fig. S6–S15)

Spectra of esters of simple FTOHs were rather simple – the main ion was M+1, two other significant ions, M+29 and M – 19, had intensity of 10–20% of the M+1.

The spectrum of hydroxy-FTOH methacrylate was more complex. M+1 ion (613) was one of the three strongest ions with similar intensity (491, 527, 613). M+29 was present, but not M-19. M – 17 was present instead (40%). Other abundant ions had *m*/*z* of 455, 507, 555, 575.

In the spectrum of 10:2 FTOH phenylcarbamate the “normal” FTOH ester pattern of M+1, M+29 and M – 19 were present, but also ions with *m*/*z* 565 (60%) and 527 (30%) were significant. The latter two are two main ions in the PCI MS spetrum of 10:2 FTOH. This type of fragmentation was observed only for carbamate ester and not for acrylate, isobutyrate or any of the methacrylate esters of 5:2 to 10:2 FTOHs. The plausible explanation is fragmentation of a protonated molecular ion of carbamate to protonated FTOH ion and neutral phenylisocyanate; such pathway is less likely for other studied esters.

PCI mass-spectra of ω-1 branched N:2 FTOHs are not so different

Table 1
FTOHs in textile samples after simple extraction and after hydrolysis.

Sample no.	6:2 FTOH, μg/g		8:2 FTOH, μg/g		10:2 FTOH, μg/g	
	No hydrolysis	After hydrolysis	No hydrolysis	After hydrolysis	No hydrolysis	After hydrolysis
1	0.13	45.4	1.21	607	0.33	214
2	0.13	71.1	<0.15	887	0.69	312
3	<0.1	0.98	<0.15	0.71	<0.1	0.20
4	<0.1	<0.1	<0.15	0.67	<0.1	0.19

from those of straight chain N:2 FTOHs. The two main ions are protonated molecular ion M+1 and M-37. The latter, presumably, is a fragmentation product of the former after loss of HF and H_2O.

EI Mass-spectra of FTOH esters (SI, Figs. 17–25)

Ion with *m/z* 69.0335 (C_4H_5O) was the most intense in the EI spectra of FTOH esters of methacrylic acid. Most likely, this is a methacryloyl cation. Molecular ions were present and pronounced (10–20%) in spectra of all but one ester, the hydroxy-9:3-FTOH methacrylate (CAS 17527-29-6). Similarly, the major ion in the spectrum of 6:2 FTOH acrylate was the ion with *m/z* 55.0177 (C_3H_3O), likely, the acryloyl cation. Molecular ion was less pronounced than in spectra of methacrylates, barely 2% of the most intense ion. In the spectrum of 6:2 FTOH isobutyrate the most intense ion had *m/z* 73.0284 ($C_3H_5O_2$), the molecular ion was ca 16% of that, and another ion with high *m/z*, M – CH_3, was present (ca 8%). In the EI mass-spectrum of 10:2 FTOH phenylcarbamate the most intense ion was 93.0573 (C_6H_7N) and molecular ions intensity was ca 30% (Fig. S25). The most intense common ion for all FTOH esters was C_3F_5 (*m/z* 131.9915), with intensity of 7–21%.

3.3. Analysis of textile samples

The four textile samples were hydrolyzed in the same manner as model substances.

The results are presented in Table 1.

The most important results were obtained for samples 1 and 2, which were already known for presence of FTOHs. However, after hydrolysis the apparent concentration of sum of the three FTOHs increased ca 520 and ca 1300 times, respectively. After hydrolysis, the dominating congener was 8:2 FTOH in both samples, while without hydrolysis that was 8:2 FTOH for sample 1, but 10:2 FTOH for sample 2.

Even for presumably non-contaminated samples 3 and 4 low levels of FTOHs were detected. Noteworthy, these lower levels after hydrolysis were in the same range, as levels in contaminated samples, determined by traditional method.

Thus the usefulness of the hydrolysis method was confirmed immediately. The method revealed the presence of a 8:2 FTOH precursor (accompanied with smaller amounts of precursors of 6:2 and 10:2 FTOHs) in total amount of up to 1.3 mg/g or 0.3 g/m^2.

It was shown on model substances that corresponding FTOH is the only reaction product. Therefore, it is highly likley that the hydrolysis shall not alter the congener profile and the method can be used for source identification. It is likely that congener profile after hydrolysis reflects the original congener profile more accurately, than FTOH profile after simple extraction.

Expansion of the method to broad range of precursors other than FTOH esters will be a subject for future investigation.

4. Conclusion

A simple method was developed for hydrolysis of FTOH precursors. Complete conversion of model FTOH esters was achieved after 16 h at 60 °C in 1 N sodium hydroxide in methanol-water (9:1) mixtures.

The method was successfully applied to textile samples. For two textile samples with suspected fluorine content the hydrolysis method revealed presence of FTOH precursor at concentration up to 1300 times higher than that of FTOHs after simple extraction.

Hydrolysis, as a pre-treatment method for PFAS analysis has the following potential advantages: preservation of structure of perfluorinated part, preservation of congener profile, full compatibility with isotope-labeled internal standards, simplicity, reliability and safety.

Credit author statement

Credit author statement is nonsense for a single author, right?

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2021.130044.

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