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# Identification of novel non-ionic, cationic, zwitterionic, and anionic polyfluoroalkyl substances using UPLC–TOF–MS$^E$ high-resolution parent ion search

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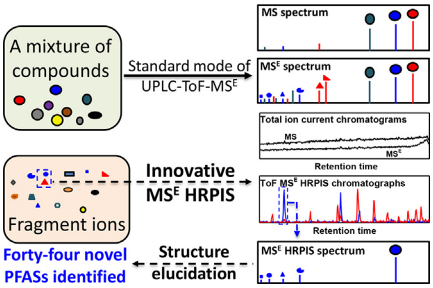
## HIGHLIGHTS

- An innovative ToF–MS$^E$ HRPIS approach was established.
- This approach was validated with certified standards of 24 PFASs.
- A workflow for non-targeted identification was developed.
- Two novel classes of PFASs and 47 new PFASs were identified.

## GRAPHICAL ABSTRACT



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## ABSTRACT

Poly- and perfluoroalkyl substances (poly- and per-PFASs) are a large group of organic compounds that have become the target of investigation due to their widespread occurrence in the environment and biota, coupled with their known or suspected impacts on human health. Recent studies have shown that a significant portion of poly-PFASs remain unidentified. This study presents a time-of-flight mass spectrometry approach based on continuously interleaving scans at low and high collision energies (ToF-MS$^E$) for the rapid identification and characterization of unknown PFASs. The MS$^E$ mode allowed for the simultaneous acquisition of full-spectrum accurate mass data of both parent and fragment ions in a single chromatographic run. Specific to PFASs, the hypothesis that PFASs can be selectively detected by the ToF–MS$^E$ high-resolution parent-ion search (HRPIS) of their characteristic fragments was confirmed with certified standards of 24 poly- and per-PFAS. After being validated with these certified standards, the innovative HRPIS approach was applied to a group of commercial surfactants, which led to the identification of 47 new and 43 infrequently reported PFASs, including 40 non-ionic, 30 cationic, 15 zwitterionic, and five anionic compounds. It is envisaged that the results, especially the identification of new non-ionic PFASs, may provide important insights into the historical occupational and non-occupational exposure to PFASs from the production and application of these surfactants.

## 1. Introduction

Poly- and perfluoroalkyl substances (poly- and per-PFASs) are anthropogenic chemicals with important industrial and consumer

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applications. They have been mass-produced since the 1950s as ingredients in aqueous film-forming forms (AFFFs) used by military and airports to suppress fires and as surface-treatment surfactants for a range of consumer products [1,2]. However, there has been a growing concern since 2000 regarding the widespread distribution of PFASs in the environment and adverse human health effects due to the exposure to these chemicals. Two moderately hydrophobic per-PFASs, perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA), have been measured in many components of the biosphere since 2000 [3–6]. A wealth of information has been generated on PFOS and PFOA regarding their fate [2,7,8], transport [2,9], effects [10–12], and removal [13–15] from water. The U.S. EPA recently released updated drinking-water guidelines for PFOS and PFOA; the lifetime health advisory suggests a maximum combined level of 70 ng/L [16]. However, PFOS, PFOA, and a few other legacy PFASs account for only a small fraction of PFASs manufactured since the 1950s. A significant portion of PFASs still remain unidentified [17–20], including potential precursor compounds that lead to the secondary formation of PFOS and PFOA during natural and engineered abiotic and biotic transformation processes [21–23]. In terms of analytical method development, it can generally be concluded that detection methods for targeted PFASs have reached a very high level of reliability (accuracy and precision) [24–27]. However, transparent, easy-to-use non-targeted identification methods for previously unknown PFASs are still underdeveloped.

With the increasing availability of high-resolution mass spectrometry (HRMS) systems, important progress has been made recently in the identification of novel PFASs. Xiao in a recent review mentioned that more than 400 emerging PFASs have been identified in studies published since 2009 [28]. In a pioneering study, Place and Field identified 27 new poly-PFASs in AFFFs [29]. AFFF samples were first analyzed by fast atom bombardment mass spectrometry. Ions in series characterized by *m*/*z* differences of 50 ($CF_2$) and 100 ($C_2F_4$) were selected that were believed to represent PFASs produced by electrochemical fluorination and telomerization, respectively. The candidate ions were then analyzed by quadrupole time-of-flight mass spectrometry (QToF-MS) to obtain accurate mass data [29]. In another study, D'Agostino and Mabury identified 76 new and 27 infrequently reported poly-PFASs in AFFFs and two commercial surfactant products using three MS systems [30]. More recently, Higgins, Field, and coworkers reported the identification of 40 novel poly-PFAS classes in AFFFs, AFFF-affected groundwater, and three commercial surfactants made by 3M [31]. Common approaches in these previous studies include the identification of 1) mass defects as PFASs tend to have negative mass defects and 2) homologues that differ from each other by *m*/*z* 50 ($CF_2$) or 100 ($C_2F_4$). However, it is worth mentioning that other fluorine-free compounds containing oxygen, nitrogen, sulfur, and phosphorus also typically have negative mass defects. Alternative non-targeted identification approaches are needed.

Furthermore, it has been estimated that AFFFs account for only less than 10% of the total production volume of perfluorooctane sulfonyl fluoride (POSF) manufactured by 3M (~96,000 t between 1970 and 2002 [1]). POSF was produced by electrochemical fluorination during which the C–H bonds of an educt (e.g., octanesulfonyl) are replaced by C–F bonds [32–34]. The production of POSF is not clean, which generates a range of cleaved, branched, or cyclic byproducts or isomers [32–34]. POSF was employed as the starting chemical to generate substances used in several mainstream commercial products including Fluorad brand surfactants as the additives in household chemicals, insecticides, and chemical intermediates [32–34]. The identities and structures of PFASs in these commercial surfactants remain largely unknown.

This study presents a new non-targeted identification approach for PFASs based on HR parent (precursor) ion search (PIS) experiments carried out on a ToF-MS system with continuously interleaving scans at low and high collision energies ($MS^E$). PIS has been used previously in a triple quadrupole MS system (QqQ-MS) for the detection of novel chlorinated and brominated disinfection by-products with the relative abundance ratio of chlorine or bromine isotopes as a diagnostic tool [35–38]. Fluorine has only one stable isotope ($^{19}F$). However, it has been demonstrated that anionic PFASs in a sample can be selectively detected by performing QqQ-$ESI^-$-MS/MS PIS of their fragment ions (e.g., $C_3F_7^-$, *m*/*z* 169) (unpublished results of F.X.) and by in-source fragmentation flagging scans using a linear ion trap Orbitrap MS [39]. QqQ-MS, by nature, has a limited ability for non-targeted analysis, as it requires pre-selected fragment ions or predetermined transitions to capture parent ions and yields a much lower resolution than HRMS. A particular disadvantage to linear ion traps for small molecule analysis is that fragment ions with *m*/*z* less than 1/3 of the parent *m*/*z* may be ejected from the ion trap and thus not appear in MS spectra [40]. The authors in this study explore the possibility of performing PIS-like experiments using ToF–$MS^E$ in both negative and positive ion modes.

A QToF or ToF MS does not have the PIS function as in QqQ-MS. However, the $MS^E$ technology expands the capacity of QToF by allowing the simultaneous acquisition of both MS and MS/MS fragmentation data during a single chromatographic run using alternating low- and high-collision energy scans [41]. The authors employed PFAS fragments generated during ToF $MS^E$ as the marker for searching the parent PFAS compounds. This approach was validated with certified standards of 24 PFASs, and further applied to a group of Fluorad brand surfactants. A total of 90 emerging poly-PFASs were identified in these surfactants. Among them, 40 nonionic, five zwitterionic, and two cationic PFASs were identified for the first time in this study. The authors believe that the new non-targeted approach may become a good complementary tool to other screening methods for PFASs using HRMS. The study also provides a foundation for future studies on the detection, fate/transport, removal/transformation, and exposure/effects of these newly identified PFASs in natural and engineered environmental systems.

## 2. Materials and methods

Certified standards of 24 PFASs in methanol were purchased from Wellington Laboratories (Guelph, Canada). Chemicals in group #1 (per-PFAS group) included 1) five linear perfluoroalkyl sulfonates (per-PFSAs): perfluorobutanesulfonate (PFBS), perfluorohexanesulfonate (PFHxS), perfluoroheptanesulfonate (PFHpS), PFOS, perfluorodecanesulfonate (PFDS); and 2) ten linear perfluoroalkyl carboxylates (per-PFCAs): perfluoropentanoate (PFPeA), perfluorohexanoate (PFHxA), perfluoroheptanoate (PFHpA), PFOA, perfluorononanoate (PFNA), perfluorodecanoate (PFDA), perfluoroundecanoate (PFUnDA), perfluorododecanoate (PFDoDA), perfluorotridecanoate (PFTrDA), perfluorotetradecanoate (PFTeDA). Group #2 (poly-PFAS group) chemicals included 1) four alternative compounds to PFOS/PFOA [42–50]: 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy) propanoic acid (HFPO-DA or GenX [42–45]), dodecafluoro-3H-4,8-dioxanonanoate (ADONA [42,46]), 6:2 and 8:2 chlorinated polyfluorinated ether sulfonates (6:2 and 8:2 Cl-PFAESs or F-53B [42,47–50]); and 2) five poly-PFASs: 6:2 and 8:2 fluorotelomer sulfonates (6:2 and 8:2 FTS), 8:2 fluorotelomer unsaturated acid