Time trends of PFASs in human blood: closing the mass balance

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Credits: 45 or 60

Start date: January 2018 or later

Background

It is estimated that >3000 commercial per- and polyfluoroalkyl substances (PFASs) exist on the global market. Considering that only a few dozen PFASs are included in routine monitoring programs, it is very likely that exposure to these substances is underestimated. Recently, new analytical techniques - namely combustion ion chromatography (CIC) and suspect screening - have been developed to specifically address this problem. In CIC, all molecules containing fluorine are combusted to inorganic fluorine which is then measured by ion chromatography. When combined with data from targeted (LC-MS/MS) analysis, the fraction of organofluorine associated with as-of-yet unidentified fluorine-containing substances in the sample can be quantified. Applications of this technique in samples of biota, water, sediments and human serum has revealed that considerable fraction of EOF cannot be accounted for by known PFASs (Miyake et al. 2007a, Yeung et al. 2009, Loi et al. 2011, Yeung and Mabury 2013, Weiner et al. 2013).

While CIC measurements enable reliable quantification of organofluorine compounds present in environmental samples this method does not provide information about chemical structure. For this purpose, high-resolution mass spectrometry (HRMS) is a powerful tool for assignment of molecular formulas to observed mass/charge peaks through the combination of high spectral resolving power and high mass accuracy. For PFASs there are a handful of studies that have detected novel PFASs in environmental samples using LC-HRMS (Liu et al. 2015; Baygi et al. 2016; Newton et al. 2017; Barzen-Hanson 2017; Munoz et al. 2017). In this projects, ACES will develop an approach which produces both quantitative data for known PFASs, while also aquiring full-scan data which can be retrospectively interrogated for suspect PFASs (or any other contaminant) which may be present in the sample. The proposed approach is coined 'target/non-target (TNT)' screening.

Research Objectives

In this 45-60-credit Master's project we will develop the TNT approach and apply it, together with CIC to pooled human serum samples collected from 1997-2017 as part of the 'POPUP' study. ACES and LMV have previously investigated samples from 1997 – 2015 using a targeted, LC-MS/MS-based approach. The objectives of this study are as follows:

1) Develop and validate the new TNT-based approach and compare this method to that of a traditional, LC-MS/MS-based approach performance in terms of accuracy, precision, and detection limits.

2) Quantify the fraction of organofluorine which is unaccounted-for in human serum using CIC and determine whether this fraction is increasing, decreasing or staying the same over time.

3) Carry out a suspect screening approach to determine whether any of the novel PFASs reported in the literature are present in any of the human serum samples.

4) Extend the current time trend beyond 2015 for 'known' PFASs, while building the first time trends for 'novel' PFASs.

Training Objectives

- Gain hands-on experience in ultra-high performance liquid chromatography-high resolution (Orbitrap) mass spectrometry.

- Gain hands-on experience with combustion ion chromatography.
- Develop understanding for biomonitoring of emerging organic pollutants, in particular per- and polyfluoroalkyl substances (PFASs).
- Gain experience in the lab preparing samples and processing data.

Methods

A total of 3 replicates of a single pooled sample are required for the entire analysis. The first sample is fortified with internal standards, extracted, and analyzed by UHPLC-Orbitrap-MS (i.e. TNT screening). The second portion is combusted directly without internal standards (the internal standards will interfere with the CIC analysis) for determination of total fluorine (i.e. organic + inorganic) using CIC. The 3rd portion is extracted without internal standards and a wash step is used to remove the inorganic fluorine. The resulting extract is then subjected to combustion IC for determination of extractable organofluorine. An overview of the various replicates is provided in figure 1.

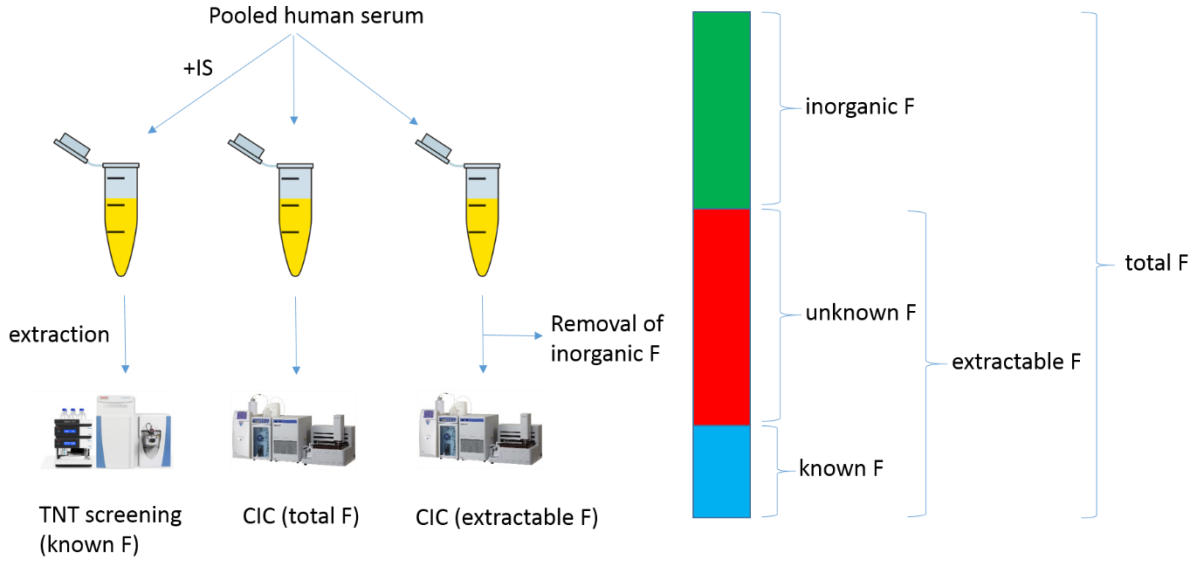

Figure 1. Relationship between organic-, inorganic-, extractable-, and total-fluorine.