Discovering Novel Chemicals in Drinking Water: Point-of-use Filters with Non-Targeted Analysis using GC and LC

Seth R. Newton[1], Hannah K. Liberatore[1], John T. Sloop[1,2]

1) Office of Research and Development US EPA 2) Oak Ridge Institute for Science and Education

Introduction

Drinking water is one of the most important sources of exposure to chemicals and studies have shown that hundreds to thousands of unidentified compounds exist in drinking water. It has been demonstrated that commercially available, activated carbon point-of-use (POU) filters can accumulate a wide range of organic compounds[1]. Non-targeted analysis (NTA) using high resolution mass spectrometry (HRMS) combined with POU filters is an excellent tool to discover novel compounds and examine differences in drinking water samples. Gas Chromatography (GC) has been under-utilized in the NTA community and drinking water contains compounds that require both LC and GC.

Sampling

Six participants were selected to represent two large water systems: DeKalb County in Atlanta (ATL), Georgia and New York City (NYC). Residents of DeKalb are served by a single treatment facility while resident of NYC are served by multiple treatment facilities using the same source water. Faucet filters (Figure 1) were mailed to participants who installed them on their kitchen faucets for sampling periods of 3 months. Sampling was conducted from April 2021 to December 2021 with most participants stopping after the first time period (April – June). Two participants in ATL continued sampling for three time periods.

Objectives

- Develop a method for non-targeted analysis of drinking water filters that utilizes both LC and GC
- Explore differences between houses that receive water from different treatment facilities vs. the same facility
- Explore seasonal differences in drinking water
- Discover important drinking water contaminants that are not currently monitored

This presentation does not necessarily reflect agency policy

Extract 1: Sonication in DCM:Acetone

Liquid/Liquid Extraction to separate DCM from residual water

Extract 2: Sonication in Methanol

Extract 1

Extracts 1 + 2 Combined

1 mL aliquot

Reduced to 1 mL

NTA by GC-HRMS

NTA by LC-HRMS

Figure 1 – Summary of analytical method

Data Processing

LC Data Workflow - MS1 data were matched to MS-ready formulas from the DSSTox Database[2] and subsequently processed using the NTA WebApp.[3] Candidate compounds were ranked by data sources and assigned a ToxPi score. Candidates with the highest data source ranking and top ToxPi score were considered for further prioritization. MS2 data was processed using Agilent Workflows and matched to Personal Compound Databases and Libraries.

GC Data Workflow – EI data was processed using Compound Discoverer 3.3, matching to the NIST20 and Wiley 11 databases. Cutoff scores of RHRF > 75 and SI > 600 were used. Retention indices were considered when available. PCI and NCI data were examined for evidence of the molecular ion to boost confidence in candidate compounds from EI data.

Location and Time Trends

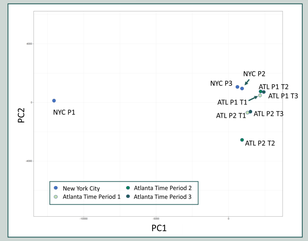


Figure 2 – PCA of samples using all detected features. NYC = New York City, ATL = Atlanta, P = Participant number, T = Time period

Location vs. Time
Samples collected from the same house but at different times had a smaller Euclidean distance on the PCA plot than samples from different houses at the same time, indicating differences in drinking water between houses served from the same treatment facilities are greater than time differences. However, some time trends were observed.

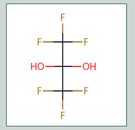
Time trends
A decrease in abundance of priority compounds was observed from spring to fall, resulting in a statistically significant difference between the first and last time periods ($p = 0.045$, paired t-test).

Figure 3 – Time trends from two houses

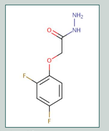
What are the highest-ranking compounds in drinking water?

ToxPi Score = Toxicity Score + Detection Frequency + Average Abundance

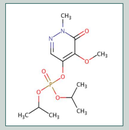
Where Toxicity score = sum of three TEST model[4] predictions:
Oral rat 50 percent lethal dose + Developmental Toxicity + Ames Mutagenicity
All individual terms are normalized to a max value of 1, for a max ToxPi score of 3



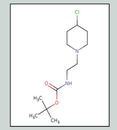
1,1,1,3,3,3-Hexafluoropropane-2,2-diol
ToxPi = 1.32



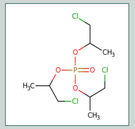
2-(2,4-difluorophenoxy)-acetohydrazide
ToxPi = 2.24



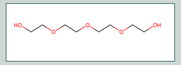
Phosphoric acid, 1,6-dihydro-5-methoxy-1-methyl-6-oxo-4-pyridazinyl bis(1-methylethyl) ester
ToxPi = 1.47



tert-Butyl [2-(4-chloropiperidin-1-yl)ethyl]carbamate
ToxPi = 1.08



Tris(2-chloroisopropyl)phosphate
ToxPi = 1.47



Tetraethylene glycol
ToxPi = 0.54

Figure 4 – Top Compounds by ToxPi Score

Conclusions

- Many unknown compounds exist in drinking water
- Concentration of water samples onto a POU filter followed by NTA is an excellent approach to discovering novel contaminants
- The use of both LC and GC expands the chemical space of NTA
- There is less variability in time than from between houses although some time trends are still observed

*Reference:

1) Newton, Seth R., et al. "Suspect screening and non-targeted analysis of drinking water using point-of-use filters." *Environmental pollution* 234 (2018): 297-306.
2) McEachran, Andrew D., et al. ""MS-Ready" structures for non-targeted high-resolution mass spectrometry screening studies." *Journal of cheminformatics* 10.1 (2018): 1-16.
3) NTA: non-targeted analysis of MS data (beta): https://github.com/quanted/nta_app/
4) U.S. EPA (2020). "User's Guide for T.E.S.T. (version 5.1) (Toxicity Estimation Software Tool): A Program to Estimate Toxicity from Molecular Structure." https://www.epa.gov/chemical-research/toxicity-estimation-software-tool-test