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Evaluating Analytical Methods for Detecting Unknown Chemicals in Recycled Water

CALIFORNIA Water Boards
STATE WATER RESOURCES CONTROL BOARD
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Evaluating Analytical Methods for Detecting Unknown Chemicals in Recycled Water

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Southern California Coastal Water Research Project Authority

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Abstract and Benefits

Abstract:

This report provides a synopsis of the current state-of-the-science for analytical methods to identify and measure unknown trace organic compounds (TOrCs) in recycled water. It proposes is an integrated framework that includes targeted analysis of known contaminants, as well as semi- and non-targeted analysis of unknown contaminants by both instrumental methods and by bioassays, along with the advantages and limitations of each approach. A research plan is also presented to evaluate the utility of using these strategies for identifying unknown TOrCs. Finally, a communications strategy is outlined for regulators, managers, and the general public with regards to monitoring for unknown TOrCs using the methods discussed.

Benefits:

- Demonstrates that recycled water can contain a plethora of known and unknown TOrCs that affect water quality and potential reuse of this resource.
- Demonstrates that a variety of instrumental methods exist for both targeted and semi-/ non-targeted analysis of TOrCs, each with advantages and limitations.
- Demonstrates that an integrated approach that uses targeted analysis, instrumental semi-/ non-targeted analysis, and bioassays as appropriate can address unknown TOrCs well.
- Demonstrates that the proposed research plan evaluates whether candidate analytical methods can correctly identify model “unknown” compounds.
- Demonstrates that later phases of the proposed research determine if indicator compounds can be used to signal the presence of TOrCs.
- Demonstrates that accuracy, transparency, and timeliness are crucial for disseminating results around unknown TOrCs to stakeholders: regulators, customers, and the general public.

Keywords: Recycled water, trace organic compounds, targeted analysis, non-targeted analysis, bioassays, potable reuse.

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Acronyms and Abbreviations

AhR	Aryl hydrocarbon receptor
AOP	Advanced oxidation process
AR	Androgen receptor
AWTF	Advanced water treatment facility
BAC	Biological activated carbon
BEQs	Bioassay equivalent concentrations
CDOM	Chromophoric dissolved organic matter
CECs	Contaminants of emerging concern
CRM/SRM	Certified/standard reference materials
CWA	Clean Water Act
DBPs	Disinfection byproducts
DOC	Dissolved organic carbon
DOM	Dissolved organic matter
DPR	Direct potable reuse
EDCs	Endocrine disrupting compounds
EEM	Excitation-emission matrix
ER-α	Estrogen receptor
GR	Glucocorticoid receptor
HLB	Hydrophilic/lipophilic balance
HRMS	High-resolution mass spectrometry
IC	Ion chromatography
ICP/MS	Inductively coupled mass spectrometry
ICP-OES	Inductively coupled plasma-optical emission spectroscopy
IR	Infrared spectrometry
IVBs	In vitro biossays
LC	Liquid chromatography
LMW	Low molecular weight
LRW	Laboratory reagent water
MCL	Maximum contaminant level
MDLs	Method detection limits
MQOs	Measurement quality objectives
MRLs	Method reporting limits
MS	Mass spectrometry
NDELA	N-nitrosodiethanolamine
NDMA	N-nitrosodimethylamine
NOM	Natural organic matter
NTA	Non-target analyses
PAC	Powdered activated carbon

PFAAs	Perfluoroalkyl acids
PFCs	Perfluorinated compounds
PPCP	Pharmaceuticals and personal care products
PR	Progesterone receptor
QA/QC	Quality assurance/quality control
QQQ	Triple quadrupole
QSAR	Quantitative structural-activity relationships
QTOF	Quadrupole-time of flight
RCRA	Resource Conservation and Recovery Act
RO	Reverse osmosis
SDWA	Safe Drinking Water Act
SIM	Selected ion monitoring
SPE	Solid phase extraction
STPs	Sewage treatment plants
SWRCB	California State Water Resources Control Board
TF	Total fluorescence
TOC	Total organic carbon
TOF	Time-of-flight
TOrCs	Trace organic compounds
TOX	Total organic halide
TPs	Transformation products
TTHMs	Total trihalomethanes
UCMR	Unregulated Contaminant Monitoring Rule
U.S. EPA	United States Environmental Protection Agency
UV	Ultraviolet
UVA	Ultraviolet absorbance
VOCs	Volatile organic compounds
WWTP	Wastewater treatment plant

Executive Summary

The goals of this report are three-fold: 1) to document the current state-of-the-science for analytical methods that target and identify unknown trace organic compounds (TOrCs) in recycled water; 2) to develop a research plan to evaluate the utility of the most promising methods for identifying unknown TOrCs; and 3) to outline a communications strategy for regulators, managers, and the general public regarding monitoring of unknown TOrCs using these methods.

Goal 1: Conduct an assessment of the current state-of-the-science for analytical methods that target unknown contaminants, particularly low molecular weight compounds that survive advanced water treatment.

Analytical methods for low molecular weight compounds surviving advanced water treatment can be categorized into targeted methods, and semi- and non-targeted methods. Targeted methods can provide information both qualitative (i.e., confirmation of chemical identity) and quantitative (i.e., analyte concentration) for known compounds with authentic standards, while semi- and non-targeted methods focus more on identifying chemical structure of unknown analytes.

Targeted analysis makes use of a variety of chemical instrumentation. In particular, mass spectrometric techniques are most commonly used, for which low-mass resolution instruments are popular given their suitability for quantitative analysis and lower capital and operational costs compared to high mass resolution instruments.

The approach for semi-targeted methods, for which some information is known about the unknown analytes (e.g., analytes structurally similar to known compounds, suspected transformation products, similar bioreactivity), is similar to that for non-targeted methods. In both, a workflow, a sequence of analytical and data processing steps is followed to narrow down possible compound structures, and if successful, to identify the compound outright. High mass resolution mass spectrometric techniques are preferred for such methods, given their sensitivity and selectivity. However, low mass resolution mass spectrometers can quite valuable as well under specific conditions. One such condition is if the workflow can take advantage of the larger database of mass spectral libraries available for such instruments. Another is if chromatographic separation techniques, such as comprehensive two-dimensional gas chromatography, can be employed. Bioassays that detect in vitro responses of a class of analytes to an endpoint are also highly sensitive and selective, and have the advantages of being cheaper and easier to use (if available, and once validated) than mass spectrometric techniques, and providing toxicity information for the sample.

A tiered approach is recommended for robust evaluation of waters for unknown TOrCs. Monitoring for surrogate that would co-occur with different classes of TOrCs or with source waters (e.g., wastewater) is an initial screening tier. Positive results from such screening can trigger targeted analysis to monitor for known indicator compounds representing commonly-found TOrCs of concern. The presence of TOrCs above specified action thresholds (e.g., levels exceeding health-based guidelines, or suggesting the presence of co-contaminants) can trigger a third tier of semi- or non-targeted instrumental or bioassay analysis to identify and evaluate occurrence and effects associated with unknown compounds.

Goal 2: Suggest a scope of work and research team, for conducting analytical work, as appropriate, to assess and demonstrate the utility of the analytical methods in Task 1, and address resultant knowledge gaps.

A three-phase research project is proposed to address the relative capabilities of the various analytical techniques for TOrCs. Phase 1 will consist of comparisons of candidate NTA methods using both high resolution mass spectrometric techniques coupled with gas and liquid chromatography (e.g., quadrupole-time of flight, Orbitrap) platforms compared to comprehensive two-dimensional gas chromatography-time of flight mass spectrometry. Model TOrCs would be spiked into clean water matrices. Those methods demonstrating acceptable performance based on QA/QC measurement goals would be subjected to challenge testing using a more realistic simulated source water matrix that comprises a more complex mixture of a broader suite of TOrCs as well as natural background interferences. Phase 2 would develop and evaluate surrogates to detect changes in bulk water quality in real time, with candidates recommended by previous panels on CECs in recycled water. Phase 3 would develop and evaluate targeted and bioanalytical methods to inform identification of suspected and unknown contaminants missed by existing monitoring methods, to address knowledge gaps resulting from previous phases.

Goal 3: Provide guidance on an approach to communicate analytical results for identifying unknown contaminants to regulators, government officials, and the general public.

It is necessary to have a clear, simplified, and accurate description of the need for an integrated approach to assessing low molecular weight compounds, known and unknown, in waters. Existing monitoring efforts only provide information on the chemicals for which it specifically measures. While useful (for example in indicating that health or regulatory guidelines are not exceeded), it cannot quantify what is not measured. It is possible that many other chemicals that are unknown or remain unidentified in water treatment systems. Hence the need for non-targeted analysis methods. These can identify such unknowns by isolating and enriching them from a water sample, and applying either state-of-the-art instrumentation to identify their chemical structures, or bioassays that measure for a specific overall toxic response from all chemicals (known or unknown) present that can trigger it. These non-targeted approaches go hand-in-hand, in that measuring toxicity can trigger instrumental analysis to determine what unknown chemicals might be involved, and identification of unknown compounds that may be structurally similar to known toxicants can trigger evaluation of actual toxicity via bioassays. Targeted monitoring, in turn, can trigger the need for non-targeted approaches, which for instrumental analysis can be expensive in terms of capital and operating costs, and which for bioassays cannot identify specific chemicals or their individual toxicological responses.

CHAPTER 1

Introduction

1.1 Study Goals

The goals of this report are to 1) document the current state-of-the-science for analytical methods that target and identify unknown trace organic compounds (TOrCs) in recycled water; 2) develop a research plan to evaluate the utility of the most promising methods for identifying unknown TOrCs; and 3) outline a communications strategy for regulators, managers, and the general public regarding monitoring of unknown TOrCs using these methods.

1.2 Problem Statement

Treated municipal wastewater effluent as the "source" water for potable reuse undergoes a series of purification steps to remove biological and chemical contaminants which may pose a risk to human health. Even the most rigorous treatment trains (e.g., reverse osmosis followed by an advanced oxidation process (RO/AOP)), cannot remove all detectable contaminants, including TOrCs in the final "product" water slated for indirect and direct potable reuse (DPR) applications. Current analytical methods are capable of monitoring hundreds of known TOrCs. However, they fall short of addressing all chemicals of interest, including transformation products and otherwise unknown chemicals that may occur in source and product water. Assuming RO/AOP as the de facto requirement for DPR treatment trains, low molecular weight (LMW) compounds that can penetrate RO membranes are of particular interest. Based on the recommendations of water quality experts, the development of new analytical methods, including those based on non-targeted analysis (NTA), is needed to fill this gap in monitoring capability.

1.3 Scope and Organization

Chapter 1 provides study goals, statement of the problem to be discussed, scope, and organization, as well as definitions of common terms used in this report. In Chapter 2, analytical methods that can screen for, and if warranted, identify unknown low molecular weight (LMW) trace organic compounds (TOrCs) in matrices of interest for direct potable reuse (DPR) are identified. In Chapter 3, a research plan is defined to evaluate the utility of the methods identified in Chapter 2. Chapter 4 provides guiding principles for communicating the need for and the results of analysis for unknown LMW TOrCs are provided.

Supporting information is included in several Appendices. Appendix A describes the research plan for surrogate and indicator compounds, a part of the overall proposed research plan to develop and evaluate means by which to identify unknown low molecular weight compounds in recycled water. Appendix B summarizes criteria for bioanalytical screening of water quality. Appendix C characterizes quality assurance/quality control procedures for evaluating analytical methods of Chapter 3, and Appendices A and B. Appendix D provides summaries of interviews with technical experts who provided insight into the knowledge and approaches within this report. Appendix E details peer-reviewed literature providing the scientific basis for the information and recommendations of this report, as well as the means by which this literature was found.

The universe of TOrCs addressed in this report are previously unidentified ("known unknowns") and unknown ("unknown unknowns") TOrCs (e.g., those that are not currently addressed by existing monitoring methods). Matrices of primary interest are treated municipal wastewater effluent before ("source") and after ("product") advanced treatment for DPR. The evaluation of candidate methods described in Chapter 2 constitutes a preliminary "proof of concept", and is not intended to serve as an exhaustive or formal validation process for such methods.

1.4 Definitions

Adduct: Product of a direct addition of two or more distinct molecules, resulting in a single reaction product containing all atoms of all components. The resulting "adduct" is considered a distinct molecular species.

Continuous or Online Method: Methods that measure water quality parameters at a high frequency.

Direct Potable Reuse (DPR): Planned introduction of recycled water either directly into a public water system, or into a raw water supply immediately upstream of a water treatment plant.

Discrete Sampling: Collection of a water sample that is processed and analyzed offline.

Indicator: A compound that can be used to track the fate of a group or family of chemicals (e.g., through a treatment process). In addition to its ability to mimic the behavior of a larger group of chemicals, an ideal indicator is ubiquitous and easily detectable at some point in the treatment or distribution system.

Instrumental (Determinative) Method: Pertains to procedures that describe the identification and quantitation (or "measurement") of a parameter that is indicative of the quality of an aqueous sample.

High-Resolution Mass Spectrometry (HRMS): An instrumental method capable of mass determination at fractional accuracy ("exact mass"). In contrast, low resolution mass spectrometry performs at integer level mass accuracy.

Mass Accuracy: The ability to assign a "true" structural mass to charge ratio.

Mass to Charge Ratio (*m/z*): A number indicating the mass of an ion produced in mass spectrometry, divided by the number of charges (positive or negative) on that ion, and expressed in units of Daltons (Da).

Mass Resolution: The ability to distinguish between two different but adjacent mass to charge ratios

Mass Spectrometry (MS): A technique that identifies a trace compound based on its molecular structure (mass to charge ratio), isotopic and fragmentation pattern, and adduct formation.

Non-Target (unknown) Analysis (NTA): Identification of an unknown compound, with no prior knowledge of its structure, adduct formation or fragmentation behavior.

Preparative Method: Pertains to procedures that describe the collection, storage, extraction, clean-up, and concentration of target analytes found in an aqueous sample.

Product Water: Water subjected to AWTF that is discharged to a potable water supply.

Recycled Water: Treated municipal wastewater effluent that is further purified for discharge into natural or engineered water supply systems.

Reverse Osmosis (RO): A membrane-based water purification process that rejects a broad suite of chemicals.

Source Water: Feed for a recycled water facility that is typically secondary or tertiary effluent from a municipal WWTP.

Surrogate: A quantifiable change in a parameter that can serve as a performance measure that is

relatable to the removal of a specific chemical, or groups of chemicals.

Semi-Targeted Analysis (Suspect screening): Analysis of a sample/extract and/or identification of a known/unknown/previously unidentified compound with *a priori* knowledge of possible/probable structures.

Targeted Analysis: Analysis of a pre-determined list of analytes that are identified and quantified using authentic (high purity) standards.

Total Fluorescence (TF): Integrated measure of light energy emitted ("fluorescing") from a sample illuminated by incident light energy.

Ultraviolet Absorbance (UVA): Energy attenuated by a sample illuminated by incident light energy of a fixed wavelength, or across a scanned range of wavelengths.

CHAPTER 2

Analytical Methods for Low Molecular Weight Unknown Compounds in Water

In this chapter, the means by which analytical methods are developed and promulgated for monitoring and regulatory purposes is first briefly discussed. A treatise follows on analytical methods suitable for targeted analysis as well as semi- and non-targeted analysis, for the purpose of detecting and identifying low molecular weight unknown compounds in waters.

2.1 Developing Analytical Methods for Water Quality Monitoring

The two primary federal regulatory vehicles by which analytical methods are developed and applied for water quality monitoring are the Safe Drinking Water Act (SDWA) and Clean Water Act (CWA). Analytical methods for drinking water applications have historically been adapted and/or applied for monitoring of regulated and unregulated contaminants, the list of which over time has evolved via the process known as the Unregulated Contaminant Monitoring Rule (UCMR), now in its fourth iteration. The U.S. EPA administers the UCMR effort in part to spur development of analytical methods for contaminants deemed necessary to protect public health. The method development process focuses on demonstration of robust performance for sample preservation, preparation, and analytical (instrumental) protocols (e.g., that these steps produce data that meet monitoring objectives and that ultimately allow managers to make informed decisions). Among the most important aspects in ensuring robust method performance are the stability and recovery of target analytes during sample collection, storage and preparation; as well as the sensitivity (detectability), accuracy (relative to some known or accepted "gold standard"), precision, repeatability, and comparability of the measured parameter (Figure 2-1) (U.S. EPA 2018).

For pollutants in environmental matrices, including natural and receiving waters, the U.S. EPA provides guidance for analytical methods intended to support national programs covered under the Resource Conservation and Recovery Act (RCRA). In this guidance, method development occurs in two phases, the first of which demonstrates the feasibility of a proposed method, followed by a formal validation phase that encompasses 11 key elements, including delineation of method performance and quality assurance/quality control (QA/QC) requirements, identification of interfering substances and appropriate matrices, and demonstration of comparability of results by multiple measuring entities. *The feasibility stage typically involves characterizing basic performance parameters, such as recovery of spiked or native analytes and intrasample precision, using replicate samples with at least two different concentration levels. This phase can also include samples of different matrices (e.g., source vs. product water) that represent the range of matrices for which the method is intended.* The compendium of methods that successfully pass the validation sequence is published as "Test Methods for Evaluating Solid Waste" (or SW-846).

2.2 Sample Handling and Processing

For discrete samples (i.e., those collected at a specific location in the treatment train or water supply system and processed/analyzed offline), analytical methods are typically comprised of a preparative (extraction/cleanup) and a determinative (instrumental or measurement) step. Table 2-1 summarizes preparative methods commonly used to isolate TOrCs from aqueous samples. Instrumental methods that allow for direct injection of aqueous sample (i.e., without pre-concentration or isolation)

notwithstanding, selection of a preparative method that quantitatively isolates and recovers the analyte(s) of interest is a key consideration in meeting monitoring goals. Certain classes of TOrCs may require specific conditions and/or extraction materials for optimal isolation (e.g., acetone as an example of a volatile, non-purgeable, water soluble compound); however, solid phase extraction (SPE) using a hydrophobic/hydrophilic balance sorbent, such as Oasis HLB, captures a wide range of TOrCs and results in a solvent extract that can readily be analyzed by various instrumental methods. *For offline determination of non-polar and polar TOrCs (including known TPs and unknowns), SPE with Oasis HLB is recommended as the preferred preparative method.* The wide use of Oasis HLB for sequestering many classes of TOrCs means that its use is effectively a de facto standard for collection and processing of these chemicals in waters, thus reducing variability associated with differing pre-analysis steps. Other important considerations in developing and evaluating processing method (or methods) are 1) the reduction or elimination of extraction/pre-concentration steps, to minimize the handling steps that can result in loss or contamination; 2) the availability of purified standards and/or radiolabeled analogs for robust quantification, and 3) inclusion of related and/or other TOrCs of interest as target analytes for more inclusive, robust analyses.

Further details on recommended sample collection, preservation, and collection are available from previous expert panels on TOrCs in waters (Anderson et al. 2010, Drewes et al. 2018) and other guidance documents (Dodder et al. 2015). These are summarized in Appendix C.

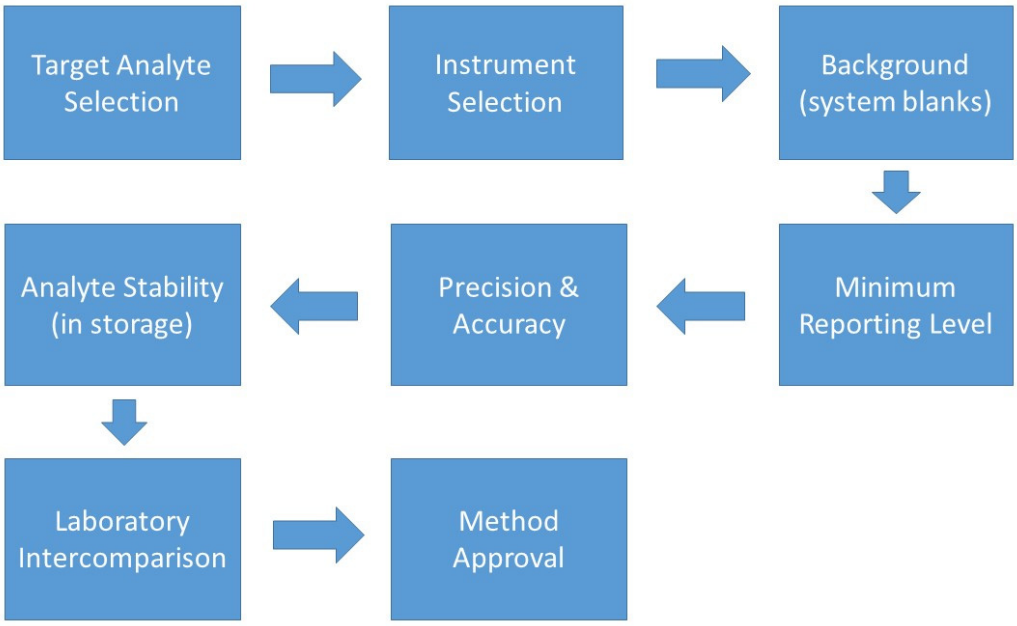

Figure 2-1. Method Development Sequence for Drinking Water Methods for Monitoring Purposes.
Adapted from W. Adams, U.S. EPA 2018.

Table 2-1. Sample Preparation Methods for Determination of TOrCs in Aqueous Matrices, Along with Typical References for Such Methods.

Method	Target Analytes	Reference
Solid phase extraction (SPE), activated carbon	Non-polar, polar organics	EPA Methods 521, 522
SPE, cation exchange, acidic conditions	NDMA precursors	Hanigan et al (2016)
SPE, hydrophobic/hydrophilic balance (Oasis HLB)	PPCPs, TPs (oxybenzone)	EPA Method 1694; Zhang et al. (2016)
SPE, hydrophobic sorbent (e.g., C-18; XAD, HP-20)	Non- and semi-polar organics	Plewa et al. (2004)
Derivatization	Polar, non-volatile organics, DBPs	EPA Methods 8041, 8151; Vincenti et al. (2010)
Purge and trap extraction	Volatile organic compounds (VOCs)	EPA Method 5030
Azeotropic distillation	Volatile, non-purgeable, water soluble organics	EPA Method 5031
Liquid-liquid extraction (LLE)	Non- and semi-polar organics	EPA Methods 3510, 3520

2.3 Analytical Methods for Identifying Known and Unknown Contaminants

There is a wide variety of analytical methods now available for identifying known and unknown contaminants in waters. In this chapter, the methods available are summarized, in terms of both targeted methods, as well as semi- and non-targeted methods. This summary was developed from searches of the peer-reviewed scientific literature addressing the analysis of relevant chemicals in wastewater and recycled water. Abstracts of the results of this exercise, with key advances of each study highlighted in boldface, are detailed in Appendix E.

2.3.1 Targeted Methods

Tremendous progress has been made over the past several years on methods to measure exceedingly low levels of known TOrCs and inorganic contaminants of concern in aqueous samples (Table 2-2). As a general rule, the analysis of volatile or semi-volatile organic compounds is best performed by gas chromatography (GC)-based instrumental methods, whereas non-volatile (ionizable, water soluble) organic compounds are amenable to liquid chromatography (LC). Some TOrCs, however, can be analyzed using either GC- or LC-based methods, with the choice of method dependent on a number of factors, such as the type of other TOrCs being analyzed (e.g., if volatile compounds are of interest, then GC-based methods should be used) and availability of instrumentation for detection.

In providing excellent selectivity and sensitivity, mass spectrometry (MS) is the clear choice for detection of most TOrCs. As a result, GC-MS and LC-MS are by far the most widely applied instrumental methods for detection and quantification of TOrCs. Mass spectrometers now come in many different configurations and degrees of operational complexity and robustness. Single quadrupole or ion trap, time-of-flight (TOF), and tandem (MS/MS) triple quadrupole (QQQ), hybrid (quadrupole-TOF or QTOF) and Orbitrap instruments constitute a wide spectrum of performance in terms of sensitivity, selectivity, robust operation, complexity and cost.

In general, more complex instruments provide greater capability and flexibility for targeted chemical analysis, but for greater capital and operating costs. That said, the suitability of different types of mass spectrometers for targeted analysis varies. In general, single quadrupole and triple quadrupole mass spectrometers provide excellent performance for targeted analysis, in terms of sensitivity and linear dynamic range, and are also less expensive to acquire and operate compared to more complex mass

spectrometers such as hybrid and Orbitrap instruments. For LC, triple quadrupole MS is greatly preferred over single quadrupole MS for trace environmental analysis given greater selectivity, which is necessary because of the generally lower separation efficiency in LC (including ultra-high resolution LC, or UHPLC) compared to GC. QTOF and Orbitrap instruments, while unparalleled for non-targeted analysis due to their capability to identify unknown compounds as discussed in Section 2.2.2, are generally less suitable for quantitative targeted analysis given much more limited linear dynamic range compared to single and triple quadrupole instruments. Although ion chromatography (IC) and inductively coupled mass spectrometry (ICP/MS) are geared for inorganic compounds, they are useful as they can specifically address the analysis of ionizable TPs and inorganic indicators.

Table 2-2. Candidate Targeted Instrumental Methods for TOrCs in Aqueous Samples.
[1]Direct sample injection and online SPE reduce turnaround time and sample processing cost, if available and possible.

Analyte	Method[1]	Performance	Relative Cost
Organics, non-volatile	LC-MS	Medium selectivity, high sensitivity, precision, intermediate turnaround	Medium capital, recurring & labor
	LC-MS/MS (QQQ)	High selectivity, sensitivity, precision, extended turnaround	High capital, recurring & labor
	LC-ICP/MS	Medium selectivity, high sensitivity, precision, intermediate turnaround	Medium capital, recurring & labor
Organics, semi-volatile and volatile	GC-MS	Medium selectivity, high sensitivity, precision, intermediate turnaround	Medium capital, recurring & labor
	GC-MS/MS (QQQ)	High selectivity, sensitivity, precision, extended turnaround	High capital, recurring & labor
Inorganic (anionic)	LC-MS/MS (QQQ)	High selectivity, sensitivity, precision, extended turnaround	High capital, recurring & labor
	IC-UV/VIS; -MS/MS; ICP/MS	Medium to high selectivity, low to high sensitivity, precision; intermediate to extended turnaround	Medium to high capital, recurring & labor
Inorganic (cationic)	ICP/MS	High selectivity, medium sensitivity; intermediate turnaround	Medium capital, recurring & labor
Organics (bioreactive)	Immunoassays	Medium selectivity & sensitivity, rapid turnaround	Low capital, recurring & labor

2.3.2 Semi- and Non-Targeted Methods

To screen for and identify TOrCs not addressed by existing targeted methods (e.g., new chemicals, known and unknown transformation products), a semi- or non-targeted approach is needed. If some knowledge exists of the chemical structure or bioactivity associated with the compound (i.e., the compound is a “known unknown”), a semi-targeted approach (aka “suspect screening”) is useful, as it would reduce the universe of possible chemical structures, and with that knowledge comes reduced uncertainty, and therefore time and effort needed for identification of analytes. On the other hand, a

non-targeted approach applies when the analyst has no *a priori* knowledge of the compound present in a sample ("unknown unknown"). In this situation, a sequence of analytical and data processing steps is followed (aka "workflow") to narrow down the possible structures of these "unknown unknown" compounds, and if successful, to identify the compound outright.

Examples of methods used for semi- and non-targeted analysis from the literature (Appendix E) are summarized in Table 2-3. In general, chromophoric techniques, such as UV-visible absorbance detection, are not suitable for semi- and non-targeted analysis given limited sensitivity and low selectivity. Fluorescence spectrometry can be quite valuable for identification of specific compounds, namely those that fluoresce, but are not suitable given lack of response for non-fluorescent compounds. Low mass resolution MS, such as those in single and triple quadrupole instruments, are optimized for quantification of known compounds. While they can be used for identification of unknown compounds, the most effective use of such instruments generally requires spectral libraries. These are most consistent only for GC-MS-based systems using electron impact ionization for which spectra are widely available for thousands of compounds by various sources (e.g., NIST, and instrument vendors). Under these circumstances, low resolution mass spectrometric instruments can be quite powerful for NTA, particularly as analogous mass spectral databases for high resolution instruments are not widely available to date. In addition, LC-MS ionization techniques, such as electrospray and atmospheric pressure chemical ionization, are softer techniques than electron impact, and therefore produce fewer mass fragments that can be utilized to identify compounds unambiguously. Also, mass spectra from both major LC ionization techniques can be dependent on solution chemistry, particularly for electrospray ionization. For these reasons, low mass resolution LC-MS is typically not widely used for suspect screening or non-targeted analysis.

Table 2-3. Candidate Semi-Targeted and Non-Targeted Analysis Systems for TOrCs in Aqueous Samples.

Analyte	Method[1]	Performance	Relative Cost
Organics, non-volatile	LC-HRMS (MS/MS, QTOF, Orbitrap)	High selectivity, medium sensitivity, low precision; extended turnaround	High capital, recurring, and labor
Organics, semi-volatile and volatile	GC-HRMS (MS/MS, QTOF, Orbitrap)	High selectivity, medium sensitivity, low precision; extended turnaround	High capital, recurring, and labor
	GCxGC/TOF-MS	High selectivity, medium sensitivity, medium precision; extended turnaround	High capital, recurring, and labor
Organics, non-volatile, and Inorganic (anionic)	LS-MS/MS (QQQ)	High selectivity, medium to high sensitivity, precision; extended turnaround	High capital, recurring, and labor
Organics, chromophoric	UV-visible spectrophotometry (UV Absorbance)	Low selectivity; medium sensitivity, precision; rapid response (online)	Medium capital, low recurring and labor
	Fluorescence Spectrophotometry (Total Fluorescence)	Low selectivity; medium sensitivity; rapid response (online)	Medium capital, low recurring and labor
Organics, bioactive	Bioanalytical (cell-based)	Medium selectivity, precision; high sensitivity, rapid turnaround	Low capital, recurring and medium labor

Accurate or exact mass instruments, aka high-resolution mass spectrometers (GC-HRMS or LC-HRMS) are among the most powerful analytical tools to identify suspected and unknown TOrCs. The two most common types of high mass resolution used for trace environmental chemical analysis include time-of-flight (TOF) mass spectrometry, including hybrid detectors such as QTOF, and Orbitrap mass spectrometry. Both can provide sufficient mass resolution (e.g., 10,000+) for identification of unknown compounds of low molecular weight, compared to ~100-1,000 for low mass resolution instruments. Orbitrap instruments are particularly popular for this purpose, as mass resolution in such instruments increases with decreasing ion mass-to-charge ratio; for low molecular weight compounds typical of aquatic environmental contaminants, mass resolution exceeding 100,000 is common. In addition, resolution increases with increasing scan time in such instruments. However, implementation of HRMS methods is costly from both a capital equipment and required expertise (labor) standpoint, particularly for Orbitrap instruments. Although data processing workflows, necessary for non-targeted analysis, are being automated to reduce expert personnel time, building consensus on appropriate and effective standardized protocols is still very much a work in progress.

To circumvent some of these issues, a technique known as two-dimensional gas chromatography – time of flight mass spectrometry (GC×GC-TOF/MS) has been applied for suspect and non-targeted screening of aqueous media, including samples from an operating recycled water facility. By using two separate chromatographic stationary phases to resolve individual compounds in a complex sample mixture prior to mass analysis, GC×GC-TOF/MS does not require high mass accuracy in detection to provide high confidence in identifying unknowns, although some vendors do use high mass resolution TOF instruments to link with GC×GC systems at the price of additional capital and operating expense. Data processing is also simplified relative to HRMS workflows as the electron ionization (EI) spectra obtained by TOF/MS are more readily searchable using spectral libraries that are far more populated and vetted compared with “soft ionization” libraries and databases.

In contrast to MS-based methods, receptor-based cell assays that provide an integrated measure of chemical exposure in a relatively short time period (one to two days), have been adapted and more recently applied for water quality monitoring applications. Many of these assays provide the added benefit of gleaning information regarding potential effects that are plausibly linked to the assay-specific response. For example, the estrogen receptor (ER-α) transactivation assay responds to estrogenic chemicals present in a sample by initiating a cascade of biochemical events that can result in a toxic response at the tissue and/or organism level. Applied in conjunction with targeted and non-targeted monitoring methods, cell assays can better inform and streamline efforts to identify bioactive (and potentially problematic) TOrCs in recycled water (see also Task 1D – Data Interpretation). The State of California recently adopted the recommendation of the Science Advisory Panel to use cell assays, including the ER-α assay, to screen recycled water quality for potable reuse facilities (SWRCB 2018).

It is recommended that the utility for screening recycled water quality afforded by cell assays be further evaluated. It is also recommended that the diagnostic capabilities of HRMS-based and GCxGC-TOF/MS methods be further evaluated. These recommendations are discussed in further detail in Chapter 3.

2.4 Tiered Monitoring Strategy for Recycled Water

As no one single group or set of analytical methods (and most certainly no single method) can address all possible chemicals of interest across a wide range of aqueous matrices, a multi-tiered monitoring approach is recommended by leading experts in the field (Appendix D). A three-tiered approach described here utilizes multiple methods to screen first for surrogates and indicators of TOrCs using continuous and/or robust offline methods, and if warranted, then identify problematic TOrCs using more advanced, diagnostic methods (Figure 2-2).

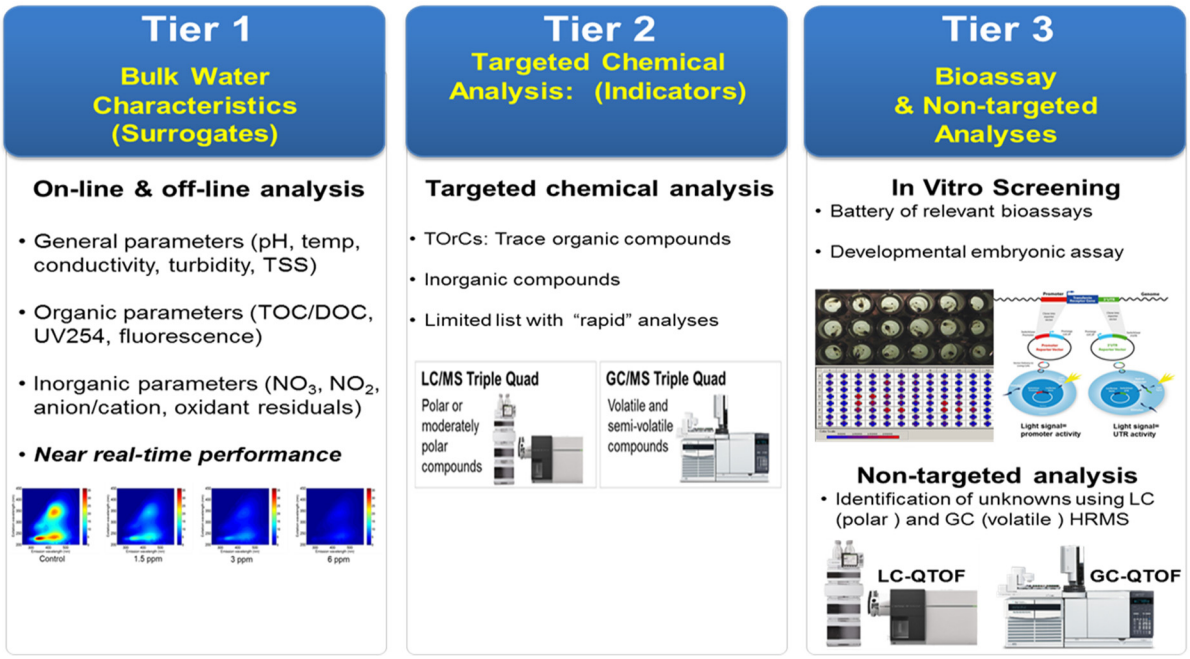

Figure 2-2. A Three-Tiered Approach for Monitoring of Recycled Water Quality Allows for Efficient Utilization of Currently Available Technology and Human Resources.
Courtesy of S. Snyder, University of Arizona.

2.4.1 Tier 1: Bulk Water Analysis for Surrogates of TOrCs

Tier 1 represents online *in situ* measurement of surrogate parameters for TOrCs in water, as per Figure 2-2, that is subject to minimal modification and/or disturbance. These parameters include general water quality parameters such as pH, temperature, conductivity, and turbidity for which monitoring efforts (e.g., in wastewater) typically exist as a matter of course. They can also include organic parameters, such as TOC/DOC, UV absorbance at 254 nm, and fluorescence; as well as inorganic parameters such as nitrate/nitrite content. Sudden increases in such parameter can be indicators of greater contamination (e.g., increases in conductivity can be due to the general presence of wastewater) requiring more detailed Tier 2 or Tier 3 analysis. The efficacy of such surrogates in correlating with the water-borne presence of TrOCs, both known and unknown, is a research topic addressed in Chapter 3.

2.4.2 Tier 2: Targeted Chemical Analysis for Indicator TOrCs

Tier 2 represents periodic measurement of indicator TOrCs, including those known or suspected to occur in recycled water treatment trains that may be of health concern and/or that provides information on treatment performance. Unlike Tier 1 surrogate monitoring, the "targeted" analysis of indicators is typically performed offline, requiring sample collection, preservation and processing protocols prior to instrumental analysis using separation or ionization interfaces (GC, LC, or ICP) coupled to single or tandem mass detectors (MS or MS/MS, respectively) (Figure 2-3). The type of analytical technique to use depends on the analytes of interest, as described previously. For example, metals and metal complexes are best analyzed using ICP-MS, while dedicated analysis of inorganic ionic species is more suited to IC.

Surrogate and/or indicator monitoring results are quantitative, meaning that absolute and/or changes in concentrations of measured parameters can be interpreted against action thresholds established in advance to warn AWTF operators and managers of "off-spec" conditions. In the case of health-based indicators, the quantitative monitoring data can be used to assess incremental risk of exposure to "off-spec" water, and ultimately to inform appropriate management actions.

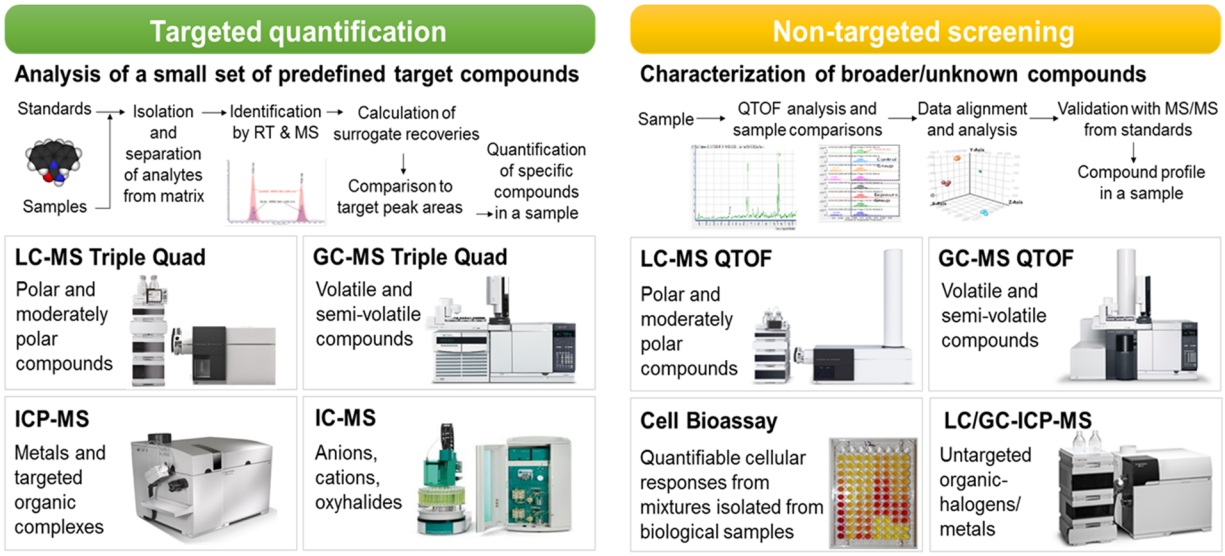

Figure 2-3. Workflows and Instrumental Techniques Differ for Targeted and Non-Target Analyses (NTA), with NTA to Identify Unknown TOrCs Requiring Rapid Scanning, Accurate Mass Instrumentation and Multi-Step Data Processing Sequences.

Which techniques to use is dependent on analyte properties and on availability of instrumentation and expertise to use it effectively. Courtesy of S. Snyder, University of Arizona.

2.4.3 Tier 3: Instrumental Non-Targeted Analysis

Tier 3 analyses are used to screen for and identify TOrCs not addressed by targeted methods (e.g., new chemicals, transformation products, or previously unidentified or unknown compounds). In such cases, semi- or non-targeted methods are needed, for example if the sample site is suspected to have new chemicals present, or if weathering of chemicals resulting in the potential formation of transformation products is likely. Non-target analysis is applied under the most challenging of situations, such as when the analyst has no *a priori* knowledge of the compound present in a sample. If some knowledge of the chemical structure or bioactivity associated with the unknown compound of interest exists, a semi-targeted approach (aka "suspect screening") reduces the universe of possible chemical structures. As a result, the instrumental analysis is much the same as for NTA but the data workflow is simplified, and the uncertainty associated with suspect compound identification is also (in theory) reduced. Examples of detection methods used for semi- and NTA are summarized in Table 2-3. For elucidation of a chemical structure resulting in a positive identification of a previously unidentified or unknown TOrC, mass spectrometry-based instrumental techniques are preferred. MS-based methods that have shown the most promise to date for NTA and suspect screening are two-dimensional gas chromatography coupled to a fast scanning mass spectrometer, such as a time-of-flight detector (GC×GC/TOF-MS); and GC or LC coupled to accurate mass detectors, aka high-resolution mass spectrometers (HRMS) (Figure 2-3). As before, the choice of instrumental analysis technique to use will depend on the properties of the analytes, as well as on logistical constraints on availability of capital equipment and appropriate expertise to use the equipment in an effective and efficient manner.

Because of the large volume and complexity of data produced, NTA also requires a sequence of analytical and data processing steps (referred to as "workflows") above and beyond what is employed for targeted analysis. A typical example of the logic and structure of such workflows is found in Figure 2-4, and examples of successful use are described in case studies below. Moreover, specialized expertise is required to conduct data analysis for NTA results, and subsequently to interpret the output from such

workflows. Automation of data processing is limited to date, and data-mining is typically done and tailored for specific objectives that are generally difficult to adapt beyond their intended use. Custom data processing workflows are currently instrument-specific. This is due in part to the fact that standardized mass spectral databases for usable across the myriad of platforms available from different vendors have not yet been established. In turn, this is due to the difficulty of creating common mass spectral databases for LC-based ionization processes as previously discussed. Few public-databases exist in any event. The combined result of workflow complexity and the limited availability of specialized expertise typically results in a timeframe to complete suspect screening or NTA for a given sample of weeks to months, and even years.

As with targeted analysis, the results of NTA are also incumbent on sample collection, preservation and processing protocols. Whereas specific classes of TOrCs require specialized extraction protocols, isolating a broad spectrum of TOrCs from water relies on sorbents that capture both hydrophilic and lipophilic chemicals (e.g., hydrophilic/lipophilic balance (HLB) type resins) (Table 2-1). To minimize loss of TOrCs, the collection and storage of water samples in amber glass bottles containing ascorbic acid and sodium azide as quenching and preserving agents has been shown to provide good recovery of TOrCs (Vanderford et al. 2011). Timely extraction after sample collection is another important consideration to ensure a representative analysis is performed.

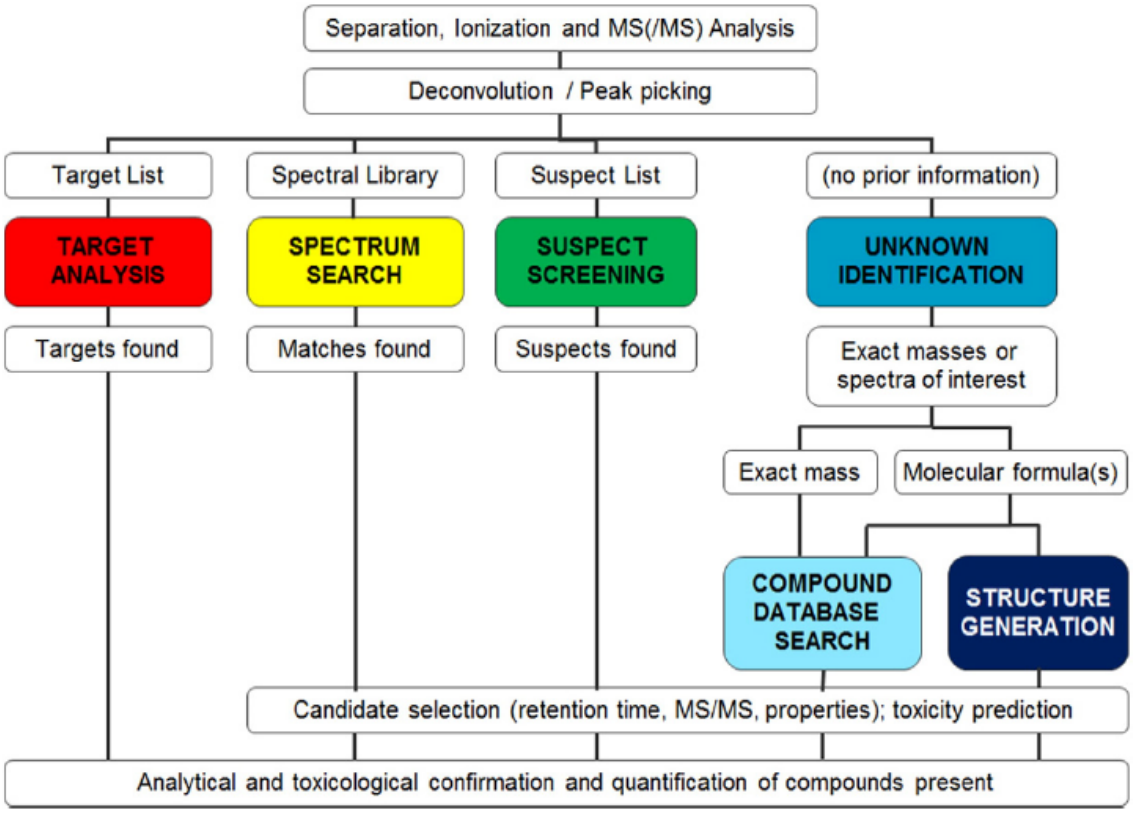

Figure 2-4. Because Analytical Standards are (by Definition) Not Available, Data Processing Workflows, Such as This One, to Identify Unknown TOrCs Using Non-Targeted Analysis Involve Multiple Steps Beyond What is Applied for Known or Suspected Chemicals.
From Brack et al. 2016.

2.4.3.1 Case Studies for Instrumental Non-Targeted Analysis

Perhaps the best known and most comprehensive application of NTA for water quality monitoring and assessment was performed on the Rhine River, the source of drinking water for countless communities along its banks, as described in Ruff et al. (2015) and Hollender et al. (2017). A five-step workflow beginning with sampling and instrumental analysis followed by a sequence of three data processing steps, similar to those shown in Figure 2-4, was followed. In a pilot study to standardize such workflows for more intensive baseline monitoring, seven-day composite samples from 10 stations on the Rhine were extracted by multiple SPE phases and analyzed by Orbitrap LC-HRMS, resulting in the confirmed identification of seven previously unidentified TOrCs and 10 additional tentatively identified structures (Ruff et al. 2015). Of the 17 chemicals identified using the NTA workflow, roughly half were identified using a simplified "empirical" approach, whereas the remaining TOrCs were identified using the more rigorous "systematic" approach.

The pilot study was followed by daily monitoring of water quality at a single station near Basel, Switzerland, resulting in collection and analysis of nearly 2000 samples between 2012 and 2016. In addition to target and suspect screening, NTA was implemented to safeguard against periodic inputs (i.e., spills) of previously unidentified or unknown TOrCs into the river. This effort confirmed the presence of 2-phenyl-2-(2-piperidinyl)acetamide, or PPA, a precursor in the synthesis of methylphenidate (Ritalin) commonly prescribed to treat attention deficit disorders, which triggered additional investigation to identify its source(s). Both Hollender et al. (2017) and Ruff et al. (2015) concluded that such "non-target concepts can easily be applied and adapted" and that the case studies "demonstrates the potential for NTA to be an effective complementary analysis technique in a regulatory framework." However, they also acknowledged that" such programs are costly" (Hollender et al. 2016) in part because the final unknown identification step requires "time consuming and systematic analysis of the dataset" (Ruff et al. 2015).

The negative impact of not standardizing NTA workflows was illustrated in an interlaboratory comparison of HRMS involving 18 European labs who analyzed a single common extract of a Danube River water sample using their own instruments and workflows (Schymanski et al. 2015). Incorporating the three-pronged screening approach (i.e., target, suspect, and non-target) shown in Figure 2-4, the participants reported the number of TOrCs identified using a five-level confidence matrix "scorecard". Out of thousands of peaks appearing in the extract, the number of tentatively identified unknowns (Level 2 or 3) ranged between one to 26, with only six of 17 labs reporting. The number of unidentified peaks in the extract reported by 13 of 17 laboratories ranged from three to 8,535. The wide range of NTA results clearly illustrated the lack of consensus among participants, and thus the degree of development and evaluation needed to standardize NTA workflows for identifying unknowns in water samples.

Very few if any published studies have demonstrated the utility of GC-based HRMS applications for identifying unknown TOrCs (i.e., in true non-target mode) in recycled, potable and/or a similarly highly treated water matrix. One recent study, however, applied both LC- and GC-HRMS to comprehensively screen ambient water samples from the Sacramento-San Joaquin River Delta complex (CA, USA) (Moschet et al. 2017). A total of 51 water samples were collected, extracted by Oasis HLB SPE and analyzed by GC-QTOF-MS/MS in the EI mode to facilitate spectral matching. Using a retention time based peak processing software, 45 compounds were identified with 17 reported as being unique to this method compared with the results of parallel LC-QTOF-MS/MS analyses. Of the 45 TOrCs identified, 39 were confirmed using authentic standards. The majority of identified compounds were pesticides and/or their transformation products, with the remaining TOrCs derived from wastewater and/or other non-point sources in the watershed.

2.4.4 Tier 3: Bioassay Directed Identification of Unknowns

In contrast to MS-based detection methods, receptor-based cell assays that provide an integrated measure of chemical occurrence (and thus exposure) have been adapted and applied for benchmarking the quality of source and product water samples from pilot and/or full scale AWTFs (Escher et al. 2014; Mehinto et al. 2015). Measurement protocols for these high throughput assays can be completed in a relatively short time period (on to two days). As with targeted and NTA methods, bioassay methods require separate offline sample collection, preservation and processing protocols that generate an extract suitable for such analysis. A subset of these assays provides the added benefit of screening a potentially wide spectrum of TOrCs that may be present in a sample for potential overall toxicity (e.g., the estrogen receptor (ER-α) transactivation assay responds to estrogenic chemicals than are known to affect reproductive success in model animal species) (Mehinto et al. 2018). Applied in conjunction with analytical chemistry, cell assays applied in semi-targeted mode can streamline efforts to identify problematic TOrCs (Brack et al. 2008; Brack et al. 2016; Snyder 2014). This was recognized by a panel of experts charged with recommended monitoring practices for recycled water applications statewide in California (Drewes et al. 2018).

Bioassays have been combined with targeted analysis to identify problematic TOrCs since Snyder et al. (2001) reported the presence of natural and synthetic estrogens in water receiving treated wastewater effluent. Since then, receptor-based bioassays have been applied to screen for the occurrence of other endocrine disrupting chemicals in wastewater impacted waters, including gluococorticoid steroids (Jia et al. 2015), and followed up with targeted LC-MS/MS analyses to identify the specific glucorcorticoids responsible for such bioactivity (Jia et al. 2016). More recently, Zhang et al. (2019) applied LC-QTOF-MS in suspect screening mode to identify transformation products (TPs) that modulated genotoxic responses of *Salmonella* bacterial strains exposed to extracts of water subject to different advanced water treatment processes. Although the application of LC-HRMS did not result in confirmed compound identifications of the most bioactive TPs in this latter study, the combination of bioassay directed HRMS analysis narrowed the field of possible chemical structures to nitrogenous compounds that could be further identified in additional, follow-up studies. This follow-up would be necessary to identify the toxicity associated with such unknown compounds; while their potential toxicity may be estimated from their structure via quantitative structural-activity relationships (QSAR), these may not necessarily be available (e.g., only limited predictive capability currently exists) or applicable (e.g., chemical may not have a structure amenable for predictive modeling, or endpoints differ). The linkages among targeted analysis, instrumental non-targeted analysis, and bioassays provides synergy for increasing our understanding of TrOCs and their effects in waters.

2.5 Interpretation of Analytical Results for Unknown Contaminants

At present, the infrastructure, expertise, effort/time, and ultimately cost to perform suspect screening and non-targeted analysis of known unknown and unknown unknown greatly outdistances the cost to perform surrogate, targeted and semi-targeted cell assay analyses (Snyder 2014; Leusch and Snyder 2015). Thus, it would be highly cost inefficient and thus fruitless to approach the identification of unknowns without first screening for the possible/likely occurrence of problematic TOrCs, both known and unknown. Such a screening approach has been proposed by multiple investigators, including the recent California Science Advisory Panel for CECs in recycled water (Drewes et al. 2018). In their proposed framework for unmonitored TOrCs (aka CECs), non-targeted analysis for unknowns plays a “last ditch” diagnostic role when targeted methods fail to identify problematic TorCs (Figure 2-5). Furthermore, the incorporation of cell assays that screen for groups of TorCs that share common biological response modes (or “modes of action”) into the screening framework serves to inform and narrow the candidate compound structures/classes responsible for the cell bioactivity. This additional information also serves to reduce and/or focus the effort needed for subsequent diagnostic

investigation from non-targeted unknown to suspect screening identification, also referred to "exploratory" phase screening (Leusch and Snyder 2015).

Inherent in the screening frameworks proposed by Leusch and Snyder (2015) and Drewes et al. (2018) is the ability to respond to monitoring data, once unknowns have been identified and appropriate methods have been established to generate robust exposure and effects information using a traditional risk assessment paradigm. It also follows that successful non-targeted identification of a previously unknown or unidentified TorC would be useful for source control measures employed by the affected utility.

In summary (Figure 2-5), both targeted and non-targeted analysis (by both instrumental and bioassay), are integrated parts of the screening and monitoring for occurrence and effects of low molecular weight compounds in waters. Targeted analysis is valuable for monitoring for known TOrCs of concern, particularly those with defined action levels for regulatory and compliance purposes. This analysis can trigger the necessity for non-targeted analysis on its own, depending on criteria (e.g., waters at a specific site are suspected to have compounds not routinely measured by targeted analysis, or may contain transformation products that are problematic). Bioassays can provide a measure of overall toxicity to an endpoint of interest, which itself can trigger appropriate targeted or non-targeted instrumental analysis (e.g., if overall toxicity exceeds that of known chemical constituents) to identify unknown compounds of concern, or even quantify them as standards become available. For recycled water, these integrated approaches can be applied to various stages of advanced water treatment to evaluate occurrence and effects of known and unknown TOrCs of interest and concern.

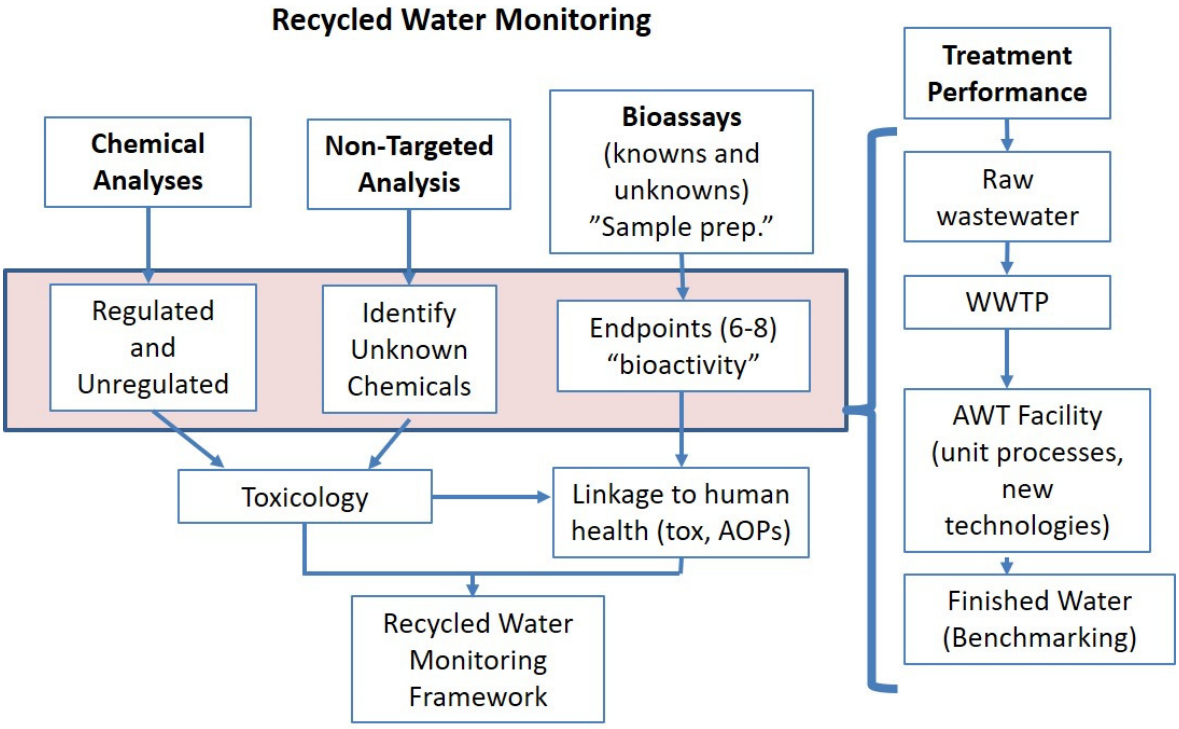

Figure 2-5. Non-Targeted Analysis Complements Current "Targeted" Chemical Analyses and Newly Developed Bioanalytical Tools for Monitoring Recycled Water Quality and for Assessing Treatment Performance.
Adapted from Drewes et al. 2018.

2.6 Data Support Tools for Non-Targeted Methods

As summarized by Schymanski et al. (2015), there is a clear need to harmonize and standardize data processing workflows for mass spectrometric based suspect and unknown identification. It is also accepted that EI mass spectral libraries, i.e., those populated by MS instruments that utilize hard ionization energies, are more easily standardized and accessed than those being developed and compared for ESI-based HRMS techniques (i.e., LC-MS, -QQQ, -QTOF and Orbitrap MS). Moreover, it has been acknowledged that mass spectra acquired by the various HRMS instruments available to analysts may differ, creating a difficult challenge in harmonizing HRMS spectral databases and/or additional steps in HRMS data workflows. At present, such harmonization and standardization are viewed as a long-term, multi-million dollar endeavors that are well beyond the scope of this investigation. However, initial steps can be taken toward understanding and defining the practical capabilities of non-targeted methods for recycled water monitoring and assessment. These include:

1. Creation and standardization of an EI mass spectral database for water quality assessment;
2. Characterization of overlap in the occurrence profile of “known unknowns” and “unknown unknowns: detected in recycled water samples using LC-HRMS, GC-HRMS and GC×GC-TOF/MS;
3. Streamlining and standardization of HRMS workflows for suspect and unknown identification.

2.7 Frequency of Monitoring

Short of directing hundreds of thousands (and likely millions) of U.S. dollars for application of non-targeted methods in routine monitoring of recycled water, it is not currently feasible to recommend a regular schedule for these methods. Rather, as the California Science Advisory Panel has most recently recommended (Drewes et al. 2018), the application of non-targeted methods is most effectively tied to the results of more frequent, robust and cost-effective screening methods, namely the surrogate, targeted and semi-targeted cell assay methods described herein. For fully operational water recycled facilities, semi-annual monitoring of targeted indicator TOrCs and cell assay parameters in product water prior to discharge to the subsurface or surface aquifer was recommended (Anderson et al. 2010; Drewes et al. 2018). During pilot testing and facility start-up, more frequent (i.e., quarterly) monitoring at additional locations within the treatment train is recommended (Drewes et al. 2018). As online monitoring technology matures, surrogate data collected continuously will allow for screening of relative water quality on a near real-time basis. It was emphasized that only when surrogate, indicator and cell assay results consistently exceeded monitoring thresholds, that diagnostic investigation, which includes in sequence 1) targeted and 2) non-targeted analysis is warranted.

To be clear, non-targeted analysis by itself is not currently a cost-effective means of screening for unknowns in recycled water (Drewes et al. 2018). These recommendations may change in the future as non-targeted techniques mature and become as/more cost-effective as current targeted and semi-targeted screening methods.
Thus, it is recommended that non-targeted “screening” of recycled water not be implemented on a fixed time schedule, but rather, appropriately and prudently applied in response to results of currently recommended screening methods.

CHAPTER 3

Proposed Research Plan

A phased approach is described to compartmentalize and sequence methods evaluation for identifying LMW unknown TOrCs in recycled water. *Phase 1*, described in detail in this chapter, will focus on identification of unknowns in product and source water matrices using the Tier 3 non-targeted mass spectrometric methods described in Section 2.4.3. Because no single method can cover the broad range of possible LMW unknown TOrCs, both the LC- and GC-based methods highlighted in Table 2-3 will be assessed. The challenge task for *Phase I* will evaluate whether the candidate methods can correctly identify model "unknowns" spiked into carbon-filtered Milli-Q ("zero") water, followed by a second challenge on a more complex, "real life" mixture of unknowns (e.g., tertiary wastewater effluent that has undergone advanced oxidation). A five-year project is proposed, at an estimated cost of $1.2M, with approximately 50% of the total cost reserved for evaluation of each of the two proposed matrices.

Following the approach utilized for development of RCRA methods, investigators shall first characterize the measurement performance of candidate NTA methods using clean water matrices spiked with model TOrCs. Methods that demonstrate acceptable performance based on QA/QC measurement goals shall then be subject to challenge testing using a more realistic "source" water matrix (e.g., one that represents a complex mixture of a broader suite of TOrCs as well as natural background interferences). Challenge testing results from the different methods shall be assessed for comparability, relevance, and utility as part of a tiered monitoring framework (Figure 2-2). Investigators shall provide a ranking of evaluated methods based on their performance and utility, as well as suggested next steps for method development.

Subsequent phases deemed necessary to take full advantage of Tier 3 NTA methods that perform satisfactorily in the *Phase 1* evaluation will focus on further aims. *Phase 2* work is the development and evaluation of surrogates to detect changes in bulk water quality in real time. A listing and description of candidate surrogates and indicator methods, recommended by previous expert panels on CECs in recycled water (Drewes et al. 2018), is provided in Appendix A. *Phase 3* work would develop and evaluate targeted and bioanalytical methods, summarized in Appendix B, to inform identification of suspected and/or unknown contaminants missed by existing monitoring methods.

The *Phase 2* evaluation of promising surrogate methods will follow a similar design as described for *Phase 1*, but would also incorporate comparisons, as appropriate, between analysis of spiked surrogates in samples, with analysis of model TrOCs present in waters being monitored. *Phase 2* has an estimated cost of $300K for a two-year project.

The *Phase 3* evaluation of targeted and bioanalytical methods would also follow a similar plan as that described below for *Phase 1*, but will require a longer list of endpoints and known chemicals to spike and conduct in representative source and product water matrices. The choice of endpoints will depend on the results of *Phase 1* and *Phase 2* testing. *Phase 3* has an estimated cost of $700K for a three-year project.

3.1 Sample Collection, Preservation, Transport, and Processing

3.1.1 Sample Collection, Preservation, and Transport

Duplicate 1-L aliquots of spiked clean water or candidate source and product water samples shall be collected in pre-cleaned amber glass bottles with pre-added ascorbic acid and sodium azide using trace organics research grade protocols (see Appendix C). Immediately after collection, each sample bottle shall be capped and placed in ice-filled coolers or directly in refrigerator storage (maintained at 4°C). If

overnight shipping is necessary, sample bottles shall be shipped on ice and delivered to the investigator within 24 hours of collection. Upon receipt of sample bottles, investigators should measure and record the interior temperature of the shipping container, and immediately store and maintain the sample bottles at 4°C.

3.1.2 Sample Processing

Within two weeks of spiking or collection, aliquots of water samples (500 mL minimum) shall be extracted by SPE using a broad-spectrum or mixed mode sorbent, such as Oasis HLB, to capture a wide variety of TOrCs in the sample. Each 500 mL aliquot equivalent shall be reduced in volume and exchanged to the appropriate solvent for instrumental analysis (methanol for LC-based NTA; dichloromethane or iso-octane for GC-based NTA). A minimum of three 500-mL equivalent sample extracts – one for each instrumental method described in Section 3.2 – shall be prepared.

3.2 Instrumental Analysis

3.2.1 LC- and GC-HRMS

Per Table 2-3, sample extracts representing 500 mL equivalent volumes of spiked clean water, source and/or product water shall be analyzed by LC-and GC-based high-resolution mass spectrometry. Different HRMS instruments are currently available for feature identification, suspect screening and/or unknown identification, including quadrupole-time of flight (QTOF) (e.g., Vanderford et al. 2008; Anumol et al. 2016; Moschet et al. 2017) and Orbitrap (Wang and Gardinali 2014; Prasse and Ternes 2016; Hu et al. 2018) instruments. Custom data processing workflows are currently instrument-specific, as standardized mass spectral databases have not yet been established. The investigators shall identify instruments and workflows that, as a minimum, have been partially validated for identifying suspect or unknown TOrCs.

3.2.2 GC×GC-TOF/MS

Per Table 2-3, sample extracts representing 500 mL equivalent volumes of spiked clean water, source and/or product water shall be analyzed by comprehensive two-dimensional GC coupled to time-of-flight mass spectrometry (GC×GC/TOF-MS) to detect previously unidentified semi-volatile and volatile organic compounds. This technique relies on a rapid scanning mass spectrometer (hence the TOF/MS) and high resolution of chromatographic separation from GC×GC to resolve and identify closely eluting peaks in a complex sample. Data processing workflows for feature identification, suspect screening and/or unknown identification that have been developed for various water qualities from an AWTF (Hoh et al. 2018) shall be followed. For suspect screening, GC×GC/TOF-MS has a great advantage because the largest mass spectral library (NIST EI mass spectral library) that contains 250,000 mass spectra is available.

3.3 Study Design

3.3.1 Initial Evaluation of Method Performance

In the first step of the proposed two-step evaluation process, investigators shall characterize the baseline measurement performance of the candidate methods using highly purified, low TOC (“Milli-Q” grade) water spiked with low levels of model TOrCs selected to represent unknown or otherwise problematic chemical classes that may be expected to occur in source and product water. The evaluated methods should exhibit suitable “background” performance for ultrapure (“Zero”) water, as well as low TOC water. Model TOrCs may include synthesized or commercially available disinfection by-products (DBPs) that represent “known unknowns” generated and/or not fully removed by an AWTF, as well as known indicator compounds (see Appendix A, Table A-2).

3.3.2 Challenge Testing

An important consideration for building confidence in new methods is the demonstration of their performance, when competently applied, and utility in providing the relevant information to support hazard assessment or unknown compound identification. Since the matrices of interest for DPR monitoring are narrowly defined (e.g., the California Department of Drinking Water), investigators shall identify those methods that demonstrate adequate performance for such matrices (e.g., source and product water) in the initial evaluation (Section 3.3.1). It should be noted that application of the analytical methods under consideration to a broader range of water qualities (e.g., receiving waters that contain complex mixtures of TOrCs and natural background substances including elevated levels of total suspended solids (TSS) and/or dissolved organic matter (DOM)), is possible but beyond the scope of the current research plan. For DPR applications, two matrices of interest shall be considered for this phase of the evaluation: 1) source water (filtered secondary/tertiary municipal effluent); and 2) product water (post RO, or RO-permeate). Split samples of well characterized source and product water samples from participating AWTFs that represent a range of water qualities shall be employed for challenge testing.

3.3.3 Measurement Performance Goals

The investigators shall apply measurement performance goals for mass spectrometry based semi- and non-target methods that address range of mass (compound) identification, sensitivity of detection and uncertainty associated with compound (mass spectral) identification, as listed in Table 3-1, in their assessment of semi- and non-target methods. Detailed QA/QC guidelines for candidate NTA methods are included in Appendix C.

3.4 Data Analysis and Synthesis

3.4.1 Assessment of Data Quality

The quality of data collected in both the initial performance and challenge testing phases of this evaluation for semi- and non-target methods shall be assessed against the measurement performance goals in Table 3-1. The quality of compound identification or confirmation of a known TOrC shall be based on the spectral match score for LC-based methods; and the combination of spectral and retention time match for GC-based methods (Table 3-1). For all candidate methods, the number and magnitude of exceedances of numeric goals shall be compiled into a composite score to rank the methods in terms of their overall performance.

3.4.2 Method Comparability

For semi- and non-target methods, there is expected to be some overlap in the TOrCs that are detectable using the three different approaches. Thus, the investigators are expected to provide the numbers and lists of identified TOrCs using each of the mass spectrometric methods. Heat maps and/or Venn diagrams shall be generated to visualize the overlap in identified TOrCs among these methods.

3.4.3 Method Relevance and Utility

The investigators are tasked to comment on the utility efficacy of each individual NTA method using relevant metrics for assessment of analytical methods, if available.

3.5 Research Team Qualifications

A multi-disciplinary team with expertise in analytical chemistry, advanced (non-target) environmental mass spectrometry, and water quality monitoring and assessment and recycled water treatment practices shall be formed to carry out this study. A highly experienced practitioner who understands the monitoring requirements and gaps for TOrCs in recycled water for potable reuse, as well as the current state-of-the-art of monitoring technologies proposed herein shall lead this effort. Some potential candidates for lead PI include Dr. Jorg Drewes (TU Munich), Dr. Shane Snyder (NTU and the University of

Arizona) and Dr. Shane Trussell (Trussell Technologies, Inc.). The above candidates would also be qualified to manage and evaluate the performance of surrogate and indicator methods as described in *Phase 2*. In addition to Drs. Snyder and Drewes, Drs. Thomas Young (UC Davis) and Lee Ferguson (Duke University) are potential candidates knowledgeable in evaluating and applying LC- and GC-HRMS methods; Dr. Eunha Hoh (San Diego State University) is a potential candidate recommended for evaluating GC×GC-TOF/MS; and Drs. Michael Denison (UC Davis), Daniel Schlenk (UC Riverside) and Alvina Mehinto (SCCWRP) are potential lead candidates for evaluating bioanalytical tools.

Currently, the vast majority of NTA is done in academic and public-sector research laboratories. Few commercial laboratories have both the equipment and the requisite expertise to perform NTA in an efficient and effective manner.

Table 3-1. Measurement Performance Goals for Suspect Screening and Non-Target Analysis of Unknown Compounds.

Method/Parameter	Sensitivity[1]	Retention Time[2]	Mass Range[3]	Mass Accuracy[4]	Mass Resolution[5]	Spectral Match
LC-HRMS	≤ 0.01 ug/L (S/N = 5)	± 0.2 min	20-2000 Da	± 5 ppm	≥ 25 000	≥ 70%
GC-HRMS	≤ 0.01 ug/L (S/N = 5)	± 0.04 min	50-1000 Da	1 Da	≥ 10 000	≥ 70%
GCxGC-TOF/MS	≤ 0.01 ug/L (S/N = 5)	± 0.04 min	50-1000 Da	1 Da	unit	≥ 70%

[1] per analyte; may require pre-concentration of sample (e.g., by SPE)
[2] Ibáñez et al. (2017); Hernández et al. (2015); E. Hoh (pers. comm.)
[3] Da - Daltons
[4] Mass Accuracy (ppm) = 10^6 × [(mass error)/(exact mass)]
[5] m/Δm; nominal value across mass range

CHAPTER 4

Communication Strategy

4.1 Key Concepts

Accuracy, transparency, and timeliness are the key concepts for effective communication of monitoring results to the "community" that includes regulators, customers, and the general public as ultimate consumers of potable water supplied (in part) by DPR projects. In addition, a proactive outreach effort to educate the community on the importance and implications of monitoring for unknown TOrCs is needed to provide context for the results, which may not always be definitive and/or straightforward to interpret. These concepts are reflected in the recommendations of different Advisory Panels convened in the State of California over the years to address 1) monitoring of constituents of emerging concern or CECs in recycled water (aka TOrCs) (Drewes et al. 2018); and 2) the feasibility of establishing regulatory criteria for DPR (NWRI 2016) regarding the development of communication protocols for monitoring results.

From *Monitoring Strategies for Chemicals of Emerging Concern (CECs) in Recycled Water. Recommendations of a Science Advisory Panel. Final Report* by Drewes et al. (2018):

"*The State and Regional Water Boards ("regulatory agencies") should develop a protocol outlining the roles and responsibilities for reviewing and communicating CEC data from potable reuse projects. These protocols should include a process for communicating with the utilities*."

"*The State Water Board ("regulatory agency") should develop a protocol for providing the public an annual report summarizing performance of potable reuse projects. Public transparency is a key element to public acceptability. The intent is to be able to have a web portal for potable reuse projects and post annual utility reports and any State Water Board staff reports on the operations of the State Water Board program*."

From *Recommendations of the Advisory Group on the Feasibility of Developing Uniform Water Recycling Criteria for Direct Potable Reuse* by NWRI (2016):

To garner public confidence in the safety of DPR, "*a robust, comprehensive and continuous monitoring regimen should be required…*" and "*…should include a methodical and robust search for CECs and other potentially harmful constituents*."

"In addition, *monitoring requirements and water quality results should be made available to the public. Data and results should be routinely posted to the utility's website and included in Consumer Confidence Reports (CCRs). Water quality data and relevant public health information should also be made available on a continuous basis."*

"*Utilities should develop a proactive and comprehensive education outreach program early in the development of a DPR project. A well planned and well-executed public educational effort by project proponents is essential to obtain public acceptance*."

4.2 Challenges

The current chemical-specific monitoring paradigm compares concentrations of individual chemicals to pre-determined screening or trigger levels. In the case of regulated chemicals, maximum contaminant levels and/or guidelines (MCLs, MCLGs), established from toxicological information to be protective of human and/or environmental health, serve as benchmarks for estimating risks associated with

consumption of/exposure to chemicals in water. The persistence and magnitude of exceedance of established MCLs/PHGs are key factors in informing what management action(s), if any, is/are warranted. The existence of mature decision-making frameworks for regulated chemicals thus render the interpretation of monitoring results to be a relatively straightforward undertaking.

For unknown contaminants, however, a dearth of monitoring data can be expected, and even less toxicological information typically will be available to allow for a rigorous chemical-specific, risk-based assessment. Thus, identifying unknown TOrCs using NTA methods is but a single step in a multi-component monitoring and assessment framework (Figure 2-5). As a result, utility managers will be faced with difficult questions from the community at large regarding the potential impacts of unknown contaminants on potable water quality without the benefit of an established, proven interpretive framework for analytical results collected for the purposes of identifying unknowns. As such frameworks develop and mature, their role in establishing public confidence in the safety of DPR should be explained and incorporated into outreach materials.

4.3 Guidance for Effective Communication

A clear, simplified and accurate description of the need and implications of NTA results, coupled with a pre-defined channel of communication are the central elements of an effective strategy for communicating the results for identifying unknown TOrCs in DPR applications. For the former element, explanations for why and in what instances is NTA necessary should be provided in a clear and concise manner, followed by a concise and timely accounting of what was found, the implications to human health (if any), and finally what actions (if any) were taken to mitigate the incidence. Some examples of anticipated questions from the community, along with example responses to such questions, that can serve as content for community outreach are given below:

Question: Do existing monitoring methods guarantee the safety of recycled water in DPR applications?

Response: Waterborne contamination (e.g., by chemicals and microbes) can occur at any point in the water supply and distribution system. While existing monitoring programs employ methods that target hundreds of individual known chemicals, it is not technically nor economically feasible to measure every known chemical that can occur in water. That said, current monitoring provides a means to objectively assess the risks associated with consuming and/or contacting water that contains trace chemicals. When such monitoring data indicate that MCLs/PHGs are not exceeded, an acceptably low risk for health impacts is expected.

***Question: What do non-targeted methods measure, and why are they being considered for recycled water monitoring*?**

Response: Whereas existing targeted monitoring efforts measure individual “known” chemicals, there are many other chemicals that are unknown or remain unidentified in water treatment systems. Non-targeted methods attempt to identify such unknowns by isolating and enriching these chemicals from a water sample, and then applying state-of-the-art instrumentation to narrow down and ultimately identify its (their) chemical structure (and thus identity). Although advanced treatment technologies for recycled water have been shown to be robust for the removal of most chemicals over several decades of operation, changes in source water quality and newly developed treatment trains necessitate a more comprehensive monitoring approach that includes non-targeted methods. However, non-targeted methods are not routine at present, and their inclusion in monitoring programs for DPR applications should be carefully constrained to address specific management questions and needs.

***Question: What does the detection of a previously unknown chemical mean relative to safety and human health*?**

Response: The detection and identification of a previously unidentified or unknown chemical in source and product water for DPR serves only to confirm its presence. Thus, non-targeted analysis stops well short of assigning risk associated with consuming water that contains said unknown. Risk assessment requires both quantitative exposure (e.g., a water concentration) and toxicological information (e.g., an effects threshold), both of which are not generated by non-targeted analysis. To complete a risk analysis, targeted analytical methods are typically employed to measure water concentrations for individual (identifiable) chemicals, and experimental/modeling/statistical methods are employed to establish screening/trigger thresholds (e.g., MCLs).

***Question: What steps should be taken to address a detection or identification of an unknown*?**

Response: The results of non-targeted analysis should be viewed as one of many pieces of evidence obtained through a multi-component, multi-method monitoring approach to assessing water quality. Taken together with other measured parameters, such as surrogates and indicators, the results of non-targeted analysis can trigger additional confirmatory monitoring (e.g., to determine the persistence of the unknown's occurrence), as well as efforts to synthesize the chemical in purified form for future targeted analytical method development and toxicity characterization. However, such responses are costly and time-consuming, and should only be undertaken if results from other monitoring elements, such as bioanalytical (cell-based) screening, indicate a reason for heightened concern.

Second, the channel of communication should begin with utilities, flow through to regulators and customers next, and as consensus is achieved, to the general public. Furthermore, the information outlined above should be readily available to the community (e.g., as they are approved through web portals, as well as in written documentation such as utility annual reports), as timeliness of response is also critical in ensuring and maintaining public confidence in DPR.

Lastly, the accuracy and veracity of information provided via outreach activities are clearly critical for maintaining credibility and thus public confidence in DPR monitoring efforts. As the results from unknown identification efforts using NTA methods are not always straightforward, expert and/or peer review of the technical information and tools used to make informed decisions is desirable.

APPENDIX A

Research Plan for Evaluating Surrogate and Indicator Methods

A.1 Surrogates

A list of candidate surrogates for DPR monitoring of TOrCs is provided in Table A-1.

Table A-1. Candidate Surrogate Parameters for TOrCs in Recycled Water Matrices of Interest.

Surrogate/Indicator	Contaminant of Interest	Reference(s)
Fluorescence (total)	TOrCs	Bergman et al. (2016); Gerrity et al. (2012); Sgroi et al. (2018)
UV absorbance (254 nm)	TOrCs	Dickenson et al. (2009); Wert et al. (2009); Gerrity et al. (2012); Sgroi et al. (2018)
Dissolved organic carbon (DOC)	TOrCs	Anumol et al. (2015)
Total organic carbon (TOC)	TOrCs	Anumol et al. (2015)
Total organic halide (TOX)	Halogenated DBPs, TPs	Plewa et al. (2004); Ackerson et al. (2018)

A.1.1 Total/Dissolved Organic Carbon (TOC/DOC)

TOC/DOC is measured by completely oxidizing carbon-containing compounds in an aqueous followed by detection of liberated CO_2 by infrared spectrometry (IR). Wet chemical (e.g., persulfate) or high temperature catalytic (e.g., using platinum) oxidation are employed in commercially available TOC/DOC instruments. If necessary, removal of inorganic carbonates by acid sparging prior to TOC/DOC measurement shall be incorporated. Because the oxidation step using current instruments can only be performed off-line, the time step for "continuous" TOC/DOC data collection is currently ~ 10 min.

A.1.2 Total Fluorescence (TF)

TF is a proxy for chromophoric dissolved organic matter (CDOM) content that is measured by illuminating an aqueous sample with light ("excitation") and detecting the light emitted from the "fluorescing" molecule ("emission") using a fluorescence spectrophotometer ("fluorometer"). TF can be measured at fixed excitation and emission wavelengths, or it can be integrated across a range of excitation and emission wavelengths. For the latter, two-dimensional maps of the fluorescent excitation-emission matrix (EEM) are generated to characterize across the wavelength range, and TF is calculated from the EEM data (Yu et al. 2015; Park and Snyder 2018). In contrast to TOC/DOC, fluorescence does not require offline processing of a given sample, thus TF can in theory be measured in real time on water flowing through a sample path/conduit, with the time step limited by instrument scanning and data processing rates.

A.1.3 Ultraviolet Absorbance (UVA)

UVA is another proxy for the presence of organic compounds in water, which as the name suggests measures the absorption of incident UV light. Like TF, UVA can be measured at a fixed wavelength, or integrated over a range of wavelengths. An absorption spectrophotometer measures the attenuation of

UV light across a fixed sample path containing the water of interest, thus lending this surrogate parameter to automated/continuous measurement. The current standard for UVA employs a fixed absorption wavelength of 254 nm (UVA-254), however, scanning a range of absorbed UV light can provide additional information on TOrCs present.

A.1.4 Total Organic Halide (TOX)

TOX measures all forms of halogenated organic molecules, whether in chlorinated, brominated or iodinated forms. Different instrumental methods, including ion chromatography, ICP-MS and GC-MS after derivatization of the parent halogen containing compound, have been utilized for TOX measurement in water samples (Plewa et al. 2004; Krasner et al. 2006; Ackerson et al. 2018). Automation is not currently available; efforts to provide online measurement capability for TOX are unknown.

A.2 Indicators

A list of candidate indicators and instrumental methods for DPR monitoring of TOrCs is provided in Tables A-2 and 2-3, respectively. Sample preparative methods are listed in Table 2-1.

Table A-2. Candidate Indicators for Monitoring of TOrCs in Recycled Water Matrices of Interest.

Surrogate/Indicator	Contaminant of Interest	Reference(s)
1-4-dioxane, gemfibrozil, iohexol, NDMA, NMOR, PFOA, PFOS, sucralose, sulfamethoxazole	TOrCs	Drewes et al. (2018)
20 PPCPs (including sucralose, iohexol, TCPP, acesulfame, gemfibrozil, DEET, caffeine, triclosan, iopromide)	TOrCs, PPCPs	Anumol & Snyder (2015)
Dilantin, DEET, meprobamate, iopromide	PPCPs	Dickenson et al. (2009)
Boron	TOrCs (LMW, neutral)	Breitner et al. (2018)

A.2.1 State of California's List of Nine Indicator TOrCs

The analysis of the nine indicator TOrCs recommended by the State of California's CEC Expert Panel (Table A-2) will generate monitoring data that will inform the effectiveness of treatment (so called "treatment" indicators) and the risk to human health associated with certain problematic chemicals (so-called "health-based" indicators) for potable reuse applications governed by the State's Recycled Water Policy. Thus, a robust set of methods that target this list of indicators for the recycled water matrices of interest is needed, and shall be developed and evaluated in this study. Indicator-specific methods and method reporting limits (MRLs) as recommended by the Expert Panel are included in Tables A-3 and A-4, respectively. A list and description of EPA methods that may be applicable for these analytes is described after Table A-4.

Table A-3. EPA Drinking Water Methods for Nine Indicator TOrCs Recommended for Monitoring in Recycled Water for Potable Reuse by the CA CEC Expert Panel.

Indicator Compound	Preparative	Instrumental	Continuous
1,4-dioxane	EPA Method 522	EPA Method 522	100 mL sample; SPE (AC), GC-MS-SIM
Gemfibrozil	EPA Method 542	EPA Method 542	100 mL sample; SPE (HLB); LC-MS/MS (ESI+ & - modes)
Iohexol	EPA Method 542	EPA Method 542	100 mL sample; SPE (HLB); LC-MS/MS (ESI- mode)
NDMA	EPA Method 521 (.1)	EPA Method 521 (.1)	100-500 mL sample; SPE (AC); GC-MS/MS (NCI mode)
NMOR	EPA Method 521 (.1)	EPA Method 521 (.1)	100-500 mL sample; SPE (AC); GC-MS/MS (NCI mode)
PFOA	EPA Method 537	EPA Method 537	250mL sample; SPE (DVB); LC-MS/MS (ESI- mode)
PFOS	EPA Method 537	EPA Method 537	250mL sample; SPE (DVB); LC-MS/MS (ESI- mode)
Sucralose	EPA Method 542	EPA Method 542	100 mL sample; SPE (HLB); LC-MS/MS (ESI- mode)
Sulfamethoxazole	EPA Method 542	EPA Method 542	100 mL sample; SPE (HLB); LC-MS/MS (ESI+ & - modes)

EPA Method 521: Determination of Nitrosamines in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionization Tandem Mass Spectrometry (MS/MS). This method established in 2004 called for an ion-trap GC-MS instrument, which is now considered antiquated and basically obsolete. The commercial services industry has since developed a new method for analysis of nitrosamines in drinking water using a GC–MS/MS (tandem quadrupole) system. The method described involved optimization of the MS/MS parameters and GC conditions to ensure a faster run time than the current EPA method 521, while providing equivalent or better sensitivity and precision and accuracy. The method used in the study does not deviate from the sample preparation procedures – SPE extraction of a 500 mL sample using activated carbon (AC) – described in the current EPA 521 but improves the analytical method performance and reliability.

EPA Method 522: Determination of 1,4-Dioxane in Drinking Water by Solid Phase Extraction (SPE) and Gas Chromatography Mass Spectrometry (GC/MS) with Selected Ion Monitoring (SIM). 1,4-Dioxane has been identified as a probable human carcinogen and an emerging contaminant in drinking water. The National Exposure Research Laboratory (NERL) has developed a method for the analysis of 1,4-dioxane

in drinking water at ng/L concentrations. The method consists of an activated carbon solid-phase extraction of 500-mL or 100-mL water samples using dichloromethane as the elution solvent. The extracts are analyzed by gas chromatography-mass spectrometry (GC/MS) in selected ion monitoring (SIM) mode. In the NERL laboratory, recovery of 1,4-dioxane ranged from 94-110% in fortified laboratory reagent water (LRW), and recoveries of 96-102% were demonstrated for fortified drinking water samples. The relative standard deviations for replicate analyses were less than 6% at concentrations exceeding the minimum reporting level.

EPA Method 542: Determination of Pharmaceuticals and Personal Care Products (PPCP) in Drinking Water by Solid Phase Extraction (SPE) and Liquid Chromatography Electrospray Ionization Tandem Mass Spectrometry (LC/ESI-MS/MS). This method utilizes Oasis HLB as a preparative step followed by LC-MS/MS in both ESI+ and ESI- modes for determination of multiple PPCP analytes. Requires a 100-fold concentration post SPE, isotopically labeled surrogate standards and multiple sample injections. Refrigerated stability of 28 days with addition of multiple preservatives (ascorbic acid, citrate and EDTA). Validated by interlab comparison for tap water matrices at MRLs of 0.28 and 1.4 ng/L for sulfamethoxazole and gemfibrozil, respectively. Other PPCP analytes in this method include diazepam, diclofenac, fluoxetine, naproxen and triclosan.

EPA Method 556.1: Determination of Carbonyl Compounds in Drinking Water by Fast Gas Chromatography September 1999. A method for aldehydes and ketones (e.g., acetaldehyde) that utilizes derivatization, solvent extraction and GC-ECD for detection of analyte derivatives in the 0.04 to 1 mg/L range for a 20 mL sample. Providing a blank water is a challenge and requires ultra-polishing (Milli-Q).

EPA Method 537: Determination of perfluoroalkyl acids (PFAAs) by Solid Phase Extraction (SPE) and Liquid Chromatography Electrospray Ionization Tandem Mass Spectrometry (LC/ESI-MS/MS) In progress. A 250 mL sample is extracted with a DVB cartridge followed by LC-MS/MS in ESI- mode for determination of 14 PFAAs, including PFOA and PFOS. Utilizes isotopically labeled surrogate standards and can be expanded to GenX components. Trizma is used as a preservative. A wide range of target analyte water solubilities and blank levels remain as challenges. No MRLs were reported. An effort to expand the analyte list for EPA Method 537 to include short chain PFASs (e.g., < C-12) into a combined method is being carried out. Suitable sample storage media (polypropylene), preservatives (trizma) and SPE sorbent (weak anion exchange resin) have been identified for MRLs in the 10 ng/L range.

A GC-MS based method for low molecular weight, water soluble contaminants in CCL4 is being developed as EPA Method 558. Nitrogen containing compounds such as aniline, carbamates and nitrosamines are targeted in samples preserved with bisulfite, isolated with multiple SPE cartridges in parallel, and analysis at the 0.2 to 2 ug/L range by GC-MS in selection ion monitoring (SIM) mode using isotopically labeled standards. Currently, the method is being optimized for two indicators – ethyl carbamate and *N*-methyl-2-pyrrolidone.

Table A-4. Monitoring Requirements for Health-Based and Performance-Based Indicator TOrCs and Performance Surrogates for Potable and Non-Potable Reuse Practices.

Reproduced from Table 9.1 in Drewes et al. 2018

Reuse Practice	Health-Based Indicator	MRL (ng/L)	Bioanalytical Methods	MRL (ng/L)	Performance-Based Indicator	Expected Removal[6]	MRL (ng/L)	Surrogate	Method	Expected Removal[6]
Surface Spreading Application (SA)	NDMA[2]	2	ER-α	0.5	ΔGemfibrozil[3]	>90%	10	ΔAmmonia	SM	>90%
	NMOR[1]	2	AhR	0.5	ΔSulfamethoxazole[4]	>30%	10	ΔNitrate	SM	>30%
	1,4-Dioxane[1]	100			ΔIohexol[3]	>90%	50	ΔDOC	SM	>30%
					ΔSucralose[5]	<25%	100	ΔUVA	SM	>30%
								ΔTotal fluorescence		>30%
Subsurface Application (Direct Injection) and Surface Water	NDMA[2]	2	ER-α	0.5	ΔSulfamethoxazole	>90%	10	ΔConductivity	SM	>90%
Augmentation (SWA)	NMOR[1]	2	AhR	0.5	ΔSucralose	>90%	100	ΔDOC	SM	>90%
	1,4-Dioxane[1]	100			ΔNDMA	25-50%	2	ΔUVA	SM	>50%
Non-potable reuse practices					None			Turbidity	SM	
								Cl_2 residual or operational UV dose	SM	
								Total coliform	SM	

[1]Industrial chemical [2]Disinfection byproduct [3]Pharmaceutical residue [4]Antibiotic [5]Food additive [6]travel time in subsurface two weeks and no dilution, see details in Drewes et al. 2008.
SM – Standard Methods; MRL – Method Reporting Limit

Table A-5. Measurement Performance Goals for Surrogates and (targeted) Indicators Recommended for Recycled Water Monitoring.

Method/Parameter	Calibration Range	Calibration Linearity	Recovery/Accuracy of Matrix Spike (MS)	Recovery/Accuracy of CRM/SRM[2]	Precision[1] (MS Duplicate)	Precision[1] (Sample Duplicate)
UV absorbance (254 nm)	0.001 - 1.0	$R^2 \geq 0.99$	N/A	N/A	N/A	≤ 30% RPD
Fluorescence, Total (RU)[3]	TBD	$R^2 \geq 0.99$	N/A	N/A	N/A	≤ 30% RPD
Total/Dissolved Organic Carbon (TOC/DOC) (mg/L)	TBD	$R^2 \geq 0.99$	90-110%	90-110%	≤ 25% RPD	≤ 30% RPD
Indicator TOrC concentration (ng/L)	Variable	$R^2 \geq 0.99$	50-150%	N/A	≤ 25% RPD	≤ 30% RPD
Bioassay equivalent concentration, BEQ (ng/L)	Variable	$R^2 \geq 0.99$	70-130%	N/A	≤ 25% RPD	≤ 30% RPD

[1] RPD = relative percent difference [2] CRM/SRM – Certified Reference Material/Standard Reference Material (if available)
[3] RU – Raman units (Yu et al. 2015) [4] N/A – not applicable [5] TBD – to be determined

A.2.2 Boron

The analysis of boron using inductively coupled plasma-optical emission spectroscopy (ICP-OES) has been proposed by Breitner et al. (2018) as an indicator of the fate of TOrCs through recycled water treatment trains that utilize RO. The reported detection limit for this method was 10 ng/L.

A.2.3 Bioanalytical Assays

A list and description of cellular transactivation assays that are potentially relevant for recycled water monitoring applications is included in Appendix B. Bioassay endpoint-specific method reporting limits (MRLs) as recommended by the Expert Panel for potable reuse applications in California are included in Table A-4. Investigators shall select and apply only those cell assays that have successfully benchmarked water quality in previous studies, and that can be quantified against a reference agonist and reported in terms of a bioassay equivalent concentration, or BEQ.

A.3 Study Design

A.3.1 Sample Collection, Preservation, Transport, and Processing

For each of the indicator methods described in Appendix A.2, investigators shall collect as much as 1-L of water sample to provide adequate sensitivity for a wide spectrum of TOrCs using the semi- and non-target methods described above. In some cases, a smaller volume (250 or 500 mL) may be sufficient for certain analyses (e.g., specific cell assay endpoints).

A.3.2 Initial Evaluation of Method Performance

See Section 3.3.1.

A.3.3 Challenge Testing

See Section 3.3.2.

A.3.4 Measurement Performance Goals

The investigators shall apply measurement performance goals listed in Table A-5. Detailed QA/QC guidelines for candidate indicator methods are included in Appendix C.

A.4 Data Analysis and Synthesis

The quality of data collected in both the initial performance and challenge testing phases of this evaluation for surrogates and indicators shall be assessed against the measurement performance goals in Table A-5. For selected parameters (e.g., TF and UVA) it may not be practical or relevant to retain measurements for all wavelengths. The investigators shall assess the magnitude and frequency of response across the wavelength ranges assessed in the evaluation, in comparison to the responses of other study parameters, to determine and recommend the wavelengths of greatest relevance for detecting TOrCs in the recycled water matrices of interest.

Investigators shall apply measurement performance goals that address range, linearity and stability of calibration, recovery of known (spiked) TOrCs, within sample precision and repeatability as listed in Table A-5 in their assessment of method performance for surrogate, indicator and bioanalytical (cell assay) methods. The investigators shall assess, via non-parametric correlation as applicable, the correspondence among surrogate parameters, as well as among surrogates and indicator concentrations. This analysis shall be used to assess the overall utility of each individual method.

The results across all three tiers of monitoring described in Section 2.3 and depicted in Figure 2-2 shall be compared to determine if the consistency in response across the methods is observable. For example, a relatively high response for TF and UVA would correspond to elevated levels of indicators (whether native or spiked), as well as the relative complexity of chromatograms or heat maps generated by semi- and/or non-target mass spectrometric methods.

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APPENDIX B

Bioanalytical Screening of Water Quality

The following discussed bioanalytical screening tools for water quality, and is adapted from Dodder et al. (2015) "M*onitoring of Constituents of Emerging Concern (CECs) in Aquatic Ecosystems – QA/QC Guidance*".

B.1 General Approach

The QA/QC criteria for these new monitoring tools were based on technical reports from EPA's Endocrine Disruptor Screening Program (U.S. EPA 2013), and recently completed research projects on adapting *in vitro* bioassays (IVBs) for water quality screening (SCCWRP 2014; WRRF 2014). A performance-based approach is adopted where each laboratory may use their method of choice.

B.2 In Vitro Bioassay (IVB) Endpoints

Cellular (*in vitro*) bioassays shall be used to screen chemicals and to determine their potential toxic effects. These tools will be applied to water samples. The IVB endpoints described in the pilot study plan (SCCWRP 2015) and listed in Table B-1 can screen for endocrine disrupting chemicals (e.g., estrogens, androgens, progestins, and glucocorticoid steroids) as well as dioxin-like chemicals.

B.2.1 Commercial Suppliers

In vitro bioassays selected for CEC monitoring are all commercially available. Selected suppliers are specified in Table B-1.

Table B-1. Recommended Commercial Suppliers for *In Vitro* Biossays (IVBs).

Endpoints	Bioassay, Supplier
Estrogen Receptor (ER)	GeneBLAzer ERα Division Arrested Assay, Life Technologies[1] ERα CALUX, BioDetection Systems[2] ERα Reporter Assay, INDIGO Biosciences[3], IONTOX[4]
Androgen Receptor (AR)	GeneBLAzer AR Division Arrested Assay, Life Technologies[1] AR CALUX, BioDetection Systems[2]
Glucocorticoid Receptor (GR)	GeneBLAzer GR Division Arrested Assay, Life Technologies[1] GR CALUX, BioDetection Systems[2] GR Reporter Assay, INDIGO Biosciences[3], IONTOX[4]
Progesterone Receptor (PR)	GeneBLAzer PR Division Arrested Assay, Life Technologies[1] PR CALUX, BioDetection Systems[2]
Aryl Hydrocarbon Receptor (AhR)	DR CALUX, BioDetection Systems[2] AhR Reporter Assay, INDIGO Biosciences[3], IONTOX[4]

[1] Madison, WI (USA) [2]Amsterdam, The Netherlands [3] State College, PA (USA) [4] Kalamazoo, MI (USA)

B.2.2 Sample Processing

Samples to be screened by IVBs shall be collected and preserved following the methods described in Section 3.1. Samples will be extracted following the same protocols used for analytical chemistry *with one critical modification*. To prevent non-sample related interference in bioassay response, addition, fortification or spiking of chemicals of any kind (e.g., internal standards or recovery surrogates), except those specifically identified to evaluate IVB performance, shall not be performed.

B.2.3 Reference Toxicants

Reference toxicants used in the IVBs shall meet the following requirements:

- High affinity for the endpoint of interest.
- Linear dose response shall have a dynamic range of five-fold minimum.
- Endpoint specific sensitivity thresholds reported in Table B-2 shall be attained.

Since there is limited information on the performance of alternative reference toxicants, it is recommended that all laboratories employ the reference toxicants listed in Table B-2. The performance of these chemicals has been evaluated in recent studies that adapted bioassay protocols for water quality measurement (SCCWRP 2014; Escher et al. 2014).

Table B-2. Recommended Reference Toxicants for *In Vitro* Bioassays (IVBs).
Agonist mode (+); antagonist mode (-).

Endpoints	Reference Toxicant	Sensitivity Threshold (ng/L)
Estrogen Receptor (ER)	17-beta estradiol (+) 4-hydroxy-tamoxifen (-)	0.5
Androgen Receptor (AR)	Flutamide (-)	20
Glucocorticoid Receptor (GR)	Dexamethasone (+)	50
Progesterone Receptor (PR)	Levonorgestrel (+)	50
Aryl Hydrocarbon Receptor (AhR)	2,3,7,8-tetrachlorodibenzo-*p*-dioxin 3,3',4,4',5-pentachlorobiphenyl (PCB 126)(+)	50

B.2.4 Measurement Quality Objectives (MQOs)

The MQOs delineated in Table B-3 are intended to provide a common foundation for laboratory performance and should be considered as the minimum requirements for bioanalytical screening of pilot study samples. Additional MQOs may be instituted by participating laboratories, as long as the MQOs presented herein are satisfied. In vitro bioassay results shall be reported as bioassay equivalent concentrations (BEQs) in units of ng/L (as reference toxicant).

Table B-3. Measurement Quality Objectives (MQOs) for *In Vitro* Bioassays (IVBs).

Measurement Parameter	Frequency of Analysis	Control Limits
Extract Cytotoxicity	Per sample extract	Dilutions of the extract shall not cause > 20% cell mortality (corrected for background).
Cell-Free Media Blank	Per assay plate	Average response for cell free blank (media only) shall be less than 75% of the solvent vehicle free blank response (cells and media). RSD of replicate wells shall be < 20%.
Vehicle Blank Response	Per assay plate	50 Average response of cells exposed to the solvent vehicle shall be within 15% RSD of the vehicle free response.
Initial Calibration	Per bioanalytical batch	Linear dose-response curve for reference toxicant; $r^2 > 0.95$. Minimum of 9 points per curve (one of them at or below sensitivity threshold).
Calibration Verification	Per subsequent assay plates within a bioanalytical batch	Continuing calibration shall remain within 15% of mean response for initial calibration.
Spiked Sample	Per extraction batch	Assay response of sample spiked with reference toxicant shall be within 70 to 130% of expected response.
Reproducibility	Per sample	Differences among replicate bioassay responses shall be less than 20% RPD within and among laboratories.

Appendix B References

Dodder, N.G., A.C. Mehinto, and K.A. Maruya. 2015. “Monitoring of Constituents of Emerging Concern (CECs) in Aquatic Ecosystems: Pilot Study Design and QA/QC Guidance.” Southern California Coastal Water Research Project. Costa Mesa, CA. Technical Report 854. 93 pgs.

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APPENDIX C

QA/QC Recommendations for Evaluating Analytical Methods

The goal of quality assurance/quality control (QA/QC) is to ensure data quality and comparability within and among participating labs, and to ensure that data can confidently be compared to other studies. Quality assurance (QA) includes design, planning, and management actions conducted prior to field sampling to ensure appropriate types and quantities of data are collected. In contrast, quality control (QC) activities are implemented during data collection to evaluate the effectiveness of the QA procedures.

QA/QC recommendations for sample collection, preservation, processing (e.g., extraction, cleanup and concentration), and instrumental analysis, as described previously (Anderson et al. 2010, Dodder et al. 2015, Drewes et al. 2018), are provided herein to ensure data quality and comparability. Methods that target surrogates, indicators, and known unknowns should include, where available, standardized and validated protocols that demonstrate acceptable recovery of target/suspect analytes and reduced uncertainty in confirming the identity of suspect (e.g., known unknown) compounds. In lieu of standardized and/or validated instrumental methods and data analysis workflows for non-target identification of unknown unknowns, performance guidelines for instrumental methods and data analysis workflows are provided.

C.1 Sample Collection and Preservation

Protocols for sample collection and preservation should be standardized to ensure quantitative capture/minimal loss of target analytes, as well as minimal addition of non-native compounds. Personnel charged with sample collection and handling must strictly adhere to established protocols to insure the collection of representative, uncontaminated samples. Guidelines for sample storage are provided in Table C-1. Changes and/or additions to these guidelines may be proposed by project participants if proper justification is provided.

- Personnel must be thoroughly trained
    - in the proper use of sample collection gear,
    - in distinguishing acceptable versus unacceptable samples in accordance with pre-established criteria,
    - to recognize and avoid potential sources of sample contamination.
- Sampling equipment and utensils that come in direct contact with the sample should be made of non-contaminating materials and should be thoroughly cleaned between sampling stations.
- Sample storage containers should be of the recommended type and must be free of contaminants.
- Conditions for sample collection, preservation and holding times should be followed, and relevant field observations should be recorded.

On the day of sampling, personnel should avoid contact with or consumption of products that contain the target analytes. This may include soaps, detergents, fragrances, sunscreen, and pharmaceuticals. Storage containers with Teflon should not be used to store samples that are slated for analysis of perfluorinated compounds (PFCs). Guidelines for storage conditions and hold times are shown in Table C-1.

Table C-1. Sample Collection and Holding Time Conditions.

Matrix	Container Type	Container Size (mL)	Preservation Requirements	Maximum Holding Time
Aqueous	Pre-cleaned amber glass	1000 (100% full)	Cold (4 °C), with preservative added as required	Two weeks

C.2 Measurement Performance Goals for Surrogate and Targeted Methods

Measurement performance goals for analysis of discrete samples include 1) initial and continuing instrument calibration performance (range and linearity); 2) method detection and reporting limits (MDLs and MRLs); 3) analysis of blanks, matrix spikes and (where available) certified/standard reference materials (CRM/SRM). Performance measurement goals for the recommended surrogate and targeted indicator methods are shown in Tables C-2, A-5, and A-6.

Table C-2. Measurement Performance Goals for Discrete Sample Analysis Using Targeted Methods.

Measurement	Frequency	Control Limit
Initial Calibration	A new response factor or calibration curve should be established for each instrumental batch.	Relative standard deviation (RSD) of the response factor ≤ 25% Coefficient of determination $r^2 \geq 0.990$ for linear and non-linear curves. First or second order curves allowed. Minimum of five points per curve.
Continuing Calibration Verification	Every 10 samples or 8 hours	Expected concentration ± 20%.
Method Blank	5% of total no. samples (1 per batch of 20 samples)	Less than the RL for target analytes.
Method Detection/Reporting Limits (MDLs/RLs)	Verified, updated annually	Not applicable.

C.2.1 Method Detection and Method Reporting Limits

MDLs and MRLs define the lowest levels at which an instrument can differentiate between a signal and noise and the lowest level at which a value may be reported, respectively. The determination of these values is especially important for the analysis of CECs, as many of these compounds occur at trace levels (sub-µg/L). Formal detection and reporting limit studies are highly recommended (see also Chapter 6 in Drewes et al. 2018). In addition, every effort should be made to determine and verify the reporting limit in each and every one of the matrices of interest to be analyzed. This should include analyzing sample matrices fortified at or slightly above the determined reporting limit of the method to detect the presence of potential interferences that may lead to false negative or positive results. Furthermore, reporting limits should be re-evaluated frequently as sample matrices change or instrumental performance varies.

C.2.2 Method Performance Goals for Semi- and Non-Target Analysis

As the expected results for semi- and non-target methods (e.g., tentative and confirmed identification of a previously unidentified or unknown TOrC) are fundamentally different than for targeted analysis, QA/QC guidelines for the former shall also be distinct from those described in the previous paragraphs. In discussions with project advisors and experts interviewed for this effort, the focus of QA/QC efforts

for mass spectrometry based suspect screening and non-target analyses is to minimize false negative and positive detection and identification of known and unknown unknowns. To prevent false negatives and positives, the specification of numeric instrumental performance goals for:

1. Minimum absolute sensitivity.
2. Minimum mass range (m/z).
3. Maximum mass accuracy/error.
4. Surrogate/matrix spike recovery.
5. Minimum "fit" for spectral matching (compound identification).

were proposed and tentatively endorsed by interviewed experts. Preliminary numeric goals for measurement parameters are proposed in Table 3-1. It should be noted that numeric goals may differ among the recommended instrumental methods. For example, goals for mass accuracy/error required for high confidence compound identification differ between HRMS-based techniques and GC×GC-TOF/MS, due to the superior peak separation performance afforded by the latter method. It should also be noted that such measurement goals are subject to change as non-target methodologies and applications to water quality monitoring and assessment evolves.

In contrast to mass spectrometric based detection systems applied in semi- and/or non-target mode, cell assays applied to screen aqueous samples for groups of TOrCs by mode of biological action utilize a reference toxicant (or agonist) that serves as both a calibrant and normalizing agent. The output of cell assay analyses calibrated in this fashion are equivalent concentrations, referred to as bioassay equivalent concentrations (BEQs), reported in molar or mass concentration units (e.g., ng/L). As such, calibrated cell assays are subject to the same performance measurement goals as targeted analysis (see Tables A-5 and A-6), with the addition of a goal to ensure cell viability (Table C-3). The application of these measurement performance goals for multiple cell assay endpoints in a lab intercomparison study produced excellent interlab agreement (16-26%) for endpoints with responses consistently above the MRL (Mehinto et al. 2015).

Table C-3. Measurement Performance Goals for Cell Assays Proposed for Semi-Targeted Screening of Recycled Water.

Adapted from Dodder et al. (2015)

Measurement Parameter	Frequency of Analysis	Control Limits
Extract Cytotoxicity	Per sample extract	Dilutions of the extract shall not cause > 20% cell mortality (corrected for background).
Cell-Free Media Blank	Per assay plate	Average response for cell free blank (media only) shall be less than 75% of the solvent vehicle free blank response (cells and media). RSD of replicate wells shall be < 20%.
Vehicle Blank Response	Per assay plate	50 Average response of cells exposed to the solvent vehicle shall be within 15% RSD of the vehicle free response.
Initial Calibration	Per bioanalytical batch	Linear dose-response curve for reference toxicant; r^2 > 0.95. Minimum of 9 points per curve (one of them at or below sensitivity threshold).
Calibration Verification	Per subsequent assay plates within a bioanalytical batch	Continuing calibration shall remain within 15% of mean response for initial calibration.
Spiked Sample	Per extraction batch	Assay response of sample spiked with reference toxicant shall be within 70 to 130% of expected response.
Reproducibility	Per sample	Differences among replicate bioassay responses shall be less than 20% RPD within and among laboratories.

C.2.3 Challenge Testing

An important consideration for building confidence in newly developed and/or adapted methodologies is to demonstrate that they can if fact (when competently applied) detect, quantify and/or provide the intended information (e.g., hazard assessment or unknown compound identification) so that informed decisions can be made. For the proposed methods, two distinct "challenge" exercises can be envisioned. For surrogate and targeted method evaluation, samples representing the aqueous matrices of interest can be spiked with known amounts of a suite of known TOrCs, e.g., including indicators recommended in Section 3.2. Samples are then subject to the entire analytical protocol (e.g., from collection through data analysis) to determine the recovery of spiked TOrCs as a measure of method effectiveness. For semi- and non-target method evaluation, the same representative sample matrices can be spiked with a combination of known TOrCs and known unknowns (e.g., synthesized DBPs) compounds for determination of recovery. Alternatively, or in addition, split samples of product water from strategic locations within pilot- or full-scale recycled water treatment plants that represent a range of water qualities can be analyzed by the recommended semi- and non-target methods to determine comparability and "accuracy" of results across labs. Criteria for comparability would include the number and list of identified TOrCs using mass spectrometric methods, as was attempted by multiple labs using Rhine River water samples (e.g., Schymanski et al. 2015). Another important comparison would be to characterize the overlap in detected TOrCs among the three recommended methods. Criteria for accuracy would prove to be more elusive, and in the strictest sense, would require availability of a reference material with certified values for the parameters of interest, or as a minimum, values agreed as "true" based on analytical expert consensus.

Appendix C References

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APPENDIX D

Summary of Interviews with Technical Experts

Four experts in the area of environmental analytical chemistry were interviewed to obtain their insights and reasoning for the data and recommendations detailed in this report. This Appendix summarizes these interviews, which occurred between November 2018 and January 2019.

Dr. Thomas Young (UC Davis). The discussion centered around 1) improving capture of unknown contaminants of interest by solid phase extraction (SPE) of water samples, and 2) possible methods for compounds missed by the status quo approach, namely SPE followed by LC- and GC-HRMS. Dr. Young described methods that target simple organic molecules (e.g., aldehydes) that are not typically amenable to separation by GC or LC, by first derivatizing such compounds followed by separation and detection using e.g., FID, ECD and/or MS. For comprehensive capture of waterborne contaminants, including polar and non-polar chemicals, Dr. Young described a SPE sequence that combined ion exchange (presumably for molecules with polar or charged functional groups) with a hydrophobic sorption material (e.g., C-18 resin), developed and applied by researchers at the Swiss Federal Institute of Aquatic Science and Technology (EAWAG).

Dr. Lee Ferguson (Duke University). This interview covered 1) possible screening methods for compounds that elude conventional targeted and/or NTA, 2) sample processing protocols to capture a broad spectrum of organic chemicals; and 3) strawman performance requirements for non-targeted methods used to identify LMW unknowns. For topic 1), Dr. Ferguson referred to the work of Dr. Susan D. Richardson (University of South Carolina) and collaborators who have applied total organic halogen/halide methods (aka TOX) to screen for unknowns and transformation products, particularly in treatment schemes that utilize chlorine or chloramination for disinfection/maintenance, or that may be subject to naturally occurring halogens (e.g., as the result of brackish or saltwater intrusion/mixing). Dr. Ferguson also described trials performed in his lab that compared the efficiency of numerous sample extraction approaches, e.g., combining different SPE and/or chromatography elements in series and/or parallel. Based on the largely unpublished results from these trials, he concluded that a single Oasis HLB SPE protocol works best overall.

The interview concluded with a discussion of general principles and performance considerations that could be applied to NTA to ensure comparability of and reduce bias in results across labs using different instrument technology and data analysis schemes. For example:

To prevent false negatives, specify uniform numeric guidelines for:

1. Minimum (uniform) absolute sensitivity.
2. Minimum mass range (m/z): e.g., 50 to 1000.
3. Maximum mass error: e.g., < 5 ppm over m/z range of interest.
4. Surrogate/matrix spike recovery (50-150%).
5. Peak detection criteria, e.g., signal to noise relative to baseline or blank.
6. Minimum no. and spectral accuracy of features/compounds in available spectral libraries.

To prevent false positives, specify uniform numeric guidelines for:

1. Maximum (uniform) absolute sensitivity
2. Maximum mass range (m/z)

3-6. Same as false negatives

Dr. Eunha Hoh (San Diego State University). Dr. Hoh's recommendations are based on a study she led, which was commissioned by the Orange County Water District (OCWD) to assess the utility of NTA in identifying trace organic compounds, including transformation products, in samples of reverse osmosis permeate (ROP) and product water of ROP subjected to UV/AOP treatment (UVP). Samples of ROP, UVP and controls of ultrapure water were collected in triplicate on five separate days, extracted by Oasis HLB and analyzed by two-dimensional gas chromatography coupled to time-of-flight mass spectrometry (GCxGC/TOF-MS). This technique combines powerful separation of individual features (GCxGC) and structural identification by HRMS. Using a combination of automated/manual data analysis, a compound was reported if it was 1) detected in all three replicates; and 2) observed with a peak abundance > five times the control, and its structure was reported if 3) the mass spectrum scored a similarity of 70% or higher to a compound contained in the NIST EI library (tentative), or 4) the mass spectrum and retention time matched that of an injected authentic standard (confirmed). The number of confirmed detections and tentatively identified compounds (12-39) was similar for ROP and tap water (sampled in triplicate on two different occasions), whereas UVP samples contained fewer (6-11) identifiable compounds. Approximately 80% of detectable compounds were identifiable.

For ROP samples, 10 compounds were detected in three or more events, with nine tentatively identified and five confirmed using authentic standards (including three benzotriazoles). None of the 10 compounds detected in ROP were detected in either UVP or tap water samples. For UVP samples, more than half (17 of 33) of unique compounds detected eluted in <20 min, suggesting these to be of LMW. Eleven and five compounds were reported to be halogenated or nitrogen containing, respectively. Of the 25 compounds tentatively identified, 12 were confirmed using standards, including dichloroacetonitrile, bromochloroacetonitrile, dibromoactonitrile and bromodichloromethane. Roughly similar numbers of compounds were reduced, unchanged in abundance and/or appeared in the UVP samples, suggesting reduction of some, and formation of others during UV/AOP treatment. Analysis of tap water revealed that none of the five compounds identified (two of which also contained halogens) were detected in either UVP or ROP.

In summary, Dr. Hoh concluded that NTA profiles (or "fingerprints") of ROP and UVP were different, the majority (80%) of detectable compounds were tentatively or positively identified, and that RO and

UV/AOP reduced the number of compounds detectable by SPE coupled to GCxGC/TOF-MS. These preliminary results were presented at the National WateReuse Symposium in January 2018. Final study results are pending.

Additional observations by Dr. Hoh regarding performance characteristics of GCxGC-TOF/MS analysis:

- *m/z* range: 50-1000; (sensitivity is uniform across range).
- Mass accuracy: TBD, (noting that the larger 250K compound library does not rely on high mass
- accuracy).
- Sensitivity: ~1 ug/L per individual (basis: 1L sample; SPE using Oasis HLB).
- Data processing is time consuming and labor-intensive (particularly compound identification).
- Stepwise data workflow recommended, e.g., Step 1 peak prioritization; Step 2 fingerprinting; Step 3 compound identification.

Dr. Shane Snyder (NTU Singapore). As a principal investigator for multiple research projects and a member of numerous expert panels addressing potable and recycled water quality for the past several years, including the State of California's Science Advisory Panel for Monitoring of CECs in Recycled Water, Dr. Snyder is considered a pre-eminent scholar, advisor and technologist on such issues. He discussed 1) candidate methods for specific groups of unknown chemicals and low molecular weight (LMW) organics that may not be rejected by reverse osmosis (RO) treatment processes, as well as 2) an

overall strategy to address unknowns and LMW organics, regardless of treatment afforded to recycled water. Dr. Snyder stressed that RO is not an absolute barrier, and that even though salt rejection (atoms) may be as high as 99% (2-log), some CECs occur at levels high enough that detectable levels will still remain after 2-log reduction. Further, RO salt rejection is due in large part to electrostatic rejection due to charges on the membrane surface, which may not be effective for neutral organics. Therefore, Dr. Snyder recommended a comprehensive screening program that is applied in a tiered approach.

Dr. Snyder's three-tiered approach involves 1) surrogates/bulk parameters that can be monitored on-line or with rapid methods that can be easily applied at high frequency, 2) targeted analysis of indicator compounds that are representative of those compounds that would be highly likely to occur in wastewater and based upon particular treatment barriers, and 3) non-targeted analyses that are comprised of both mass spectrometric and bioassay methods. Tier 1 bulk water physicochemical parameters (e.g., turbidity, DOC, and nitrate-N) for which robust, continuous monitoring technology is available would serve as the first indicator of water quality. It has been shown in numerous studies that these surrogate measures of water quality are indicative of the presence/concentration of individual chemicals of concern (i.e., CECs, unknowns). Thus, their measurement on a frequent/continuous timeline serves as an early warning of fluctuating/unacceptable water quality. For instance, Dr. Snyder's team has shown that fluorescence and dissolved organic carbon (DOC) are excellent predictors of RO performance that are superior to conductivity alone. For Tier 2, Dr. Snyder suggested periodic monitoring of the established list of targeted analytes which would serve to provide a second layer of compliance by comparing measured occurrence of indicators which are known to be well and poor rejected by a particular treatment barrier. For instance, for RO performance indicator compounds would include larger molecular weight substances such as perfluorinated organics as well as neutrally charged lower molecular weight volatile substances such as acetone, benzene, and/or 1,4-dioxane. Targeted analysis methods would be subject to strict quality assurance/quality control (QA/QC) performance guidelines such as those established for EPA methods. As a final component ("Tier 3") to demonstrate acceptable water quality, or in response to repeated/persistent non-compliant or non-resolvable monitoring results in Tiers 1 and 2, NTA is available to a) quantify the potential for bioactivity of recycled water using *in vitro* bioassays and/or mass spectrometric methodologies. Ideally, *in vitro* bioassay techniques would be combined with mass spectrometric techniques. Specifically, if bioactivity is continuously detected, Dr. Snyder recommended chemical fractionation (e.g., size exclusion chromatography and/or reverse-phase chromatography) followed by iterative bioassay analyses and mass spectrometry of bioactive fractions. In this way, substances with bioactivity have a higher likelihood of identification and semi-quantification. As the resources and time needed to complete Tier 3 monitoring are currently much greater than that associated with Tiers 1 and 2, NTA, this step in the sequence would only be carried out if/when the results of Tiers 1 and 2 warrant such action. The increased cost/effort is particularly true for the MS-based NTA techniques, as the effort needed to perform cell bioassay measurements is currently estimated to be similar (or less than) that required for Tier 2 targeted analysis.

In terms of analytical approaches, Dr. Snyder suggested a toolbox for comprehensive monitoring that considers the broader chemical universe that is present as complex mixtures in wastewater. In order to be comprehensive, chemical properties must be considered, such as volatility, organic vs. inorganic, and polarity. These methods are further divided into 1) targeted methods for a broad range of set of known chemicals; and 2) non-targeted methods for a broader universe of chemicals, including those missed by targeted screening methods and unknowns (Figure 2). Within these two categories, Dr. Snyder identified multiple instrumental techniques that target groups of chemicals based on their charge, speciation, volatility and polarity (e.g., GC-MS, ICP-MS and LC-MS) for which robust methods are/can be established. Although high resolution mass spectrometry is generally applied for NTA, Dr. Snyder

suggested that even low resolution mass spectrometric instruments can be quite powerful for NTA, particularly for GC-MS where most structural databases are established for low-resolution instruments (and not widely available for high-resolution instruments). Similarly, LC-MS and ICP-MS instruments without high mass resolution/accuracy often can provide sufficient information to identify yet unknown contaminants found in recycled water systems.

That said, Dr. Snyder did advocate for high-resolution LC-MS systems if, and only if, extremely skillful chemists were employed AND rather sophisticated and complex software platforms were available. Even then, Dr. Snyder pointed out that often recycled water samples will have thousands of peaks and attempts to identify each peak are generally fruitless and vastly impractical. For this reason, Dr. Snyder is a greater advocate of in vitro bioassays, including cell bioassays such as those recently adopted by the State of California as a required monitoring tool for monitoring of potable reuse applications, as a non-targeted screening technique. Dr. Snyder reemphasized that he does not see high-resolution MS alone as a viable solution for unknown monitoring in general, though GC-MS (even with low resolution) can be more viable for volatile/semi-volatile species due to the availability of standardized databases (e.g., NIST). However, he further cautioned that sample preparation techniques for NTA, both analytical and bioassay, often are not appropriate for low molecular weight volatile species which are “lost” during sample preparation and concentration steps.

Dr. Snyder was adamant that QA/QC is critical for each tier of testing suggested. Each category also relies on i) standardized protocols for sample collection and processing to ensure quantitative capture/minimal loss of target analytes, and ii) validated data analysis work flows that demonstrate acceptable recovery of target analytes and reduced uncertainty in identifying unknown compounds (i.e., by their chemical structure). However, for surrogates (Tier 1) and targeted indicator analyses (Tier 2), QA/QC procedures are relatively well established. Conversely, non-targeted analysis suffers greatly for lack of standardized QA/QC procedures, particularly for mass spectrometric techniques. For instance, ion-suppression is common with LC-MS technologies and varies by substance depending on ionization potential, which is different for every structure. Thus, many substances may not be detected simply because of ion-suppression or other instrumental factors that lead to a false sense of “non-detect”. For bioassays, QA/QC procedures are far more straightforward and similar to those that would be used for targeted analyses.

APPENDIX E

Bibliography for Low Molecular Weight Unknown Compounds

To determine the state of science around analytical measurement of unknown low molecular weight compounds in waters, peer-reviewed literature was identified through external computerized searches using the Scopus platform. This search was conducted 15 February 2019. Searches were conducted using a list of keywords or the names of authors known to be active in development and application of analytical methods for characterizing LMW chemicals and/or unknowns in wastewater and/or recycled water, or combinations of both. Abstracts were screened for content related to 1) unknowns or problematic chemicals associated with wastewater and/or recycled water, or 2) novel analytical methods for identifying CECs, unknowns and/or transformation products in environmental media, including water. External source literature deemed to be relevant to the project have been incorporated into the updated bibliography, and entries from previous searches that have been deemed to be of no/little relevance to the topics of interest have been deleted.

Breitner, L.N., Howe, K.J., Minakata, D. Boron Can Be Used to Predict Trace Organic Rejection through Reverse Osmosis Membranes for Potable Reuse (2018) Environmental Science and Technology, 52 (23), pp. 13871-13878. DOI: 10.1021/acs.est.8b03390.

AFFILIATIONS: Department of Civil, Construction, and Environmental Engineering, University of New Mexico, Albuquerque, NM 87131, United States; Michigan Technological University, Houghton, MI 49931, United States.

ABSTRACT: Potable water reuse is a viable option for communities with extreme water scarcity. Improvements in measurement capabilities and greater occurrence of contaminants of emerging concern (CECs) have made the investigation of the removal of CECs through advanced treatment facilities essential for further reuse considerations. ***Reverse osmosis (RO) has been demonstrated to remove many CECs, but poor removal has been observed for many low molecular weight (MW), neutral organic compounds***. With the availability of many RO membrane products on the market, it is increasingly important to be able to predict organics rejection through different products without detailed information about the RO membrane's properties or structure. This laboratory-scale study investigated the rejection of low-MW, neutral organics, boron, and sodium chloride by six RO membrane products. ***The experimental results were used to develop a correlation between the removal of organics and boron. If the rejection of boron and a neutral organic through one reference membrane is available, then the rejection of that organic through any other membrane product can be estimated using the rejection of boron through that membrane.***
DOCUMENT TYPE: Article

Roback, S.L., Ferrer, I., Thurman, E.M., Ishida, K.P., Plumlee, M.H., Poustie, A., Westerhoff, P., Hanigan, D. Non-target mass spectrometry analysis of NDMA precursors in advanced treatment for potable reuse (2018) Environmental Science: Water Research and Technology, 4 (12), pp. 1944-1955. DOI: 10.1039/c8ew00401c

AFFILIATIONS: Research and Development Department, Orange County Water District, Fountain Valley, CA, United States; Center for Environmental Mass Spectrometry, University of Colorado, Boulder, CO,

United States; School of Sustainable Engineering and the Built Environment, Arizona State University, Tempe, AZ, United States; Civil and Environmental Engineering Department, University of Nevada, Reno, NV, United States.

ABSTRACT: N-Nitrosodimethylamine (NDMA) is a disinfection by-product of concern in water reuse applications due to its potential human carcinogenicity. NDMA forms via the reaction of organic amine precursors with chloramines during water treatment. Advanced treatment for potable reuse reduces NDMA to non-detectable levels and removes most precursors. ***However, historical data from a full-scale potable reuse facility indicates NDMA can form after advanced treatment due to the presence of residual chloramine and NDMA precursors that are not removed during advanced treatment***. ***This study used non-target high-resolution mass spectrometry to identify NDMA precursors and other trace organic compounds during advanced treatment for reuse. Inspection of the total ion chromatograms indicated that there was a substantial reduction of total ionizable compounds by reverse osmosis (RO). The RO feed water contained approximately 22 putative identifications of NDMA precursors across two sampling events. Only one of these precursors was found post-RO and none were found in the subsequent UV/advanced oxidation process (AOP) product water. In addition to the 22 NDMA precursors, the RO feed water contained 41 pharmaceuticals and pesticides that are not likely to be NDMA precursors. Similarly, these compounds were generally well removed by RO. Two compounds with unknown NDMA formation potential, one a suspected benzotriazole trimer with chemical formula C18H16N6O3 and the other with an unassigned formula, were identified in the UV/AOP product water that were not present prior to UV/AOP (after RO), indicating they may be transformation products.*** Overall, this research demonstrates the utility of non-target analysis for water quality investigations. © 2018 The Royal Society of Chemistry.
DOCUMENT TYPE: Article

Prasse, C., Ford, B., Nomura, D.K., Sedlak, D.L. Unexpected transformation of dissolved phenols to toxic dicarbonyls by hydroxyl radicals and UV light (2018) Proceedings of the National Academy of Sciences of the United States of America, 115 (10), pp. 2311-2316. DOI: 10.1073/pnas.1715821115.

AFFILIATIONS: Department of Civil and Environmental Engineering, University of California, Berkeley, CA 94720, United States; Department of Environmental Health and Engineering, Johns Hopkins University, Baltimore, MD 21218, United States; Department of Nutritional Sciences and Toxicology, University of California, Berkeley, CA 94720, United States; Department of Chemistry, University of California, Berkeley, CA 94720, United States; Department of Molecular and Cell Biology, University of California, Berkeley, CA 94720, United States.

ABSTRACT: ***Water treatment systems frequently use strong oxidants or UV light to degrade chemicals that pose human health risks. Unfortunately, these treatments can result in the unintended transformation of organic contaminants into toxic products. We report an unexpected reaction through which exposure of phenolic compounds to hydroxyl radicals (•OH) or UV light results in the formation of toxic?,?-unsaturated enedials and oxoenals. We show that these transformation products damage proteins by reacting with lysine and cysteine moieties. We demonstrate that phenolic compounds react with •OH produced by the increasingly popular UV/ hydrogen peroxide (H2O2) water treatment process or UV light to form toxic enedials and oxoenals.*** In addition to raising concerns about potential health risks of oxidative water treatment, our findings suggest the potential for formation of these toxic compounds in sunlit surface waters, atmospheric water, and living cells. For the latter, our findings may be particularly relevant to efforts to understand cellular damage caused by in vivo production of reactive oxygen species. In particular, we demonstrate that exposure of the amino acid tyrosine to •OH yields an electrophilic enedial product that undergoes cross-linking reaction with both lysine and cysteine residues.
AUTHOR KEYWORDS: Advanced oxidation processes; Chemoproteomics; Exposome; Reactive

transformation products; Water treatment
DOCUMENT TYPE: Article

Zeng, T., Plewa, M.J., Mitch, W.A. N-Nitrosamines and halogenated disinfection byproducts in U.S. Full Advanced Treatment trains for potable reuse (2016) Water Research, 101, pp. 176-186. DOI: 10.1016/j.watres.2016.03.062.

AFFILIATIONS: Department of Civil and Environmental Engineering, Syracuse University, 151 Link Hall, Syracuse, NY 13244, United States; Department of Civil and Environmental Engineering, Stanford University, 473 Via Ortega, Stanford, CA 94305, United States; National Sci. Found. Eng. Research Center for Re-inventing the Nation's Urban Water Infrastructure, 473 Via Ortega, Stanford, CA 94305, United States; Department of Crop Sciences and Safe Global Water Institute, University of Illinois at Urbana-Champaign, Urbana, IL 61801, United States.

ABSTRACT: Water utilities are increasingly considering indirect and direct potable reuse of municipal wastewater effluents. Disinfection byproducts (DBPs), particularly N-nitrosamines, are key contaminants of potential health concern for potable reuse. ***This study quantified the concentrations of N-nitrosamines and a suite of regulated and unregulated halogenated DBPs across five U.S. potable reuse Full Advanced Treatment trains incorporating microfiltration, reverse osmosis, and UV-based advanced oxidation.*** Low μg/L concentrations of trihalomethanes, haloacetic acids, dichloroacetonitrile, and dichloroacetamide were detected in the secondary or tertiary wastewater effluents serving as influents to potable reuse treatment trains, while the concentrations of N-nitrosamines were more variable (e.g., <2-320 ng/L for N-nitrosodimethylamine). Ozonation promoted the formation of N-nitrosamines, haloacetaldehydes, and haloacetamides, but biological activated carbon effectively reduced concentrations of these DBPs. ***Application of chloramines upstream of microfiltration for biofouling control increased DBP concentrations to their highest levels observed along the treatment trains. Reverse osmosis rejected DBPs to varying degrees, ranging from low for some (e.g., N-nitrosamines, trihalomethanes, and haloacetonitriles) to high for other DBPs. UV-based advanced oxidation eliminated N-nitrosamines, but only partially removed halogenated DBPs.*** Chloramination of the treatment train product waters under simulated distribution system conditions formed additional DBPs, with concentrations often equaling or exceeding those in the treatment train influents. Overall, the concentration profiles of DBPs were fairly consistent within individual treatment trains for sampling campaigns separated by months and across different treatment trains for the same sampling time window. ***Weighting DBP concentrations by their toxic potencies highlighted the potential significance of haloacetonitriles, which were not effectively removed by reverse osmosis and advanced oxidation, to the DBP-associated toxicity in potable reuse waters.***
AUTHOR KEYWORDS: Advanced treatment trains; Halogenated disinfection byproducts; N-Nitrosamines; Potable reuse
DOCUMENT TYPE: Article

Funke, J., Prasse, C., Ternes, T.A. Identification of transformation products of antiviral drugs formed during biological wastewater treatment and their occurrence in the urban water cycle (2016) Water Research, 98, pp. 75-83. DOI: 10.1016/j.watres.2016.03.045.

AFFILIATIONS: Federal Institute of Hydrology (BfG), Am Mainzer Tor 1, Koblenz, 56068, Germany; Department of Civil and Environmental Engineering of California at Berkeley, Berkeley, CA 94720, United States.

ABSTRACT: ***The fate of five antiviral drugs (abacavir, emtricitabine, ganciclovir, lamivudine and zidovudine) was investigated in biological wastewater treatment.*** Investigations of degradation kinetics were accompanied by the elucidation of formed transformation products (TPs) using activated sludge lab experiments and subsequent LC-HRMS analysis. Degradation rate constants ranged between

0.46 L d-1 gSS-1 (zidovudine) and 55.8 L d-1 gSS-1 (abacavir). Despite these differences of the degradation kinetics, the same main biotransformation reaction was observed for all five compounds: oxidation of the terminal hydroxyl-moiety to the corresponding carboxylic acid (formation of carboxy-TPs). In addition, the oxidation of thioether moieties to sulfoxides was observed for emtricitabine and lamivudine. Antiviral drugs were detected in influents of municipal wastewater treatment plants (WWTPs) with concentrations up to 980 ng L-1 (emtricitabine), ***while in WWTP effluents mainly the TPs were found with concentration levels up to 1320 ng L-1 (carboxy-abacavir). Except of zidovudine none of the original antiviral drugs were detected in German rivers and streams, whereas the concentrations of the TPs ranged from 16 ng L-1 for carboxy-lamivudine up to 750 ng L-1 for carboxy-acyclovir.*** These concentrations indicate an appreciable portion from WWTP effluents present in rivers and streams, as well as the high environmental persistence of the carboxy-TPs. ***As a result three of the carboxylic TPs were detected in finished drinking water.*** © 2016 Elsevier Ltd.
AUTHOR KEYWORDS: Antiviral drugs; Drinking water; Environmental stability; Rivers; Streams; Transformation products
DOCUMENT TYPE: Article

Prasse, C., Ternes, T.A. Application of Orbitrap Mass Spectrometry for the Identification of Transformation Products of Trace Organic Contaminants Formed in the Environment (2016) Comprehensive Analytical Chemistry, 71, pp. 263-282. DOI: 10.1016/bs.coac.2016.02.010.

AFFILIATIONS: UC Berkeley, Berkeley, CA, United States; Bundesanstalt für Gewässerkunde (BfG), Koblenz, Germany.

ABSTRACT: This chapter provides a general overview of the application of high-resolution Orbitrap mass spectrometry (MS) for the investigation of the transformation of trace organic contaminants in the urban water cycle. Discussed approaches include target, suspect and nontarget screening methodologies. Biodegradation of the antiviral drug penciclovir and transformation of the antiviral drug acyclovir during ozonation are used as case studies to highlight the advantages and main challenges of Orbitrap MS for the elucidation of transformation products. ***Future research needs are outlined, particularly emphasizing the importance of the analysis of highly polar compounds and the application of complementary analytical techniques such as nuclear magnetic resonance for the unambiguous identification of transformation products.*** © 2016 Elsevier B.V.
AUTHOR KEYWORDS: Biodegradation; High-resolution mass spectrometry; Isolation of transformation products; Nontarget analysis; Orbitrap; Ozonation; Suspect analysis; Target analysis; Trace organic contaminants; Transformation products
DOCUMENT TYPE: Article

Prasse, C., Stalter, D., Schulte-Oehlmann, U., Oehlmann, J., Ternes, T.A. Spoilt for choice: A critical review on the chemical and biological assessment of current wastewater treatment technologies (2015) Water Research, 87, pp. 237-270. DOI: 10.1016/j.watres.2015.09.023.

AFFILIATIONS: Federal Institute of Hydrology (BfG), Department of Aquatic Chemistry, Koblenz, Germany; Department of Civil and Environmental Engineering, University of California at Berkeley, Berkeley, United States; National Research Centre for Environmental Toxicology, The University of QueenslandQLD, Australia; Eawag, Swiss Federal Institute of Aquatic Science and Technology, Duebendorf, Switzerland; Goethe University Frankfurt, Department Aquatic Ecotoxicology, Frankfurt, Germany.

ABSTRACT: The knowledge we have gained in recent years on the presence and effects of compounds discharged by wastewater treatment plants (WWTPs) brings us to a point where we must question the appropriateness of current water quality evaluation methodologies. An increasing number of anthropogenic chemicals is detected in treated wastewater and there is increasing evidence of adverse

environmental effects related to WWTP discharges. ***It has thus become clear that new strategies are needed to assess overall quality of conventional and advanced treated wastewaters.*** There is an urgent need for multidisciplinary approaches combining expertise from engineering, analytical and environmental chemistry, (eco)toxicology, and microbiology. ***This review summarizes the current approaches used to assess treated wastewater quality from the chemical and ecotoxicological perspective. Discussed chemical approaches include target, non-target and suspect analysis, sum parameters, identification and monitoring of transformation products, computational modeling as well as effect directed analysis and toxicity identification evaluation***. ***The discussed ecotoxicological methodologies encompass in vitro testing (cytotoxicity, genotoxicity, mutagenicity, endocrine disruption, adaptive stress response activation, toxicogenomics) and in vivo tests (single and multi-species, biomonitoring).*** We critically discuss the benefits and limitations of the different methodologies reviewed. Additionally, we provide an overview of the current state of research regarding the chemical and ecotoxicological evaluation of conventional as well as the most widely used advanced wastewater treatment technologies, i.e., ozonation, advanced oxidation processes, chlorination, activated carbon, and membrane filtration. In particular, possible directions for future research activities in this area are provided. © 2015 Elsevier Ltd.
AUTHOR KEYWORDS: Conventional and advanced treatment; Ecotoxicology; Environmental chemistry; Sewage; Toxicity; Wastewater quality assessment
DOCUMENT TYPE: Review

Dai, N., Zeng, T., Mitch, W.A. Predicting N-nitrosamines: N-nitrosodiethanolamine as a significant component of total N-nitrosamines in recycled wastewater (2015) Environmental Science and Technology Letters, 2 (3), pp. 54-58. DOI: 10.1021/acs.estlett.5b00005.

AFFILIATIONS: Department of Civil, Structural, and Environmental Engineering, University at Buffalo, 231 Jarvis Hall, Buffalo, NY 14260, United States; Department of Civil and Environmental Engineering, Stanford University, Jerry Yang and Akiko Yamazaki Energy and Environment Building, 473 Via Ortega, Stanford, CA 94305, United States; Engineering Research Center for Re-Inventing the Nation's Urban Water Infrastructure (ReNUWIt), National Science Foundation, United States.

ABSTRACT: N-Nitrosamines are key contaminants of concern for wastewater reuse. ***Although research has focused on N-nitrosodimethylamine (NDMA), measurements indicate that NDMA accounts for only ∼9% of total N-nitrosamines in wastewaters, similar to previous findings in drinking and recreational waters. Recognizing the limited time scale for biological transformation during wastewater treatment, we targeted N-nitrosodiethanolamine (NDELA) as a component of total N-nitrosamines based upon the widespread usage of its triethanolamine precursor in consumer products.*** NDELA accounted for ∼6% of total N-nitrosamines, exceeding NDMA concentrations in some cases, and those of all other specific N-nitrosamines measured. While ozone and chloramines increased NDMA concentrations by up to an order of magnitude, and chloramines increased NDELA concentrations in some cases, other N-nitrosamine concentrations did not increase. ***Total N-nitrosamine concentrations increased by only 38-89% during ozonation and 23-65% during chloramination, suggesting that, in wastewaters, the occurrence of N-nitrosamines upstream of disinfection may be more significant than their formation as disinfection byproducts. In three advanced treatment trains, reverse osmosis and UV/hydrogen peroxide advanced oxidation reduced the levels of specific N-nitrosamines below their quantification limits, although 13-30 ng/L as NDMA of uncharacterized total N-nitrosamines remained.*** © 2015 American Chemical Society.
DOCUMENT TYPE: Article

Agus, E., Zhang, L., Sedlak, D.L. A framework for identifying characteristic odor compounds in municipal wastewater effluent (2012) Water Research, 46 (18), pp. 5970-5980. DOI: 10.1016/j.watres.2012.08.018.

AFFILIATIONS: Department of Civil and Environmental Engineering, University of California, 609 Davis Hall, Berkeley, CA 94720, United States; PUB, Singapore 228231, Singapore.

ABSTRACT: Municipal wastewater often contains trace amounts of organic compounds that can compromise aesthetics of drinking water and undermine public confidence if a small amount of effluent enters the raw water source of a potable water supply. ***To efficiently identify compounds responsible for odors in wastewater effluent, an analytical framework consisting of gas chromatography with mass spectrometry (GC-MS) and gas chromatography with olfactometry detection (GC-Olf) coupled with flavor profile analysis (FPA) was used to identify and monitor compounds that could affect the aesthetics of drinking water.*** After prioritizing odor peaks detected in wastewater effluent by GC-Olf, the odorous components were tentatively identified using retention indices, mass spectra and odor descriptors. ***Wastewater effluent samples were typically dominated by earthy-musty odors with additional odors in the amine, sulfidic and fragrant categories. 2,4,6-trichloroanisole (246TCA), geosmin and 2-methylisoborneol (2MIB) were the main sources of the earthy/musty odors in wastewater effluent.*** The other odors were attributable to a suite of compounds, which were detected in some but not all of the wastewater effluents at levels well in excess of their odor thresholds. In most cases, the identities of odorants were confirmed using authentic standards. ***The fate of these odorous compounds, including 2-pyrrolidone, methylnaphthalenes, vanillin and 5-hydroxyvanillin (5-OH-vanillin), should be considered in future studies of water systems that receive effluent from upstream sources.*** © 2012 Elsevier Ltd.
AUTHOR KEYWORDS: Flavor profile analysis; Mass spectrometry; Taste and odor compounds; Water reuse
DOCUMENT TYPE: Article

Agus, E., Lim, M.H., Zhang, L., Sedlak, D.L. Odorous compounds in municipal wastewater effluent and potable water reuse systems (2011) Environmental Science and Technology, 45 (21), pp. 9347-9355.
DOI: 10.1021/es202594z.

AFFILIATIONS: Department of Civil and Environmental Engineering, University of California, Berkeley, CA 94720, United States; PUB, Singapore's National Water Agency, 228231 Singapore, Singapore.

ABSTRACT: The presence of effluent-derived compounds with low odor thresholds can compromise the aesthetics of drinking water. The potent odorants 2,4,6-trichloroanisole and geosmin dominated the profile of odorous compounds in wastewater effluent with concentrations up to two orders of magnitude above their threshold values. Additional odorous compounds (e.g., vanillin, methylnaphthalenes, 2-pyrrolidone) also were identified in wastewater effluent by gas chromatography coupled with mass-spectrometry and olfactometry detection. ***Full-scale advanced treatment plants equipped with reverse osmosis membranes decreased odorant concentrations considerably, but several compounds were still present at concentrations above their odor thresholds after treatment. Other advanced treatment processes, including ozonation followed by biological activated carbon and UV/H 2O 2 also removed effluent-derived odorants. However, no single treatment technology alone was able to reduce all odorant concentrations below their odor threshold values.*** To avoid the presence of odorous compounds in drinking water derived from wastewater effluent, it is necessary to apply multiple barriers during advanced treatment or to dilute wastewater effluent with water from other sources. © 2011 American Chemical Society.
DOCUMENT TYPE: Article

Bonvin, F., Marron, E., Sedlak, D. Odorous compounds: a barrier to DPR? Water Reuse Research Conference, dated 4 May 2015.
DOCUMENT TYPE: Presentation

Hoh, E., Luna, R., Dodder, N., Ishida, K., Plumlee, M. Non-targeted analysis to characterize trace organics in reverse osmosis and UV/AOP product waters of potable reuse facility. 33rd Annual WateReuse

Symposium, 9-12 September 2018.
DOCUMENT TYPE: Presentation

Marron, E.L., Prasse, C., Sedlak, D. Occurrence and fate of low molecular weight aldehydes in potable water reuse systems. 11th IWA Conference on Water Reclamation and Reuse, dated 23-25 July 2017.
DOCUMENT TYPE: Presentation

Schimmoller, L., Lozier, J., Mitch, W., Snyder, S. Characterization and Treatability of TOC from DPR Processes Compared to Surface Water Supplies. WRRF 15-04. Progress Report #5, dated 17 December 2017.
DOCUMENT TYPE: Report

Schimmoller, L., Mitch, W., Snyder, S., Sakaji, R., Funk, D. Characterization and Treatability of TOC from DPR Processes Compared to Surface Water Supplies. WRRF 15-04. Scope of Work, dated 31 August 2017.
DOCUMENT TYPE: Report

In addition, the Contractor conducted computerized searches, using the Scopus platform, to develop a bibliography containing the most relevant literature addressing the analysis of problematic, relevant chemicals (i.e., CECs) in wastewater/recycled water. Scopus, Elsevier's abstract and citation database launched in 2004, covers nearly 36,377 titles from approximately 11,678 publishers, of which 34,346 are peer-reviewed journals in top-level subject fields focused on engineering and the sciences (life, social, physical and health). Searches were conducted using a list of keywords or author names (see below), or combinations of both. Abstracts were screened for content related to unknowns or problematic chemicals associated with wastewater and/or recycled water. Only those citations that were deemed relevant are included in this bibliography. To date, 163 citations have been entered into this bibliography.
KEYWORDS: disinfection by-products (DBPs); organic contaminants; emerging contaminants; unknown contaminants; low molecular weight contaminants; non-targeted analysis (NTA); mass spectrometry; potable/drinking/recycled water; advanced water treatment, reverse osmosis
KEY AUTHORS: Ferguson P Lee; Gardinali Piero; Hoh Eunha; Hernandez F*; Richardson Susan D; Schymanski Emma L; Snyder Shane A; Young Thomas D; Prasse C*
* added to list during this reporting term
2/15/19 SCOPUS
AUTHOR-NAME(Hernandez, F) AND TITLE-ABS-KEY(screening AND waters) (49 docs)

Ibáñez, M., Borova, V., Boix, C., Aalizadeh, R., Bade, R., Thomaidis, N.S., Hernández, F. UHPLC-QTOF MS screening of pharmaceuticals and their metabolites in treated wastewater samples from Athens (2017) Journal of Hazardous Materials, 323, pp. 26-35. DOI: 10.1016/j.jhazmat.2016.03.078.

AFFILIATIONS: Research Institute for Pesticides and Water, University Jaume I, Castellón, 12071, Spain; Department of Chemistry, National and Kapodistrian University of Athens, Athens, 157 84, Greece.

ABSTRACT: After consumption, pharmaceuticals are excreted as parent compounds and/or metabolites in urine and faeces. Some are not completely removed during wastewater treatments, forcing sewage treatment plants (STPs) to apply alternative technologies to guarantee quality of treated water. To monitor the removal efficiency of STPs, not only unchanged compounds and metabolites have to be taken into account, but also formation of possible transformation products (TPs). **In this work, QTOF MS has been used for screening metabolites/TPs of pharmaceuticals in effluent wastewater from Athens. A customized database was built with the exact masses of metabolites reported in literature for the parent drugs found in an initial screening.** Additionally, TPs identified in previous degradation experiments performed at our laboratory were included. **Up to 34 metabolites/TPs were detected for omeprazole, venlafaxine, clindamycin, clarithromycin, clopidogrel or dipyrone, among others. Seven corresponded to TPs whose reference standards were available at our lab, seven were TPs previously identified in laboratory degradation experiments, eight were TPs tentatively identified by QTOF MS**

without reference standards, and 12 TPs were discovered after using the common fragmentation pathway approach. Tentative identification of TPs was supported by prediction of their chromatographic retention time based on the use of advanced chemometric QSRR models. © 2016 Elsevier B.V.
AUTHOR KEYWORDS: Metabolites/transformation products; Pharmaceuticals; QTOF MS; Screening; Treated wastewater
DOCUMENT TYPE: Article

Hernández, F., Ibáñez, M., Portolés, T., Cervera, M.I., Sancho, J.V., López, F.J. Advancing towards universal screening for organic pollutants in waters (2015) Journal of Hazardous Materials, 282, pp. 86-95. DOI: 10.1016/j.jhazmat.2014.08.006.

AFFILIATIONS: Research Institute for Pesticides and Water, University Jaume I, Avda. Sos Baynat, Castellón, E-12071, Spain

ABSTRACT: Environmental analytical chemists face the challenge of investigating thousands of potential organic pollutants that may be present in the aquatic environment. **High resolution mass spectrometry (HRMS) hyphenated to chromatography offers the possibility of detecting a large number of contaminants without pre-selection of analytes due to its accurate-mass full-spectrum acquisition at good sensitivity**. Interestingly, large screening can be made even without reference standards, as the valuable information provided by HRMS allows the tentative identification of the compound detected. In this work, hybrid quadrupole time-of-flight (QTOF) MS was combined with both liquid and gas chromatography (using a single instrument) for screening of around 2000 compounds in waters. **This was feasible thanks to the use of atmospheric pressure chemical ionization source in GC. The screening was qualitatively validated for around 300 compounds at three levels (0.02, 0.1, 0.5. μg/L), and screening detection limits were established.** Surface, ground water and effluent wastewater samples were analyzed, detecting and identifying a notable number of pesticides and transformation products, pharmaceuticals, personal care products, and illicit drugs, among others. This is one of the most universal approaches in terms of comprehensive measurement for broad screening of organic contaminants within a large range of polarity and volatility in waters. © 2014 Elsevier B.V.
AUTHOR KEYWORDS: Gas chromatography; Liquid chromatography; Organic micropollutants; Quadrupole time of flight mass spectrometry; Universal screening; Water samples
DOCUMENT TYPE: Article

Portolés, T., Mol, J.G.J., Sancho, J.V., Hernández, F. Use of electron ionization and atmospheric pressure chemical ionization in gas chromatography coupled to time-of-flight mass spectrometry for screening and identification of organic pollutants in waters (2014) Journal of Chromatography A, 1339, pp. 145-153. DOI: 10.1016/j.chroma.2014.03.001.

AFFILIATIONS: Research Institute for Pesticides and Water, University Jaume I, 12071 Castellón, Spain; RIKILT Institute of Food Safety, Wageningen University and Research Centre, Akkermaalsbos 2, 6708 WB Wageningen, Netherlands.

ABSTRACT: A new approach has been developed for multiclass screening of organic contaminants in water based on the use of gas chromatography coupled to hybrid quadrupole high-resolution time-of-flight mass spectrometry with atmospheric pressure chemical ionization (GC-(APCI)QTOF MS). The soft ionization promoted by the APCI source allows effective and wide-scope screening based on the investigation of the molecular ion and/or protonated molecule. This is in contrast to electron ionization (EI) where ionization typically results in extensive fragmentation, and diagnostic ions and/or spectra need to be known a priori to facilitate detection of the analytes in the raw data. **Around 170 organic contaminants from different chemical families were initially investigated by both approaches, i.e., GC-(EI)TOF and GC-(APCI)QTOF, including polycyclic aromatic hydrocarbons (PAHs), polychlorinated**

biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs) and a notable number of pesticides and relevant metabolites. The new GC-(APCI)QTOF MS approach easily allowed widening the number of compounds investigated (85 additional compounds), with more pesticides, personal care products (UV filters, musks), polychloronaphthalenes (PCNs), antimicrobials, insect repellents, etc., most of them considered as emerging contaminants. Both GC-(EI)TOF and GC-(APCI)QTOF methodologies have been applied, evaluating their potential for a wide-scope screening in the environmental field. © 2014 Elsevier B.V.
AUTHOR KEYWORDS: Atmospheric pressure chemical ionization; Emerging pollutants; Gas chromatography; Hybrid quadrupole time-of-flight mass spectrometry; Screening; Water samples
DOCUMENT TYPE: Article

12/6/18 SCOPUS Search by keywords only
TITLE-ABS-KEY (*disinfection* AND *byproducts* OR *organic* AND *contaminant* OR *unknown* OR *emerging* AND *contaminant* OR *cec*) gave 719 results.
TITLE-ABS-KEY **(*disinfection*** AND ***by-products*** **OR *organic*** AND ***contaminant*** **OR *unknown*** **OR *emerging*** AND ***contaminant*** **OR *cec*) AND** TITLE-ABS-KEY **(*drinking*** AND ***water*** **OR *potable*** AND ***water*** **OR *recycled*** AND ***water*)** gave 388 document results.
TITLE-ABS-KEY (disinfection AND by-products OR organic AND contaminant OR unknown OR emerging AND contaminant OR cec) AND TITLE-ABS-KEY (drinking AND water OR potable AND water OR recycled AND water) AND TITLE-ABS-KEY (mass AND spectrometry OR non-target OR analysis) gave 39 results. Those deemed relevant are listed below:

Kimura, S.Y., Cuthbertson, A.A., Byer, J.D., Richardson, S.D. The DBP exposome: Development of a new method to simultaneously quantify priority disinfection by-products and comprehensively identify unknowns (2019) Water Research, pp. 324-333. DOI: 10.1016/j.watres.2018.10.057.

AFFILIATIONS: Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC 29208, United States; Department of Chemistry, University of Calgary, Calgary, Alberta T2N 1N4, Canada; LECO Corp., 3000 Lakeview Ave., St. Joseph, Michigan, 49085, United States.

ABSTRACT: Disinfected drinking water contains hundreds of disinfection by-products (DBPs) that are formed by the reaction of disinfectants with natural and anthropogenic organic matter, bromide, and iodide. Understanding what these DBPs are is important because millions of people worldwide consume drinking water every day, and human epidemiologic studies have reported cancer, miscarriage, and birth defects from consuming such waters. While more than 600 DBPs are reported in the literature, very few studies quantify complete classes of chlorinated, brominated, and iodinated DBPs. Also, very few studies conduct comprehensive non-target analyses of unknown DBPs to characterize the complete DBP exposure (the exposome). ***We developed a new gas chromatography (GC)-mass spectrometry (MS) method that simultaneously quantifies 39 priority unregulated DBPs from six different chemical classes (haloacetaldehydes, haloketones, haloacetamides, haloacetonitriles, halonitromethanes, and iodinated-trihalomethanes) and analyzes unknown DBPs with mass accuracy <600 ppm under full-scan conditions. Using a new type of time-of-flight (TOF) mass spectrometer, which combines selected ion monitoring (SIM)-level sensitivity with mass accuracy of ±0.05 Da, method detection limits of 3-61 ng/L were achieved***. These levels were found to be quite comparable to those of a widely used single quadrupole mass spectrometer (2-90 ng/L) operated in SIM mode. However, analysis using this TOF mass spectrometer offers two additional advantages over traditional quadrupole-MS: 1) full-scan data, which provides additional confidence for target analytes, as well as complete mass spectra for unknown analysis, and 2) two decimal place mass accuracy, which allows additional confidence for target analytes and importantly, molecular formula indication for unknowns. High resolution accurate mass TOF was also used to validate identification of selected compounds. This new method was demonstrated on finished drinking

waters from three different drinking water plants, where target quantification and non-target unknown analyses were performed simultaneously during the same run. This enabled the quantification of 39 DBPs, along with the non-target identification of many other drinking water contaminants, including two additional non-target DBPs: N,N-dimethylacetamide and N-nitrosodibutylamine. © 2018 The Authors
AUTHOR KEYWORDS: DBPs; Disinfection by-products; Drinking water; Non-target analysis; Quantification
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Richardson, S.D., Postigo, C. Liquid Chromatography – Mass Spectrometry of Emerging Disinfection By-products (2018) Comprehensive Analytical Chemistry, 79, pp. 267-295. Cited three times. DOI: 10.1016/bs.coac.2017.07.002.

AFFILIATIONS: Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC, United States; Department of Environmental Chemistry, Institute of Environmental Assessment and Water Research - Spanish National Research Council (IDAEA-CSIC), Barcelona, Spain.

ABSTRACT: Disinfection by-products (DBPs) form by the reaction of disinfectants with natural organic matter (NOM), bromide and iodide; a few are regulated in the United States and in other countries. Due to adverse health effects observed in human epidemiological studies, including bladder cancer, colorectal cancer, miscarriage, and birth defects, much research has been conducted to discover the DBPs that are responsible. Because none of the 11 DBPs regulated in the United States cause bladder cancer in animals, most scientists believe that DBPs other than those regulated are responsible. As a result, both gas chromatography-mass spectrometry (MS) and liquid chromatography (LC)-MS have been used to uncover emerging, unregulated DBPs, many of which are more toxic than those regulated. In addition to NOM, anthropogenic contaminants can also form DBPs when they react with disinfectants after entering source waters from incomplete removal in wastewater treatment. These include pharmaceuticals, estrogens, antibacterial agents, pesticides, bisphenol A, alkylphenol ethoxylate surfactants, flame retardants, benzotriazoles, and ultraviolet filters. ***Increasingly, LC-MS is being used to identify DBPs, particularly with high-resolution MS, which provides additional molecular formula information. LC-MS is enabling the identification of more polar species, as well as high-molecular-weight species. Further, tandem MS techniques, such as precursor ion scan, used in combination with electrospray ionization, are enabling the identification of brominated and iodinated compounds. This chapter will cover the advances that LC-MS has made in the identification of new emerging DBPs and the quantification of unregulated toxicologically important DBPs.*** © 2018 Elsevier B.V.
AUTHOR KEYWORDS: DBPs; Disinfection by-products; Drinking water; Emerging contaminants; Emerging DBPs; LC-MS; Liquid chromatography-mass spectrometry; Mass spectrometry; Pharmaceuticals
DOCUMENT TYPE: Article

Wang, M., Helbling, D.E. A non-target approach to identify disinfection byproducts of structurally similar sulfonamide antibiotics (2016) Water Research, 102, pp. 241-251. Cited 13 times. DOI: 10.1016/j.watres.2016.06.042.

AFFILIATIONS: School of Civil and Environmental Engineering, Cornell University, Ithaca, NY, United States.

ABSTRACT: There is growing concern over the formation of new types of disinfection byproducts (DBPs) from pharmaceuticals and other emerging contaminants during drinking water production. Free chlorine is a widely used disinfectant that reacts non-selectively with organic molecules to form a variety of byproducts. In this research, we aimed to investigate the DBPs formed from ***three structurally similar sulfonamide antibiotics (sulfamethoxazole, sulfathiazole, and sulfadimethoxine)*** to determine how

chemical structure influences the types of chlorination reactions observed. ***We conducted free chlorination experiments and developed a non-target approach to extract masses from the experimental dataset that represent the masses of candidate DBPs.*** Structures were assigned to the candidate DBPs based on analytical data and knowledge of chlorine chemistry. Confidence levels were assigned to each proposed structure according to conventions in the field. ***In total, 11, 12, and 15 DBP structures were proposed for sulfamethoxazole, sulfathiazole, and sulfadimethoxine, respectively. The structures of the products suggest a variety of reaction types including chlorine substitution, S. C cleavage, S. N hydrolysis, desulfonation, oxidation/hydroxylation, and conjugation reactions.*** Some reaction types were common to all of the sulfonamide antibiotics, but unique reaction types were also observed for each sulfonamide antibiotic suggesting that selective prediction of DBP structures of other sulfonamide antibiotics based on chemical structure is unlikely to be possible based on these data alone. ***This research offers an approach to comprehensively identify DBPs of organic molecules and fills in much needed data on the formation of specific DBPs from three environmentally relevant sulfonamide antibiotics.***
AUTHOR KEYWORDS: Disinfection byproducts; High-resolution mass spectrometry; Non-target analysis; Sulfonamide antibiotic; Transformation products
DOCUMENT TYPE: Article

Daiber, E.J., DeMarini, D.M., Ravuri, S.A., Liberatore, H.K., Cuthbertson, A.A., Thompson-Klemish, A., Byer, J.D., Schmid, J.E., Afifi, M.Z., Blatchley, E.R., Richardson, S.D. Progressive Increase in Disinfection Byproducts and Mutagenicity from Source to Tap to Swimming Pool and Spa Water: Impact of Human Inputs (2016) Environmental Science and Technology, 50 (13), pp. 6652-6662. Cited 24 times. DOI: 10.1021/acs.est.6b00808.

AFFILIATIONS: Stud. Services Authority, U.S. Environmental Protection Agency, National Exposure Research Laboratory, Athens, GA 30605, United States; National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, United States; Department of Chemistry and Biochemistry, University of South Carolina, 631 Sumter St., Columbia, SC 29208, United States; LECO Corp., 3000 Lakeview Ave., St. Joseph, MI 49085, United States; Lyles School of Civil Engineering, Purdue University, 550 Stadium Mall Drive, West Lafayette, IN 47907, United States; Division of Environmental and Ecological Engineering, Purdue University, 500 Central Drive, West Lafayette, IN 47907, United States; Oak Ridge Associ. Universities, National Risk Management Research Laboratory, U.S. Environmental Protection Agency, Ada, OK 74820, United States; PG Assist Services, Ltd., Fourteen Enterprise Ct., Durham, S47 0PS, United Kingdom.

ABSTRACT: Pools and spas are enjoyed throughout the world for exercise and relaxation. However, there are no previous studies on mutagenicity of disinfected spa (hot tub) waters or comprehensive identification of disinfection byproducts (DBPs) formed in spas. Using 28 water samples from seven sites, ***we report the first integrated mutagenicity and comprehensive analytical chemistry of spas treated with chlorine, bromine, or ozone, along with pools treated with these same disinfectants. Gas chromatography (GC) with high-resolution mass spectrometry, membrane-introduction mass spectrometry, and GC-electron capture detection were used to comprehensively identify and quantify DBPs and other contaminants. Mutagenicity was assessed by the Salmonella mutagenicity assay. More than 100 DBPs were identified, including a new class of DBPs, bromoimidazoles. Organic extracts of brominated pool/spa waters were 1.8× more mutagenic than chlorinated ones; spa waters were 1.7× more mutagenic than pools. Pool and spa samples were 2.4 and 4.1× more mutagenic, respectively, than corresponding tap waters.*** The concentration of the sum of 21 DBPs measured quantitatively increased from finished to tap to pool to spa; and mutagenic potency increased from finished/tap to pools to spas. ***Mutagenic potencies of samples from a chlorinated site correlated best with brominated haloacetic acid concentrations (Br-HAAs) (r = 0.98) and nitrogen-containing DBPs (N-***

DBPs) (r = 0.97) and the least with Br-trihalomethanes (r = 0.29) and Br-N-DBPs (r = 0.04). The mutagenic potencies of samples from a brominated site correlated best (r = 0.82) with the concentrations of the nine HAAs, Br-HAAs, and Br-DBPs. Human use increased significantly the DBP concentrations and mutagenic potencies for most pools and spas. These data provide evidence that human precursors can increase mutagenic potencies of pools and spas and that this increase is associated with increased DBP concentrations. © 2016 American Chemical Society.
DOCUMENT TYPE: Review
ACCESS TYPE: Open Access

Bergman, L.E., Wilson, J.M., Small, M.J., Vanbriesen, J.M. Application of classification trees for predicting disinfection by-product formation targets from source water characteristics (2016) Environmental Engineering Science, 33 (7), pp. 455-470. Cited five times. DOI: 10.1089/ees.2016.0044.

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ABSTRACT: Formation and speciation of disinfection by-products (DBPs) depend on source water constituents. Many studies have sought to model the formation of DBPs using both source water and in-plant operational data, and although sometimes highly predictive of DBP formation, these models are limited in their applicability. To create regional models that could apply to multiple plants within a watershed, classification trees were used to predict finished water DBP parameters from source water constituents collected at multiple locations in a watershed. Data were from a field study conducted in the Monongahela River in southwestern PA from May, 2010 to September, 2012, incorporating six different sites. Classification trees were used to predict violation of, or compliance with, four threshold values that have regulatory and operational significance, namely, the total trihalomethanes (TTHMs) maximum contaminant level (MCL) (regulatory standard of 80 μg/L), 80% of the TTHMs MCL (64 μg/L), a bromine incorporation factor of 0.75, and 50% brominated THMs by mass. The classification trees demonstrated accuracies of 76-83%. ***Fluorescence measurements were selected in all classification trees, demonstrating their utility in DBP predictive models.*** Furthermore, model validation using data from each collection site demonstrated the potential use of classification models across this spatially variable region for drinking water plants unable to collect their own source water data. Thus, classification trees provide a valuable tool for creating watershed-level source water-based DBP models. © Mary Ann Liebert, Inc. 2016.
AUTHOR KEYWORDS: disinfection by-products; natural organic matter; organic analysis; statistical analysis
DOCUMENT TYPE: Article

Hanigan, D., Liao, X., Zhang, J., Herckes, P., Westerhoff, P. Sorption and desorption of organic matter on solid-phase extraction media to isolate and identify N-nitrosodimethylamine precursors (2016) Journal of Separation Science, 39 (14), pp. 2796-2805. Cited five times. DOI: 10.1002/jssc.201600139.

AFFILIATIONS: Department of Civil and Environmental Engineering, University of Nevada, Reno, NV, United States; Institute of Municipal and Environmental Engineering, College of Civil Engineering, Huaqiao University, Xiamen, Fujian, China; School of Molecular Sciences, Arizona State University, Tempe, AZ, United States; School of Sustainable Engineering and the Built Environment, Arizona State University, Tempe, AZ, United States

ABSTRACT: Nitrosodimethylamine is mutagenic in rodents, a drinking water contaminant, and a byproduct of drinking water disinfection by chloramination. Nitrosodimethylamine precursor identification leads to their control and improved understanding of nitrosodimethylamine formation

during chloramination. ***Mass balances on nitrosodimethylamine precursors were evaluated across solid-phase extraction cartridges and in eluates to select the best combination of solid-phase media and eluent that maximized recovery of nitrosodimethylamine precursors into a solvent amenable to time-of-flight mass spectrometry analysis.*** After reviewing literature and comparing various solid-phase cartridges and eluent combinations, a method was obtained to efficiently recover nitrosodimethylamine precursors. ***The approach with the greatest recoveries of nitrosodimethylamine precursors involved cation exchange resin loaded with water samples at pH 3 and eluted with 5% NH4OH in methanol. This indicated that nitrosodimethylamine precursors are amines that protonate at low pH and deprotonate at high pH. Quaternary amines were irreversibly sorbed to the cation exchange cartridge and did not account for a large fraction of precursors. Overall, a median recovery of 82% for nitrosodimethylamine precursors was achieved from 11 surface waters and one wastewater.*** Applying this method allowed discovery of methadone as a new nitrosodimethylamine precursor in wastewater effluent and drinking water treatment plant intakes.
AUTHOR KEYWORDS: Disinfection byproducts; Fractionation; Isolation; N-Nitrosodimethylamine; Precursors
DOCUMENT TYPE: Article

Zhang, S., Wang, X., Yang, H., Xie, Y.F. Chlorination of oxybenzone: Kinetics, transformation, disinfection byproducts formation, and genotoxicity changes (2016) Chemosphere, 154, pp. 521-527. Cited 12 times. DOI: 10.1016/j.chemosphere.2016.03.116.

AFFILIATIONS: State Key Joint Laboratory of Environmental Simulation and Pollution Control, School of Environment, Tsinghua University, Beijing, 100084, China; The Pennsylvania State University, Middletown, PA 17057, United States.

ABSTRACT: UV filters are a kind of emerging contaminant, and their transformation behavior in water treatment processes has aroused great concern. In particular, toxic products might be produced during reaction with disinfectants during the disinfection process. As one of the most widely used UV filters, oxybenzone has received significant attention, because its transformation and toxicity changes during chlorine oxidation are a concern. ***In our study, the reaction between oxybenzone and chlorine followed pseudo-first-order and second-order kinetics. Three transformation products were detected by LC-MS/MS, and the stability of products followed the order of tri-chloro-methoxyphenoyl > di-chlorinated oxybenzone > mono-chlorinated oxybenzone. Disinfection byproducts (DBPs) including chloroform, trichloroacetic acid, dichloroacetic acid and chloral hydrate were quickly formed, and increased at a slower rate until their concentrations remained constant.*** The maximum DBP/oxybenzone molar yields for the four compounds were 12.02%, 6.28%, 0.90% and 0.23%, respectively. SOS/umu genotoxicity test indicated that genotoxicity was highly elevated after chlorination, and genotoxicity showed a significantly positive correlation with the response of tri-chloro-methoxyphenoyl. ***Our results indicated that more genotoxic transformation products were produced in spite of the elimination of oxybenzone, posing potential threats to drinking water safety.*** This study shed light on the formation of DBPs and toxicity changes during the chlorination process of oxybenzone.
AUTHOR KEYWORDS: Chlorination; Disinfection byproducts; Genotoxicity; Oxybenzone; Product
DOCUMENT TYPE: Article

Richardson, S.D., Postigo, C. Discovery of New Emerging DBPs by High-Resolution Mass Spectrometry (2016) Comprehensive Analytical Chemistry, 71, pp. 335-356. Cited five times. DOI: 10.1016/bs.coac.2016.01.008.

AFFILIATIONS: University of South Carolina, Columbia, SC, United States; Inst. for Environmental Assessment and Water Res. - Spanish National Research Council (IDAEA-CSIC), Barcelona, Spain.

ABSTRACT: ***More than 50% of the halogenated disinfection by-products (DBPs) formed during disinfection treatments are still unknown, and they may be relevant for the potential toxicity exerted by DBP mixtures of disinfected waters.*** High-resolution mass spectrometry (HR-MS) technology has contributed to reduce the amount of unknown DBPs. ***This chapter discusses the role of magnetic sectors, time-of-flight, Orbitrap and Fourier transform ion cyclotron resonance (FT-ICR) instruments in the comprehensive identification of DBPs in disinfected waters (including drinking water, swimming pool water, disinfected ballast water and disinfected wastewater-impacted waters) and reviews the most relevant DBP discoveries found in the peer-reviewed literature***, in terms of novel DBP chemical classes or highly toxic compounds. Furthermore, the use of HR-MS analyzers to quantify target DBPs in biological samples is also briefly discussed. © 2016 Elsevier B.V.
AUTHOR KEYWORDS: DBPs; Disinfection by-products; Drinking water; Emerging contaminants; High-resolution mass spectrometry; Structure elucidation
DOCUMENT TYPE: Book Chapter

West, D.M., Mu, R., Gamagedara, S., Ma, Y., Adams, C., Eichholz, T., Burken, J.G., Shi, H. Simultaneous detection of perchlorate and bromate using rapid high-performance ion exchange chromatography – tandem mass spectrometry and perchlorate removal in drinking water (2015) Environmental Science and Pollution Research, 22 (11), pp. 8594-8602. Cited seven times. DOI: 10.1007/s11356-014-4028-8.

AFFILIATIONS: Department of Chemistry, Missouri University of Science and Technology, 400 West 11th Street, Rolla, MO 65409, United States; Environmental Research Center, Missouri University of Science and Technology, Rolla, MO 65409, United States; Department of Civil and Environmental Engineering, Utah State University, Logan, UT 84322, United States; Missouri Department of Natural Resources, Jefferson City, MO 65102, United States; Department of Civil, Architectural and Environmental Engineering, Missouri University of Science and Technology, Rolla, MO 65409, United States.

ABSTRACT: ***Perchlorate and bromate occurrence in drinking water causes health concerns due to their effects on thyroid function and carcinogenicity, respectively.*** The purpose of this study was threefold: 1) to advance a sensitive method for simultaneous rapid detection of perchlorate and bromate in drinking water system, 2) to systematically study the occurrence of these two contaminants in Missouri drinking water treatment systems, and 3) to examine effective sorbents for minimizing perchlorate in drinking water. ***A rapid high-performance ion exchange chromatography – tandem mass spectrometry (HPIC-MS/MS) method was advanced for simultaneous detection of perchlorate and bromate in drinking water. The HPIC-MS/MS method was rapid, required no preconcentration of the water samples, and had detection limits for perchlorate and bromate of 0.04 and 0.01 µg/L, respectively.*** The method was applied to determine perchlorate and bromate concentrations in total of 23 selected Missouri drinking water treatment systems during differing seasons. The water systems selected include different source waters: groundwater, lake water, river water, and groundwater influenced by surface water. The concentrations of perchlorate and bromate were lower than or near to method detection limits in most of the drinking water samples monitored. The removal of perchlorate by various adsorbents was studied. A cationic organoclay (TC-99) exhibited effective removal of perchlorate from drinking water matrices. © 2015, Springer-Verlag Berlin Heidelberg.
AUTHOR KEYWORDS: Bromate detection; Drinking water disinfection by-product; High-performance ion chromatography – mass spectrometry; Perchlorate removal; TC-99 organoclay
DOCUMENT TYPE: Article

Kadmi, Y., Favier, L., Mouni, L., Nasrallah, N., Wolbert, D. A highly sensitive liquid chromatography-tandem mass spectrometry method for the analysis of a toxic water disinfection by-product, N-nitrosomethylethylamine (2014) Analytical Methods, 6 (10), pp. 3231-3234. Cited five times. DOI: 10.1039/c4ay00146j.

AFFILIATIONS: Ecole Nationale Supérieure de Chimie de Rennes, CNRS, UMR 6226, 11 Allée de Beaulieu, CS 50837, 35708 Rennes Cedex 7, France; Faculté des Sciences de la Nature et de la Vie et des Sciences de la Terre, Université Akli Mohand Oulhadj, Bouira, Algeria; Faculté de Génie Mécanique et Génie des Procédés, Laboratoire de Génie de la Réaction, Chimique, BP 32 El-Alia, Bab-Ezzouar, 16000 Alger, Algeria.

ABSTRACT: ***Recently, among the emerging contaminants, N-nitrosomethylethylamine has become of special concern because it is a potent human mutagenic and carcinogenic contaminant detected in chlorinated or chloraminated drinking waters and wastewaters. In this work a sensitive and robust method, which was based on solid-phase extraction followed by ultra-high-pressure liquid chromatography coupled with tandem mass spectrometry, was developed for the determination of N-nitrosomethylethylamine in water at ultra-trace levels. Chromatographic separation was performed on a C18 column. Quantification of N-nitrosomethylethylamine was achieved by using a triple quadrupole mass spectrometer that was equipped with an electrospray interface and was operated in positive ionization mode.*** Under optimized conditions, the calibration curve was linear from 0.1 to 100 µg L-1 (r2 ≥ 0.999). The precision of the intra- and inter-day values was found to be less than 2.5%, and the accuracy of the method was within ±3%. Moreover, an extraction efficiency greater than 86% was obtained at different concentration levels with relative standard deviation, RSD < 4.2%. Therefore, ***the experimental results showed that the proposed analytical method can be used successfully to determine N-nitrosomethylethylamine at ultra-trace levels (ng L-1) in aqueous samples.*** © the Partner Organisations 2014.
DOCUMENT TYPE: Article

Al-Shatri, M.A., Nuhu, A.A., Basheer, C. Determination of Haloacetic Acids in Bottled and Tap Water Sources by Dispersive Liquid-Liquid Microextraction and GC-MS Analysis (2014) Scientific World Journal, 2014, art. no. 695049. Cited 2 times. DOI: 10.1155/2014/695049.

AFFILIATIONS: Department of Chemistry, King Fahd University of Petroleum and Minerals, KFUPM, Box 1059, Dhahran, 31261, Saudi Arabia; Department of Chemistry, Ahmadu Bello University, PMB 1069, Zaria, Kaduna, 2222, Nigeria

ABSTRACT: ***Haloacetic acids are toxic organic pollutants that can be formed as by-products of disinfection of water by chlorination.*** In this study, we developed a fast and efficient method for the determination of ***six species of these compounds in water using dispersive liquid-liquid microextraction followed by GC-MS analysis. To be suitable for GC analysis, the acidic analytes were derivatized using n-octanol.*** One-factor-at-a-time optimization was carried out on several factors including temperature, extraction time, amount of catalyst, and dispersive solvent. The optimized conditions were then used to determine calibration parameters. Linearity, as demonstrated by coefficient of determination, ranged between 0.9900 and 0.9966 for the concentration range of 0.05-0.57 µg/L. The proposed method has good repeatability; intraday precision was calculated as %RSD of 2.38-9.34%, while interday precision was 4.69-8.06%. The method was applied to real samples in bottled water and tap water sources. ***Results indicated that the total concentrations of the analytes in these sources (2.97-5.30 µg/L) were far below the maximum contaminant levels set by both the World Health Organization and the United States Environmental Protection Agency.*** The proposed method compared favorably with methods reported in the literature. ©2014 Mohsen A. Al-shatri et al.
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Allard, S., Charrois, J.W.A., Joll, C.A., Heitz, A. Simultaneous analysis of 10 trihalomethanes at nanogram per liter levels in water using solid-phase microextraction and gas chromatography mass-

spectrometry (2012) Journal of Chromatography A, 1238, pp. 15-21. Cited 37 times. DOI: 10.1016/j.chroma.2012.03.020.

AFFILIATIONS: Curtin Water Quality Research Centre, Department of Chemistry, Curtin University, GPO Box U1987, Perth, WA 6845, Australia.

ABSTRACT: Trihalomethanes are predominantly formed during disinfection of water via reactions of the oxidant with natural organic matter. Even though chlorinated and brominated trihalomethanes are the most widespread organic contaminants in drinking water, when iodide is present in raw water iodinated trihalomethanes can also be formed. The formation of iodinated trihalomethanes can lead to taste and odor problems and is a potential health concern since they have been reported to be more toxic than their brominated or chlorinated analogs. ***Currently, there is no published standard analytical method for I-THMs in water. The analysis of 10 trihalomethanes in water samples in a single run is challenging because the iodinated trihalomethanes are found at very low concentrations (ng/L range), while the regulated chlorinated and brominated trihalomethanes are present at much higher concentrations (above µg/L). An automated headspace solid-phase microextraction technique, with a programmed temperature vaporizer inlet coupled with gas chromatography-mass spectrometry, was developed for routine analysis of 10 trihalomethanes i.e., bromo-, chloro- and iodo-trihalomethanes in water samples. The carboxen/polydimethylsiloxane/divinylbenzene fiber was found to be the most suitable.*** The optimization, linearity range, accuracy and precision of the method are discussed. ***The limits of detection range from 1. ng/L to 20. ng/L for iodoform and chloroform, respectively. Matrix effects in treated groundwater, surface water, seawater, and secondary wastewater were investigated and it was shown that the method is suitable for the analysis of trace levels of iodinated trihalomethanes in a wide range of waters.*** The method developed in the present study has the advantage of being rapid, simple and sensitive. A survey conducted throughout various process stages in an advanced water recycling plant showed the presence of iodinated trihalomethanes at ng/L levels. © 2012 Elsevier B.V.
AUTHOR KEYWORDS: Headspace analysis; Iodinated disinfection by-products; Iodinated trihalomethanes; Iodoform; Programmed temperature vaporizer; Solid-phase microextraction
DOCUMENT TYPE: Article

Müller, A., Weiss, S.C., Beißwenger, J., Leukhardt, H.G., Schulz, W., Seitz, W., Ruck, W.K.L., Weber, W.H. Identification of ozonation by-products of 4- and 5-methyl-1H-benzotriazole during the treatment of surface water to drinking water (2012) Water Research, 46 (3), pp. 679-690. Cited 29 times. DOI: 10.1016/j.watres.2011.11.033.

AFFILIATIONS: Zweckverband Landeswasserversorgung, Betriebs- und Forschungslaboratorium, Am Spitzigen Berg 1, 89129 Langenau, Germany; Leuphana Universität Lüneburg, Institut für Umweltchemie, Scharnhorststr. 1, 21335 Lüneburg, Germany; Hochschule Aalen, Fakultät Chemie, Beethovenstraße 1, 73430 Aalen, Germany

ABSTRACT: During the treatment of surface water to drinking water, ***ozonation is often used for disinfection and to remove organic trace substances, whereby oxidation by-products can be formed. Here we use the example of tolyltriazole to describe an approach for identifying relevant oxidation by-products in the laboratory and subsequently detecting them in an industrial-scale process.*** The identification process involves ozonation experiments with pure substances at laboratory level (concentration range mgL -1). ***The reaction solutions from different ozone contact times were analyzed by high performance liquid chromatography - quadrupole time-of-flight mass spectrometry (HPLC-QTOF-MS) in full scan mode. Various approaches were used to detect the oxidation by-products: (i) target searches of postulated oxidation by-products, (ii) comparisons of chromatograms (e.g., UV/VIS) of the different samples, and (iii) color-coded abundance time courses (kinetic) of all detected compounds were illustrated in a kind of a heat map. MS/MS, H/D exchange, and derivatization***

experiments were used for structure elucidation for the detected by-product. Due to the low contaminant concentrations (ngL -1-range) of contaminants in the untreated water, the conversion of results from laboratory experiments to an industrial-scale ***required the use of HPLC-MS/MS with sample enrichment (e.g., solid phase extraction.)*** In cases where reference substances were not available or oxidation by-products without clear structures were detected, reaction solutions from laboratory experiments were used to optimize the analytical method to detect ngL -1 in the samples of the industrial processes. We exemplarily demonstrated the effectiveness of the methodology with the industrial chemicals 4- and 5-methyl-1H-benzotriazole (4- and 5-MBT) as an example. Moreover, not only did we identify several oxidation by-products in the laboratory experiments tentatively, ***but also detected three of the 11 reaction products in the outlet of the full-scale ozonation unit.*** © 2011 Elsevier Ltd.
AUTHOR KEYWORDS: HPLC-QTOF-MS; HPTLC/AMD-MS; Ozonation by-products; Tolyltriazole; Water purification
DOCUMENT TYPE: Article

Kubwabo, C., Stewart, B., Gauthier, S.A., Gauthier, B.R. Improved derivatization technique for gas chromatography-mass spectrometry determination of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone in drinking water (2009) Analytica Chimica Acta, 649 (2), pp. 222-229. Cited 10 times. DOI: 10.1016/j.aca.2009.07.035.

AFFILIATIONS: Exposure and Biomonitoring Division, Research and Radiation Directorate, Health Canada, Ottawa, Ont. K1A 0K9, Canada; Iogen Corporation, Ottawa, Ont. K1V 1C1, Canada; Food Research Division, Food Directorate, Health Canada, Ottawa, Ont. K1A 0K9, Canada

ABSTRACT: ***The quantification of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (Mutagen X or MX)*** in drinking water is difficult due to the low concentration of MX in drinking water, its high sensitivity to pH change, and matrix effects that interfere with the derivatization and analysis. Typically, the quantification of MX involves derivatization by methylation. ***We present a one-step derivatization procedure for MX using N-methyl-bis-trifluoroacetamide (MBTFA) and analysis by ion trap GC/MS/MS.*** The new method resulted in a significant reduction in analysis time, and improved detection limits. The abundant and selective ions in the mass spectrum of the trifluoroacylated MX (trifluoroacetic acid-4-chloro-3-dichloromethyl-5-oxo-2-hydro-furan-2-yl ester) allowed for a clear identification and quantification of the compound, ***with a method detection limit of 7.7 ng L-1, and a limit of quantitation of 24.4 ng L-1. The trifluoroacylated MX was shown to be stable for 30 days in an excess of the derivatization reagent.*** The new method was applied for the determination of MX in several drinking water samples, with a concentration range from not-detected to 517 ng L-1; these values are comparable to those obtained in previous studies. ***The development of this new simplified analytical method for MX is an important step forward in the field of disinfection by-product (DBP) research, particularly in light of the recent scientific recognition of halogenated furanones as emerging drinking water contaminants.*** Increased analytical ability may well be a decisive factor in the monitoring of these disinfection by-products. © 2009 Elsevier B.V.
AUTHOR KEYWORDS: Derivatization; Drinking water; Mutagen X; N-methyl-bis-trifluoroacetamide; Solid phase extraction; Tandem mass spectrometry
DOCUMENT TYPE: Article

Mhlongo, S.H., Mamba, B.B., Krause, R.W. Monitoring the prevalence of nitrosamines in South African waters and their removal using cyclodextrin polyurethanes (2009) Physics and Chemistry of the Earth, 34 (13-16), pp. 819-824. Cited 12 times. DOI: 10.1016/j.pce.2009.07.008.

AFFILIATIONS: University of Johannesburg, Department of Chemical Technology, P.O. Box 17011, Doornfontein, 2028, South Africa.

ABSTRACT: The prevalence of nitrosamines, especially N-nitrosodimethylamine (NDMA), was monitored in three South African water supplies. NDMA a disinfection by-product (DBP) and potent carcinogen, has recently been detected in many drinking water supplies internationally. Besides direct industrial or human-derived contamination, nitrosodimethylamine can be formed through a chemical reaction between monochloroamine and an organic based compound such as dimethylamine which is frequently detected in surface water. It has been suggested that chloramination of surface waters with a high concentration of dissolved organic carbon (DOC) could result in elevated NDMA formation. Growing evidence suggests that NDMA occurs more frequently and at higher concentrations in drinking water systems that practice chloramination compared to systems that use chlorination. In gauging the extent of water contamination by nitrosamines in water distribution systems, especially NDMA, water samples collected from three different water treatment plants that practice chemical drinking water disinfection were qualitatively analyzed for the presence of nitrosamines. ***Solid phase microextraction (SPME) was employed in the extraction of nitrosamines from the water samples and gas chromatography-mass spectrometry (GC-MS)***, was used in the analysis of the water samples. Trace amounts of NDMA were detected at one of the water treatment plants and in the distribution network. The application of water-insoluble cyclodextrin (CD) polymers in the removal of nitrosamines and potential amine precursors from the water samples was tested. Quantitative removal of NDMA (based on peak area) from the water samples was achieved which suggests that in the water treatment train the use of these nanosponges can be applied in the mitigation of trace contaminants such as NDMA.
AUTHOR KEYWORDS: Cyclodextrin (CD); Disinfection by-product (DBP); N-nitrosodimethylamine (NDMA); Nitrosamines; Solid phase microextraction (SPME)
DOCUMENT TYPE: Article

Zhang, X., Talley, J.W., Boggess, B., Ding, G., Birdsell, D. Fast selective detection of polar brominated disinfection byproducts in drinking water using precursor ion scans (2008) Environmental Science and Technology, 42 (17), pp. 6598-6603. Cited 71 times. DOI: 10.1021/es800855b.

AFFILIATIONS: Department of Civil Engineering, Hong Kong University of Science and Technology, Hong Kong, Hong Kong; Department of Civil and Environmental Engineering and Geological Sciences, University of Notre Dame, Notre Dame, IN 46556, United States; Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN 46556, United States; Center for Environmental Science and Technology, University of Notre Dame, Notre Dame, IN 46556, United States

ABSTRACT: ***Brominated disinfection byproducts (DBPs), formed from the reaction of disinfectant(s) with natural organic matter and bromide in raw water, are generally more cytotoxic and genotoxic than their chlorinated analogues.*** Brominated DBPs have been intensively studied over the past 35 years, yet only a fraction of the total organic bromine formed during disinfection has been identified. ***A significant portion of the unaccounted total organic bromine may be attributed to polar/highly polar brominated DBPs. In this work, a method for fast selective detection of polar/ highly polar brominated DBPs in drinking water was developed using negative ion electrospray ionization-triple quadrupole mass spectrometry (ESI-tqMS) by setting precursor ion scans of m/z 79 and 81.*** This method was conducted without liquid chromatography separation. The results demonstrate that the ESI-tqMS precursor ion scan is an effective tool for the selective detection of electrospray ionizable bromine-containing compounds in a complex mixture. Many polar/ highly polar bromine-containing DBPs were tentatively found in two drinking water samples, and some of them may be new brominated DBPs that have not been previously reported. ***This method was also extended for the selective detection of polar bromine-containing compounds/contaminants in groundwater, surface water and wastewater.***
DOCUMENT TYPE: Article

Aeppli, C., Berg, M., Hofstetter, T.B., Kipfer, R., Schwarzenbach, R.P. Simultaneous quantification of polar and non-polar volatile organic compounds in water samples by direct aqueous injection-gas chromatography/mass spectrometry (2008) Journal of Chromatography A, 1181 (1-2), pp. 116-124. Cited 29 times. DOI: 10.1016/j.chroma.2007.12.043.

AFFILIATIONS: Eawag, Swiss Federal Institute of Aquatic Science and Technology, 8600 Dübendorf, Switzerland; Institute of Biogeochemistry and Pollutant Dynamics (IBP), ETH Zurich, 8092 Zurich, Switzerland

ABSTRACT: ***A direct aqueous injection-gas chromatography/mass spectrometry (DAI-GC/MS) method for trace analysis of 24 volatile organic compounds (VOCs) in water samples is presented. The method allows for the simultaneous quantification of benzene, toluene, ethyl benzene, and xylenes (BTEX), methyl tert-butyl ether (MTBE), tert-butyl alcohol (TBA), as well as a variety of chlorinated methanes, ethanes, propane, enthenes, and benzenes.*** Applying a liquid film polyethylene glycol or a porous layer open tubular (PLOT) divinylbenzene GC capillary column to separate the water from the VOCs, ***volumes of 1-10 µL aqueous sample are directly injected into the GC.*** No enrichment or pretreatment steps are required and sample volumes as low as 100 µL are sufficient for accurate quantification. ***Method detection limits determined in natural groundwater samples were between 0.07 and 2.8 µg/L and instrument detection limits of <5 pg were achieved for 21 out of the 24 evaluated VOCs.*** DAI-GC/MS offers both good accuracy and precision (relative standard deviations ≤10%). The versatility of our method is demonstrated for contaminant quantification in drinking water disinfection (advanced oxidation of MTBE) and for VOC concentration measurements in a polluted aquifer. The wide range of detectable compounds and the lack of labor-intensive sample preparation illustrate that the DAI method is robust and easily applicable for the quantification of important organic groundwater contaminants.
AUTHOR KEYWORDS: 1,1,1-Trichloroethane; 1,1-Dichloroethene; 1,2-Dichlorobenzene; 1,2-Dichloroethane; 1,2-Dichloropropane; 1,3-Dichlorobenzene; 1,4-Dichlorobenzene; Analysis; Benzene; Carbon tetrachloride; Chlorobenzene; Chloroform; cis-1,2-Dichloroethene; Dichloromethane; Environmental aqueous samples; Groundwater; Methyl tert-butyl ether (MTBE); Perchloroethene; tert-Butyl alcohol (TBA); Toluene; trans-1,2-Dichloroethene; Trichloroethene; Vinyl chloride; VOC; Xylene
DOCUMENT TYPE: Article

Grosser, Z. Desalinated water measurement challenges (2007) Water and Wastewater International, 22 (5), p.29.

AFFILIATIONS: PerkinElmer Life and Analytical Sciences.

ABSTRACT: Desalinated water for drinking must meet regulatory requirements for microbiological, organic and inorganic contaminants. Inductively coupled plasma mass spectroscopy (ICP-MS) is one of the desalination technology used for potable water. Special Inorganic Compounds like Disinfection by-products (DBP), are used in this method. ***The measurement is performed by High performance liquid chromatography for separation of bromine compound along with ICP-MS for the detection.*** Narrow cell technology is used for removal of analyte followed by mass spectrometry. Detection limits are improved compared to other approaches and the precision in varying matrices are also improved. Brine, a by-product of desalination must be evaluated before discharge. Routine analysis for source and final drinking water can be enhanced with the use of this new technology.
DOCUMENT TYPE: Article

Plewa, M.J., Wagner, E.D., Richardson, S.D., Thruston Jr., A.D., Woo, Y.-T., McKague, A.B. Chemical and biological characterization of newly discovered iodoacid drinking water disinfection byproducts (2004) Environmental Science and Technology, 38 (18), pp. 4713-4722. Cited 308 times. DOI: 10.1021/es049971v.

AFFILIATIONS: Coll. Agric., Consum./Environ. Sci., Department of Crop Sciences, University of Illinois, Urbana, IL 61801, United States; Natl. Exposure Research Laboratory, U.S. Environmental Protection Agency, Athens, GA 30605, United States; Risk Assessment Division, Off. of Poll. Prevention and Toxics, U.S. Environmental Protection Agency, Washington, DC 20460, United States; CanSyn Chemical Corporation, 200 College Street, Toronto, Ont. M5S 3E5, Canada.

ABSTRACT: ***Iodoacid drinking water disinfection byproducts (DBPs) were recently uncovered in drinking water samples from source water with a high bromide/iodide concentration that was disinfected with chloramines.*** The purpose of this paper is to report the analytical chemical identification of iodoacetic acid (IA) and other iodoacids in drinking water samples, ***to address the cytotoxicity and genotoxicity of IA in Salmonella typhimurium and mammalian cells***, and to report a structure-function analysis of IA with its chlorinated and brominated monohalogenated analogues. The iodoacid DBPs were identified as iodoacetic acid, bromoiodoacetic acid, (Z)- and (E)-3-bromo-3-iodopropenoic acid, and (E)-2-iodo-3-methylbutenedioic acid. IA represents a new class (iodoacid DBPs) of highly toxic drinking water contaminants. The cytotoxicity of IA in S. typhimurium was 2.9× and 53.5× higher than bromoacetic acid (BA) and chloroacetic acid (CA), respectively. A similar trend was found with cytotoxicity in Chinese hamster ovary (CHO) cells; IA was 3.2× and 287.5× more potent than BA and CA, respectively. This rank order was also expressed in its genotoxicity with IA being 2.6× and 523.3× more mutagenic in S. typhimurium strain TA100 than BA and CA, respectively. IA was 2.0× more genotoxic than BA and 47.2× more genotoxicthan CA in CHO cells. The rank order of the toxicity of these monohalogenated acetic acids is correlated with the electrophilic reactivity of the DBPs. IA is the most toxic and genotoxic DBP in mammalian cells reported in the literature. ***These data suggest that chloraminated drinking waters that have high bromide and iodide source waters may contain these iodoacids and most likely other iodo-DBPs. Ultimately, it will be important to know the levels at which these iodoacids occur in drinking water in order to assess the potential for adverse environmental and human health risks.***
DOCUMENT TYPE: Article

Roehl, R., Slingsby, R., Avdalovic, N., Jackson, P.E. Applications of ion chromatography with electrospray mass spectrometric detection to the determination of environmental contaminants in water (2002) Journal of Chromatography A, 956 (1-2), pp. 245-254. Cited 77 times. DOI: 10.1016/S0021-9673(02)00041-9.

AFFILIATIONS: Dionex Corporation, 1228 Titan Way, Sunnyvale, CA 94088-3606, United States; California Dept. of Health Services, Sanitation and Radiat. Labs. Branch, 2151 Berkeley Way, Berkeley, CA 94704, United States

ABSTRACT: ***Ion chromatography (IC) is widely used for the compliance monitoring of common inorganic anions in drinking water.*** However, there has recently been considerable interest in the development of IC methods to meet regulatory requirements for analytes other than common inorganic anions, ***including disinfection byproduct anions, perchlorate, and haloacetic acids. Many of these new methods require the use of large injection volumes, high capacity columns and analyte specific detection schemes, such as inductively coupled plasma mass spectrometry or postcolumn reaction with UV-Vis detection, in order to meet current regulatory objectives. Electrospray ionization mass spectrometry (ESI-MS) is a detection technique that is particularly suitable for the analysis of permanently ionized or polar, ionizable compounds. The combination of IC with MS detection is emerging as an important tool for the analysis of ionic compounds in drinking water, as it provides increased specificity and sensitivity compared to conductivity detection.*** This paper reports on the application of IC-ESI-MS for the confirmation and quantitation of environmentally significant contaminants, i.e., compounds with adverse health effects which are either regulated or being considered for regulation, such as ***bromate, perchlorate, haloacetic acids, and selenium species, in various water samples***.

AUTHOR KEYWORDS: Bromate; Haloacetic acids; Inorganic anions; Organic acids; Perchlorate; Selenium; Water analysis
DOCUMENT TYPE: Conference Paper

Le Curieux, F., Erb, F., Marzin, D. Identification of genotoxic compounds in drinking waters [Identification de composés génotoxiques dans les eaux de boisson] (1998) Revue des Sciences de l'Eau, 11 (SPEC. ISS.), pp. 103-118. Cited one time.

AFFILIATIONS: Department of Organic Chemistry, Åbo Akademi University, Biskopsgatan 8, FIN-20500 Turku, Finland; Département Toxicologie-Hydrologie, Faculté des Sciences Pharmaceutiques et Biologiques, 3, rue du Professeur Laguesse, F-59006 Lille Cedex, France; Laboratoire de Toxicologie, Institut Pasteur de Lille, 1, rue du Professeur Calmette, F-59019 Lille Cedex, France

ABSTRACT: In 1974, two independent studies - one in the Netherlands and the other in the United States - demonstrated the occurrence of trihalomethanes in drinking water. Following studies showed that these chemicals were common contaminants of drinking water and that chloroform, i.e., one of these trihalomethanes, was carcinogenic in rodents. ***Further investigations demonstrated that extracts of chlorinated drinking water induced significant mutagenicity in the Ames/Salmonella assay.*** In the present paper we will first discuss the methods used to detect the genotoxic activity of drinking water and, then, the methods developed to identify the compounds responsible for this activity. After this, we will present the main genotoxic chemicals identified in drinking water, before finally considering several propositions to limit the exposure of populations to these genotoxic compounds. Drinking water is usually produced through a multistage process which includes one or several chlorination steps. It is now widely accepted that the genotoxic activity of drinking water mainly originates from the reaction of chlorine with humic substances present in raw water. Humic substances are natural organic matters (resulting from the degradation of plants and animal tissues) of very complex structure with most chemical functions arranged in aromatic rings or aliphatic chains. The identification of a genotoxic activity in drinking water usually requires concentration of the water samples. Even though such a process implies a probable qualitative/quantitative alteration of the constituents of water samples, the extremely low amounts of genotoxic compounds in drinking water require concentration steps. Among the many genotoxicity tests carried out, the Ames test (which detects reverse mutations in bacteria Salmonella typhimurium) is the assay which was the most frequently used in the field of drinking water mutagenicity. Other tests were performed on eucaryotic cells. Assays detecting micronuclei or chromosomal aberrations in plants, or mutations in mold, yeast, or maize enabled the detection of genotoxic effects of drinking water extracts. Tests on mammal cells also showed that drinking water extracts induced point mutations, sister chromatid exchanges, chromosomal aberrations and micronuclei. In vivo tests on aquatic organisms such as newt or mussels demonstrated the micronuclei inducing effect of unconcentrated drinking water samples. Regarding the identification of the compounds responsible for the genotoxicity, it is obviously not possible to identify all of the thousands of chemicals that may be involved. But such a process is important in order to evaluate the specific genotoxicity and the risk associated with (at least) the main chemicals occurring in drinking water. The identification process usually follows three steps: (i) concentration of the sample can be performed using reverse osmosis, freeze drying, liquid-liquid extraction, and/or adsorption on nonionic resin followed by extraction with organic solvent; (ii) the purification step uses one or a combination of chromatographic techniques (TLC, packed column liquid chromatography, HPLC or GC); (iii) structural identification of the chemical is performed using data from mass spectrometry, and proton and carbon NMR, or UV spectroscopy. ***The analysis of the genotoxic compounds of drinking water showed that they are rather non-volatile, quite acid and not stable at high pH, rather polar, and with a mean molecular weight around 200. Turning now to the identity of these compounds, it is considered that the genotoxicity of drinking water is mainly due to organohalogenated chemicals.*** Some inorganic

chemicals (this class of chemicals is usually not recovered in drinking water extracts) which induce genotoxic or carcinogenic effects must, however, be recalled. ***Arsenic, nitrates, bromates and radon are natural or human-activity-related drinking water contaminants which are responsible for cancers in rodents or in humans. Among the many genotoxic or carcinogenic organohalogenated compounds identified in drinking water, the most abundant chemicals are chlorinated and/or brominated trihalomethanes. Other important groups of compounds are chlorinated and/or brominated derivatives of acetic acids, acetonitriles, ketones, phenolic compounds. The chlorinated hydroxyfuranones, although present at concentrations lower than 0.1 µg/l in drinking water, can be responsible for more than half of the Ames mutagenicity. MX, the most potent of these chlorohydroxyfuranones, has been submitted to intensive toxicological studies worldwide and was very recently identified as a potent carcinogen in rats.*** Now that the presence of genotoxic compounds in drinking waters is a well documented and accepted fact, the perspectives lie in the better identification of the impact of these drinking water contaminants. The development of more sensitive tests such as the Comet assay (detection of DNA strand breaks) or the 32P postlabelling assay (detection of DNA adducts) should be pursued. Moreover, the interaction between genotoxic compounds and DNA must be investigated more thoroughly, including the identification of adduct structures. More globally, it is of interest to better assess the impact of these agents on public health and on the occurrence of specific human cancers. At present, even though a few individual water contaminants are classified as human probable carcinogens, the chlorinated drinking water (in itself) is not considered as carcinogenic to humans. Exposure to these potentially harmful agents can be limited with 1) improving drinking water quality - i.e., decreasing the formation of genotoxins - by using raw water containing lower amounts of organic matter; and 2) modifying the water chemical treatment by using lower amounts of chlorine and/or combining chlorine with other disinfectants. The public health can also be protected by the setting of guidelines for drinking water: each compound identified as dangerous would be given a concentration threshold which should never be exceeded. The Environmental Protection Agency in the USA and the World Health Organization are authorities setting such guidelines. Finally, we believe it is important to limit the concentration of genotoxic compounds in drinking water as much as possible, and one way to do so is to use chlorine in smaller amounts and in a more efficient way. But it is of paramount importance to keep in mind that the disinfection process (in which chlorine still plays a major role) and the providing of a microbiologically safe drinking water should never be jeopardized.
AUTHOR KEYWORDS: Chlorination; Drinking water; Genotoxic compounds; Humic substances; Identification; Organohalogenated
DOCUMENT TYPE: Article

12/10/18 SCOPUS Search by author and keywords
AUTHOR-NAME **(*snyder,*** AND ***s*** AND ***a*****) AND** TITLE-ABS-KEY **(*water* OR *non-target* OR *unknown* OR *suspect* OR *disinfection* OR *spectrometry*) gave 215 results.**

Zhang, A., Jia, A., Park, M., Li, Y., Snyder, S.A. Genotoxicity assay and potential byproduct identification during different UV-based water treatment processes (2019) Chemosphere, 217, pp. 176-182. DOI: 10.1016/j.chemosphere.2018.11.031.

AFFILIATIONS: State Key Laboratory of Pollution Control and Resource Reuse, Tongji University, Shanghai, 200092, China; School of Environmental Science and Engineering, Donghua University, Shanghai, 201620, China; Department of Chemical & Environmental Engineering, University of Arizona, Tucson, AZ 85721, United States.

ABSTRACT: ***Formation of genotoxic byproducts during different ultraviolet (UV) -related water/wastewater treatment processes (including medium pressure (MP) UV oxidation, LP UV oxidation, chlorination, biological activated carbon (BAC) treatment, H_2O_2 oxidation, and two or more combined processes) was investigated by Ames fluctuation test using Salmonella strains TA98 and***

TA100 with and without rat liver enzyme extract S9. Byproducts responsible for genotoxicity were identified. The results showed that MP UV can induce mutagenicity and LP UV treatment does not induce mutagenicity. H_2O_2 oxidation could degrade part of genotoxic compounds. Compared with chlorination, BAC treatment is more effective in removing genotoxicity. Mutagenicity was found mostly in samples tested with TA100 instead of TA98, especially with TA100 without S9, indicating that guanosine and/or cytosine adducts contribute to mutation or toxicological effects in MP UV treated samples. Potential genotoxic byproducts were selected, most of which were nitrogenous organic compounds with more than 10 carbon atoms. Nitrosamines and histidine were excluded from potential genotoxic candidates. The results could contribute to evaluation of mutagenicity of various UV-based water treatment processes. © 2018 Elsevier Ltd
AUTHOR KEYWORDS: Ames test; Genotoxic by-products; Genotoxicity; Medium pressure ultraviolet (MP UV) treatment; Nitrogenous organic compounds
DOCUMENT TYPE: Article

Sgroi, M., Anumol, T., Roccaro, P., Vagliasindi, F.G.A., Snyder, S.A. Modeling emerging contaminants breakthrough in packed bed adsorption columns by UV absorbance and fluorescing components of dissolved organic matter (2018) Water Research, 145, pp. 667-677. DOI: 10.1016/j.watres.2018.09.018.

AFFILIATIONS: Department of Civil Engineering and Architecture, University of Catania, Viale A. Doria 6, Catania, 95125, Italy; Department of Chemical and Environmental Engineering, University of Arizona, 1133 E. James E. Rogers Way, Tucson, AZ 85721, United States; Agilent Technologies Inc., 2850 Centerville Road, Wilmington, DE 19808, United States; Nanyang Technological University;, Nanyang Environment & Water Research Institute, 1 Cleantech Loop, CleanTech One, #06-08637141, Singapore.

ABSTRACT: ***This study investigated, using rapid small-scale column testing, the breakthrough of dissolved organic matter (DOM) and 11 emerging organic contaminants (EOCs) during granular activated carbon (GAC) filtration of different water qualities, including wastewater, surface water and synthetic water (riverine organic matter dissolved in deionized water). Fluorescing organic matter was better adsorbed than UV absorbance at 254 nm (UV254) and dissolved organic carbon (DOC) in all tested water. Furthermore, highest adsorption of DOM (in terms of DOC, UV254 and fluorescence) was observed during wastewater filtration. UV absorbing DOM had fast and similar breakthrough in surface water and synthetic water, whereas fluorescence breakthrough was very rapid only in synthetic water.*** PARAFAC modeling showed that different fluorescing components were differently adsorbed during GAC process. Particularly, fluorescing components with maxima intensity at higher excitation wavelengths, which are corresponding to humic-like fluorescence substances, were better removed than other components in all waters. As opposed to DOM, EOCs were better adsorbed during synthetic water filtration, whereas the fastest EOCs breakthrough was observed during filtration of wastewater, which was the water that determined the highest carbon fouling. Exception was represented by long-chained perfluoroalkylated substances (i.e., PFOA, PFDA and PFOS). Indeed, adsorption of these compounds resulted independent of water quality. In this study was also investigated the applicability of UV254 and fluorescing PARAFAC components to act as surrogates in predicting EOCs removal by GAC in different water matrices. Empirical linear correlation for the investigated EOCs were determined with UV254 and fluorescing components in all water qualities. However, fluorescence measurements resulted more sensitive than UV254 to predict EOC breakthrough during GAC adsorption. ***When the data from all water qualities was combined, good correlations between the microbial humic-like PARAFAC component and EOC removals were still observed and they resulted independent of water quality if considering only real water matrices (wastewater and surface water). On the contrary, correlations between EOC removals and UV254 removals were independent of water quality when combining data of surface waters and synthetic water, but a different correlation model was needed to predict EOCs breakthrough in wastewater.*** © 2018

AUTHOR KEYWORDS: Fluorescence EEM; Granular activated carbon; PARAFAC; PFAS; Pharmaceutical and personal care products; Real-time monitoring
DOCUMENT TYPE: Article

Bieber, S., Snyder, S.A., Dagnino, S., Rauch-Williams, T., Drewes, J.E. Management strategies for trace organic chemicals in water – A review of international approaches (2018) Chemosphere, 195, pp. 410-426. DOI: 10.1016/j.chemosphere.2017.12.100.

AFFILIATIONS: Chair of Urban Water Systems Engineering, Technical University of Munich, Garching, Germany; Department of Chemical and Environmental Engineering, University of Arizona, Tucson, AZ, United States; Carollo Engineers, Broomfield, CO, United States.

ABSTRACT: To ensure an appropriate management of potential health risks and uncertainties from the release of trace organic chemicals (TOrCs) into the aqueous environment, many countries have evaluated and implemented strategies to manage TOrCs. ***The aim of this study was to evaluate existing management strategies for TOrCs in different countries to derive and compare underlying core principles and paradigms and to develop suggestions for more holistic management strategies to protect the environment and drinking water supplies from the discharge of undesired TOrCs.*** The strategies in different industrial countries were summarized and subsequently compared with regards to three particular questions: ***1) Do the approaches different countries have implemented manage all or only specific portions of the universe of chemicals; 2) What implementation and compliance strategies are used to manage aquatic and human health risk and what are their pros and cons; and 3) How are site-specific watershed differences being addressed?*** While management strategies of the different countries target similar TOrCs, the programs differ in several important aspects, including underlying principles, the balance between aquatic or human health protection, ***implementation methods***, and financing mechanisms used to fund regulatory programs. © 2017 Elsevier Ltd
AUTHOR KEYWORDS: Chemicals of emerging concern; Environmental health; Human health; Management strategies; Trace organic chemicals; Water regulations
DOCUMENT TYPE: Review

Park, M., Snyder, S.A. Sample handling and data processing for fluorescent excitation-emission matrix (EEM) of dissolved organic matter (DOM) (2018) Chemosphere, 193, pp. 530-537. Cited three times. DOI: 10.1016/j.chemosphere.2017.11.069.

AFFILIATIONS: Department of Chemical & Environmental Engineering, University of Arizona, 1133 E James E Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States; National University of Singapore Environmental Research Institute, T-Lab Building #02-01, 5A Engineering Drive, Singapore, 117411, Singapore.

ABSTRACT: ***In environmental engineering and science, fluorescent excitation-emission matrix (EEM) has increasingly been utilized to characterize chromophoric dissolved organic matter (CDOM). This study aims to delineate EEM data processing, including calculation of total fluorescence (TF) which is an emerging water quality parameter often used as a surrogate for micropollutant removal by advanced water treatment processes.*** In addition, sample handling procedures such as storage, use of preservatives, and oxidant quenching agents were evaluated. In this study, three antimicrobial preservatives were tested: sodium azide, sodium omadine, and thymol. All the tested preservatives altered optical properties of samples, and were therefore not suitable for the preservation of EEM samples. Without preservative, storage of samples at 4°C maintained TF within 7.5% of its original value for 21 days, while TF of samples stored at the room temperature more drastically changed (up to 15%). The impacts of three oxidant quenching agents including ascorbic acid, sodium bisulfite, and sodium thiosulfate on EEM were also tested. ***Among the quenching agents, sodium bisulfite was found to be suitable since it little influenced optical properties of samples while the other two were not favorable***

due to interference. We also scrutinized the use of TF as surrogate to monitor micropollutant rejection by nanofiltration membrane. © 2017 Elsevier Ltd
AUTHOR KEYWORDS: Chromophoric dissolved organic matter; Excitation-emission matrix (EEM); Fluorescence spectroscopy; Nanofiltration (NF); Sodium bisulfite
DOCUMENT TYPE: Article

Sgroi, M., Vagliasindi, F.G.A., Snyder, S.A., Roccaro, P. N-Nitrosodimethylamine (NDMA) and its precursors in water and wastewater: A review on formation and removal (2018) Chemosphere, 191, pp. 685-703. Cited eight times. DOI: 10.1016/j.chemosphere.2017.10.089.

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ABSTRACT: This review summarizes major findings over the last decade related to N-Nitrosodimethylamine (NDMA) in water and wastewater. In particular, the review is focused on the removal of NDMA and of its precursors by conventional and advanced water and wastewater treatment processes. New information regarding formation mechanisms and precursors are discussed as well. ***NDMA precursors are generally of anthropogenic origin and their main source in water have been recognized to be wastewater discharges. Chloramination is the most common process that results in formation of NDMA during water and wastewater treatment. However, ozonation of wastewater or highly contaminated surface water can also generate significant levels of NDMA.*** Thus, NDMA formation control and remediation has become of increasing interest, particularly during treatment of wastewater-impacted water and during potable reuse application. NDMA formation has also been associated with the use of quaternary amine-based coagulants and anion exchange resins. UV photolysis with UV fluence far higher than typical disinfection doses is generally considered the most efficient technology for NDMA mitigation. However, recent studies on the optimization of biological processes offer a potentially lower-energy solution. Options for NDMA control include attenuation of precursor materials through physical removal, biological treatment, and/or deactivation by application of oxidants. Nevertheless, NDMA precursor identification and removal can be challenging and additional research and optimization is needed. ***As municipal wastewater becomes increasingly used as a source water for drinking, NDMA formation and mitigation strategies will become increasingly more important. The following review provides a summary of the most recent information available.*** © 2017 Elsevier Ltd
AUTHOR KEYWORDS: Disinfection by-products; Drinking water; Emerging contaminants; Nitrosamines; Potable reuse; Water treatment
DOCUMENT TYPE: Review

Yan, S., Yao, B., Lian, L., Lu, X., Snyder, S.A., Li, R., Song, W. Development of Fluorescence Surrogates to Predict the Photochemical Transformation of Pharmaceuticals in Wastewater Effluents (2017) Environmental Science and Technology, 51 (5), pp. 2738-2747. Cited eight times. DOI: 10.1021/acs.est.6b05251.

AFFILIATIONS: Department of Environmental Science and Engineering, Fudan University, Shanghai, 200433, China; Department of Chemical and Environmental Engineering, University of Arizona, Tucson, AZ 85721, United States.

ABSTRACT: The photochemical transformation of pharmaceutical and personal care products (PPCPs) in wastewater effluents is an emerging concern for environmental scientists. In the current study, the photodegradation of 29 PPCPs was examined in effluents under simulated solar irradiation. Direct photodegradation, triplet state effluent organic matter (3EfOM∗)-mediated and hydroxyl radical (HO•)-

mediated degradation are three major pathways in the removal process. ***With the photodegradation of trace levels of PPCPs, the excitation-emission matrix (EEM) fluorescence intensities of the effluents were also gradually reduced. Therefore, fluorescence peaks have been identified, for the first time, as appropriate surrogates to assess the photodegradation of PPCPs.*** The humic-like fluorescence peak is linked to direct photolysis-labile PPCPs, such as naproxen, ronidazole, diclofenac, ornidazole, tinidazole, chloramphenicol, flumequine, ciprofloxacin, methadone, and dimetridazole. The tyrosine-like EEM peak is associated with HO•/CO3•--labile PPCPs, such as trimethoprim, ibuprofen, gemfibrozil, atenolol, carbamazepine, and cephalexin. The tryptophan-like peak is associated with 3EfOM∗-labile PPCPs, such as clenbuterol, metoprolol, venlafaxine, bisphenol A, propranolol, ractopamine, salbutamol, roxithromycin, clarithromycin, azithromycin, famotidine, terbutaline, and erythromycin. ***The reduction in EEM fluorescence correlates well with the removal of PPCPs, allowing a model to be constructed. The solar-driven removal of EEM fluorescence was applied to predict the attenuation of 11 PPCPs in five field samples. A close correlation between the predicted results and the experimental results suggests that fluorescence may be a suitable surrogate for monitoring the solar-driven photodegradation of PPCPs in effluents.***
DOCUMENT TYPE: Article

Wu, S., Anumol, T., Gandhi, J., Snyder, S.A. Analysis of haloacetic acids, bromate, and dalapon in natural waters by ion chromatography – tandem mass spectrometry (2017) Journal of Chromatography A, 1487, pp. 100-107. Cited one time. DOI: 10.1016/j.chroma.2017.01.006.

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ABSTRACT: ***The addition of oxidants for disinfecting water can lead to the formation of potentially carcinogenic compounds referred to as disinfection byproducts (DBPs). Haloacetic acids (HAAs) are one of the most widely detected DBPs in US water utilities and some of them are regulated by the U.S. Environmental Protection Agency (U.S. EPA). The present study developed a method to analyze all the compounds in the U.S. EPA method 557 (nine HAAs, bromate and dalapon) plus four potentially more toxic iodinated HAAs in water by coupling ion chromatography with tandem mass spectrometry (IC–MS/MS). This aqueous direct injection method has significant advantages over traditional GC methods, which require a derivatization and sample extraction that are laborious, time-consuming, and can negatively impact reproducibility.*** The method developed in this study requires half the time of the current U.S. EPA method 557 on IC–MS/MS while including more compounds and achieving sub-μg/L level method detection limits (MDLs) for all 15 target analytes. The single laboratory lowest concentration minimum reporting level (LCMRL) has also been determined in reagent water, which ranged from ***0.011 to 0.62 μg/L for the analytes. The mean recoveries of the analytes during matrix spike recovery tests were 77-125% in finished drinking water and 81-112% in surface water.*** This method was then applied to untreated, chlorinated, and chloraminated groundwater and surface water samples. Bromate and nine HAAs were detected at different levels in some of these samples. © 2017 Elsevier B.V.
AUTHOR KEYWORDS: Bromate; Dalapon; Haloacetic acids; Ion-chromatography; Tandem mass spectrometry
DOCUMENT TYPE: Article

Sgroi, M., Roccaro, P., Korshin, G.V., Greco, V., Sciuto, S., Anumol, T., Snyder, S.A., Vagliasindi, F.G.A. Use of fluorescence EEM to monitor the removal of emerging contaminants in full scale wastewater treatment plants (2017) Journal of Hazardous Materials, 323, pp. 367-376. Cited 25 times. DOI: 10.1016/j.jhazmat.2016.05.035.

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ABSTRACT: ***This study investigated the applicability of different techniques for fluorescence excitation/emission matrices data interpretations, including peak-picking method, fluorescence regional integration and PARAFAC modelling, to act as surrogates in predicting emerging trace organic compounds (ETOrCs) removal during conventional wastewater treatments that usually comprise primary and secondary treatments. Results showed that fluorescence indexes developed using alternative methodologies but indicative of a same dissolved organic matter component resulted in similar predictions of the removal of the target compounds.*** The peak index defined by the excitation/emission wavelength positions (λex/λem) 225/290 nm and related to aromatic proteins and tyrosine-like fluorescence was determined to be a particularly suitable surrogate for monitoring ETOrCs that had very high removal rates (average removal >70%) (i.e., triclosan, caffeine and ibuprofen). The peak index defined by λex/λem = 245/440 nm and the PARAFAC component with wavelength of the maxima λex/λem = 245, 350/450, both identified as humic-like fluorescence, were found remarkably well correlated with ETOrCs such as atenolol, naproxen and gemfibrozil that were moderately removed (51-70% average removal). Finally, the PARAFAC component with wavelength of the maxima λex/λem = <240, 315/380 identified as microbial humic-like fluorescence was the only index correlated with the removal of the antibiotic trimethoprim (average removal 68%). © 2016 Elsevier B.V.
AUTHOR KEYWORDS: Dissolved organic matter; Fluorescence regional integration; Parafac; Personal care products; Pharmaceuticals
DOCUMENT TYPE: Article

Park, M., Anumol, T., Daniels, K.D., Wu, S., Ziska, A.D., Snyder, S.A. Predicting trace organic compound attenuation by ozone oxidation: Development of indicator and surrogate models (2017) Water Research, 119, pp. 21-32. Cited nine times. DOI: 10.1016/j.watres.2017.04.024.

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ABSTRACT: Ozone oxidation has been demonstrated to be an effective treatment process for the attenuation of trace organic compounds (TOrCs); however, predicting TOrC attenuation by ozone processes is challenging in wastewaters. Since ozone is rapidly consumed, determining the exposure times of ozone and hydroxyl radical proves to be difficult. ***As direct potable reuse schemes continue to gain traction, there is an increasing need for the development of real-time monitoring strategies for TOrC abatement in ozone oxidation processes. Hence, this study is primarily aimed at developing indicator and surrogate models for the prediction of TOrC attenuation by ozone oxidation.*** To this end, the second-order kinetic equations with a second-phase Rct value (ratio of hydroxyl radical exposure to molecular ozone exposure) were used to calculate comparative kinetics of TOrC attenuation and the reduction of indicator and spectroscopic surrogate parameters, including UV absorbance at 254 nm (UVA254) and total fluorescence (TF). ***The developed indicator model using meprobamate as an indicator compound and the surrogate models with UVA254 and TF exhibited good predictive power for the attenuation of 13 kinetically distinct TOrCs in five filtered and unfiltered wastewater effluents (R2 values > 0.8). This study is intended to help provide a guideline for the implementation of indicator/surrogate models for real-time monitoring of TOrC abatement with ozone processes and integrate them into a regulatory framework in water reuse.*** © 2017 Elsevier Ltd

AUTHOR KEYWORDS: Indicator; Kinetics; Micropollutant; Ozone; Surrogate
DOCUMENT TYPE: Article

Goh, S.X.L., Duarah, A., Zhang, L., Snyder, S.A., Lee, H.K. Online solid phase extraction with liquid chromatography – tandem mass spectrometry for determination of estrogens and glucocorticoids in water (2016) Journal of Chromatography A, 1465, pp. 9-19. Cited 10 times. DOI: 10.1016/j.chroma.2016.08.040.

AFFILIATIONS: Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore, 117543, Singapore; NUS Environmental Research Institute, National University of Singapore, T-Lab Building #02-01, 5A Engineering Drive 1, Singapore, 117411, Singapore; Water Quality Office, Public Utilities Board, 82 Toh Guan Road East, Singapore, 608576, Singapore; Department of Chemical & Environmental Engineering, University of Arizona, 1133 E James E Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States.

ABSTRACT: ***The present work describes the development of a novel fully automated online solid phase extraction (SPE) coupled with high performance liquid chromatography-tandem mass spectrometry (LC–MS/MS) using negative electrospray ionization (ESI) for the simultaneous determination of six estrogens and six glucocorticoids in water***. ***Filtered water samples (5 mL) were preconcentrated on a HyperSep™ Retain PEP SPE cartridge, eluted in back-flush mode, and separated on an LC column before analysis by tandem mass spectrometry. The total analysis time for each sample was 17 min.*** Different experimental parameters such as the type of online SPE cartridge, loading flow rate, and composition of methanol in the loading phase were optimized. The intra-day repeatability of method ranged from 1.48 to 9.68% for all analytes, and the inter-day reproducibility ranged from 2.03 to 8.63% for all analytes, except for dexamethasone at 11.95%. These were calculated based on the peak area responses of the targeted analytes spiked at 50 ng/L in ultrapure water. ***The method also showed good linearity from 1 to 100 ng/L, with the limits of detection (LODs) ranging from 0.16 to 2.14 ng/L.*** The proposed method was applied to the analysis of municipal wastewater. This fully automated online SPE extraction coupled with LC–MS/MS method is effective and reliable to measure estrogens and glucocorticoids simultaneously due to its high throughput, relatively low solvent consumption, reusability of the online SPE cartridge, and reduction of manual labor. © 2016 Elsevier B.V.
AUTHOR KEYWORDS: Estrogens; Glucocorticoids; LC–MS/MS; Online solid phase extraction; Steroid hormones; Water
DOCUMENT TYPE: Article

Ziska, A.D., Park, M., Anumol, T., Snyder, S.A. Predicting trace organic compound attenuation with spectroscopic parameters in powdered activated carbon processes (2016) Chemosphere, 156, pp. 163-171. Cited 10 times. DOI: 10.1016/j.chemosphere.2016.04.073.

AFFILIATIONS: Department of Chemical and Environmental Engineering, University of Arizona, 1133 E James E Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States; Agilent Technologies Inc., 2850 Centerville Road, Wilmington, DE 19808, United States.

ABSTRACT: The removal of trace organic compounds (TOrCs) is of growing interest in water research and society. Powdered activated carbon (PAC) has been proven to be an effective method of removal for TOrCs in water, with the degree of effectiveness depending on dosage, contact time, and activated carbon type. In this study, the attenuation of TOrCs in three different secondary wastewater effluents using four PAC materials was studied in order to elucidate the effectiveness and efficacy of PAC for TOrC removal. With the notable exception of hydrochlorothiazide, all 14 TOrC indicators tested in this study exhibited a positive correlation of removal rate with their log Dow values, demonstrating that the main adsorption mechanism was hydrophobic interaction. As a predictive model, the modified Chick-Watson model, often used for the prediction of microorganism inactivation by disinfectants, was applied. The

applied model exhibited good predictive power for TOrC attenuation by PAC in wastewater. ***In addition, surrogate models based upon spectroscopic measurements including UV absorbance at 254 nm and total fluorescence were applied to predict TOrC removal by PAC.*** The surrogate model was found to provide an excellent prediction of TOrC attenuation for all combinations of water quality and PAC type included in this study. ***The success of spectrometric parameters as surrogates in predicting TOrC attenuation by PAC are particularly useful because of their potential application in real-time on-line sensor monitoring and process control at full-scale water treatment plants, which could lead to significantly reduced operator response times and PAC operational optimization.*** © 2016 Elsevier Ltd.
AUTHOR KEYWORDS: Indicator; Modeling; Powdered activated carbon (PAC); Surrogate; Trace organic compounds (TOrC); UV absorbance and fluorescence; Wastewater; Water reuse
DOCUMENT TYPE: Article

Maruya, K.A., Dodder, N.G., Mehinto, A.C., Denslow, N.D., Schlenk, D., Snyder, S.A., Weisberg, S.B. A tiered, integrated biological and chemical monitoring framework for contaminants of emerging concern in aquatic ecosystems (2016) Integrated Environmental Assessment and Management, 12 (3), pp. 540-547. Cited 14 times. DOI: 10.1002/ieam.1702.

AFFILIATIONS: Southern California Coastal Water Research Project Authority, Costa Mesa, CA, United States; Department of Physiological Sciences, Center for Environmental and Human Toxicology, University of Florida, Gainesville, FL, United States; Department of Environmental Sciences, University of California Riverside, Riverside, CA, United States; Department of Chemical and Environmental Engineering, University of Arizona, Tucson, AZ, United States.

ABSTRACT: The chemical-specific risk-based paradigm that informs monitoring and assessment of environmental contaminants does not apply well to the many thousands of new chemicals that are being introduced into ambient receiving waters. We propose a tiered framework that incorporates bioanalytical screening tools and diagnostic nontargeted chemical analysis to more effectively monitor for contaminants of emerging concern (CECs). ***The framework is based on a comprehensive battery of in vitro bioassays to first screen for a broad spectrum of CECs and nontargeted analytical methods to identify bioactive contaminants missed by the currently favored targeted analyses.*** Water quality managers in California have embraced this strategy with plans to further develop and test this framework in regional and statewide pilot studies on waterbodies that receive discharge from municipal wastewater treatment plants and stormwater runoff. In addition to directly informing decisions, the data obtained using this framework can be used to construct and validate models that better predict CEC occurrence and toxicity. The adaptive interplay among screening results, diagnostic assessment and predictive modeling will allow managers to make decisions based on the most current and relevant information, instead of extrapolating from parameters with questionable linkage to CEC impacts. Integr Environ Assess Manag 2016;12:540-547. © 2015 SETAC. © 2015 SETAC
AUTHOR KEYWORDS: Aquatic ecosystems; Bioanalytical tools; Contaminants of emerging concern (CECs); Monitoring; Nontargeted chemical analysis
DOCUMENT TYPE: Article

Anumol, T., Dagnino, S., Vandervort, D.R., Snyder, S.A. Transformation of Polyfluorinated compounds in natural waters by advanced oxidation processes (2016) Chemosphere, 144, pp. 1780-1787. Cited 13 times. DOI: 10.1016/j.chemosphere.2015.10.070.

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ABSTRACT: ***The presence of perfluorocarboxylic acids (PFCAs) in source and finished drinking waters is a concern with studies showing bioaccumulation and adverse toxicological effects in wildlife and potentially humans.*** Per/Polyfluoroalkyl substances (PFAS) such as fluorotelomer alcohols have been

identified as precursors for PFCAs in biological pathways. In this study, we investigated the fate of 6:2 and 8:2 homologues of the fluorotelomer unsaturated carboxylic acids (FTUCAs) during advanced oxidation process (AOPs). Results showed 6:2 FTUCA and 8:2 FTUCA transformed into 6-C PFCA (PFHxA) and 8-C PFCA (PFOA) respectively with very little other PFCA formation for all AOPs. The degradation of 6:2 FTUCA and 8:2 FTUCA was greater in the GW compared to SW for the ozone processes but similar for UV/H2O2. The formation of n-C PFCA followed O3>O3/H_2O_2 at same dose and UV/H_2O_2 had much lower formation at the doses tested. ***Non-targeted analysis with the LC-MS-qTOF indicated the production of other PFCAs which contribute to the total mass balance, although no intermediate product was discovered indicating a rapid and direct transformation from the FTUCAs to the PFCAs and/or significant volatilization of intermediates.*** With the use of AOPs essential to water reuse treatment schemes, this work raises concerns over the risk of potential formation of PFCAs in the treatment and their adverse health effects in finished drinking water. © 2015 Elsevier Ltd.
AUTHOR KEYWORDS: Fluorotelomer acids; Ozone; Perfluorinated compounds; Perfluoroalkyl carboxylic acids; UV/H2O2
DOCUMENT TYPE: Article

Sgroi, M., Roccaro, P., Oelker, G., Snyder, S.A. N-nitrosodimethylamine (NDMA) formation during ozonation of wastewater and water treatment polymers (2016) Chemosphere, 144, pp. 1618-1623. Cited 18 times. DOI: 10.1016/j.chemosphere.2015.10.023.

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ABSTRACT: N-Nitrosodimethylamine (NDMA) formation by ozonation was investigated in the effluents of four different wastewater treatment plants destined for alternative reuse. ***Very high levels of NDMA formation were observed in wastewaters from treatment plants nonoperating with biological nitrogen removal.*** Selected experiments showed that hydroxyl radical did not have a significant role in NDMA formation during ozonation of wastewater. Furthermore, ozonation of three different polymers used for water treatment, including polyDADMAC, anionic polyacrylamide, and cationic polyacrylamide, spiked in wastewater did not increase the NDMA formation. Effluent organic matter (EfOM) likely reduced the availability of ozone in water able to react with polymers and quenched the produced ·OH radicals which limited polymer degradation and subsequent NDMA production. ***Excellent correlations were observed between NDMA formation, UV absorbance at 254 nm, and total fluorescence reduction. These data provide evidence that UV and fluorescence surrogates could be used for monitoring and/or controlling NDMA formation during ozonation.*** © 2015 Elsevier Ltd.
AUTHOR KEYWORDS: Fluorescence; Hydroxyl radical; Nitrification; Polyacrylamide; PolyDADMAC; UV absorbance
DOCUMENT TYPE: Article

Sgroi, M., Roccaro, P., Oelker, G.L., Snyder, S.A. N-nitrosodimethylamine (NDMA) formation at an indirect potable reuse facility (2015) Water Research, 70, pp. 174-183. Cited 26 times. DOI: 10.1016/j.watres.2014.11.051.

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ABSTRACT: Full-scale experiments to evaluate N-nitrosodimethylamine (NDMA) formation and attenuation were performed within an advanced indirect potable reuse (IPR) treatment system, which includes, sequentially: chloramination for membrane fouling control, microfiltration (MF), reverse osmosis (RO), ultraviolet irradiation with hydrogen peroxide (UV/Hinf2/infOinf2/inf), final chloramination, and pH stabilization. ***Results of the study demonstrate that while RO does effectively remove the vast majority of NDMA precursors, RO permeate can still contain significant concentrations of NDMA precursors resulting in additional NDMA formation during chloramination.*** Thus, it is possible for this advanced treatment system to produce water with NDMA levels higher than regional requirements for potable applications (10ng/L). The presence of Hinf2/infOinf2/inf during UV oxidation reduced NDMA photolysis efficiency and increased NDMA formation (~22ng/L) during the secondary chloramination and lime stabilization. This is likely due to formation of UV/Hinf2/infOinf2/inf degradation by-products with higher NDMA formation rate than the parent compounds. However, this effect was diminished with higher UV doses. Bench-scale experiments confirmed an enhanced NDMA formation during chloramination after UV/Hinf2/infOinf2/inf treatment of dimethylformamide, a compound detected in RO permeate and used as model precursor in this study. The effect of pre-ozonation for membrane fouling control on NDMA formation was also evaluated at pilot- (ozone-MF-RO) and bench-scale. ***Relatively large NDMA formation (117-227ng/L) occurred through ozone application that was dose dependent, whereas chloramination under typical dosages and contact times of IPR systems resulted in only a relatively small increase of NDMA (~20ng/L). Thus, this research shows that NDMA formation within a potable water reuse facility can be challenging and must be carefully evaluated and controlled.*** © 2014 Elsevier Ltd.
AUTHOR KEYWORDS: Chloramination; Dimethylformamide; Hydrogen peroxide; Ozone; Reverse osmosis; UV
DOCUMENT TYPE: Article

Mehinto, A.C., Jia, A., Snyder, S.A., Jayasinghe, B.S., Denslow, N.D., Crago, J., Schlenk, D., Menzie, C., Westerheide, S.D., Leusch, F.D.L., Maruya, K.A. Interlaboratory comparison of in vitro bioassays for screening of endocrine active chemicals in recycled water (2015) Water Research, 83, pp. 303-309.
Cited 24 times. DOI: 10.1016/j.watres.2015.06.050.

AFFILIATIONS: Southern California Coastal Water Research Project Authority, Costa Mesa, CA 92626, United States; Department of Chemical and Environmental Engineering, University of Arizona, Tucson, AZ 85721, United States; Center for Environmental and Human Toxicology, Department of Physiological Sciences, University of Florida, Gainesville, FL 32611, United States; Department of Environmental Sciences, University of California Riverside, Riverside, CA 92521, United States; Department of Cell Biology, Microbiology and Molecular Biology, University of South Florida, Tampa, FL 33620, United States; Smart Water Research Centre, School of Environment, Griffith University, Southport, QLD 4222, Australia.

ABSTRACT: Invitro bioassays have shown promise as water quality monitoring tools. In this study, four commercially available in vitro bioassays (GeneBLAzer® androgen receptor (AR), estrogen receptor-alpha (ER), glucocorticoid receptor (GR) and progesterone receptor (PR) assays) were adapted to screen for endocrine active chemicals in samples from two recycled water plants. The standardized protocols were used in an interlaboratory comparison exercise to evaluate the reproducibility of in vitro bioassay results. Key performance criteria were successfully achieved, including low background response, standardized calibration parameters and high intra-laboratory precision. Only two datasets were excluded due to poor calibration performance. Good interlaboratory reproducibility was observed for GR bioassay, with 16-26% variability among the laboratories. ER and PR bioactivity was measured near

the bioassay limit of detection and showed more variability (21-54%), although interlaboratory agreement remained comparable to that of conventional analytical methods. AR bioassay showed no activity for any of the samples analyzed. Our results indicate that ER, GR and PR, were capable of screening for different water quality, i.e., the highest bioactivity was observed in the plant influent, which also contained the highest concentrations of endocrine active chemicals measured by LC-MS/MS. After advanced treatment (e.g., reverse osmosis), bioactivity and target chemical concentrations were both below limits of detection. ***Comparison of bioassay and chemical equivalent concentrations revealed that targeted chemicals accounted for ≤5% of bioassay activity, suggesting that detection limits by LC-MS/MS for some chemicals were insufficient and/or other bioactive compounds were present in these samples. Our study demonstrated that in vitro bioassays responses were reproducible, and can provide information to complement conventional analytical methods for a more comprehensive water quality assessment.*** © 2015 Elsevier Ltd.
AUTHOR KEYWORDS: Bioanalytical screening; Endocrine disrupting chemicals; Recycled water; Standardization; Water quality
DOCUMENT TYPE: Article

Yu, H.-W., Anumol, T., Park, M., Pepper, I., Scheideler, J., Snyder, S.A. On-line sensor monitoring for chemical contaminant attenuation during UV/H<inf>2</inf>O<inf>2</inf> advanced oxidation process (2015) Water Research, 81, pp. 250-260. Cited 22 times.DOI: 10.1016/j.watres.2015.05.064.

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ABSTRACT: A combination of surrogate parameters and indicator compounds were measured to predict the removal efficiency of trace organic compounds (TOrCs) using low pressure (LP)-UV/H<inf>2</inf>O<inf>2</inf> advanced oxidation process (AOP), engaged with online sensor-based monitoring system. Thirty-nine TOrCs were evaluated in two distinct secondary wastewater effluents in terms of estimated photochemical reactivity, as a function of the rate constants of UV direct photolysis (k<inf>UV</inf>) and hydroxyl radical (OH) oxidation (k<inf>OH</inf>). The selected 18 TOrCs were classified into three groups that served as indicator compounds: Group 1 for photo-susceptible TOrCs but with minor degradation by OH oxidation (diclofenac, fluoxetine, iohexol, iopamidol, iopromide, simazine and sulfamethoxazole); Group 2 for TOrCs susceptible to both direct photolysis and OH oxidation (benzotriazole, diphenhydramine, ibuprofen, naproxen and sucralose); and Group 3 for photo-resistant TOrCs showing dominant degradation by OH oxidation (atenolol, carbamazepine, DEET, gemfibrozil, primidone and trimethoprim). ***The results indicate that TOC (optical-based measurement), UVA<inf>254</inf> or UVT<inf>254</inf> (UV absorbance or transmittance at 254 nm), and total fluorescence can all be used as suitable on-line organic surrogate parameters to predict the attenuation of TOrCs. Furthermore, the automated real-time monitoring via on-line surrogate sensors and equipped with the developed degradation profiles between sensor response and a group of TOrCs removal can provide a diagnostic tool for process control during advanced treatment of reclaimed waters.*** © 2015 Elsevier Ltd.
AUTHOR KEYWORDS: Indicator; On-line sensor; Surrogate; Trace organic compound (TOrC); UV/H<inf>2</inf>O<inf>2</inf>; Water reuse
DOCUMENT TYPE: Article

Jia, A., Escher, B.I., Leusch, F.D.L., Tang, J.Y.M., Prochazka, E., Dong, B., Snyder, E.M., Snyder, S.A. In vitro bioassays to evaluate complex chemical mixtures in recycled water (2015) Water Research, 80, pp. 1-11. Cited 33 times. DOI: 10.1016/j.watres.2015.05.020.

AFFILIATIONS: University of Arizona, 1133 E. James E. Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States; The University of Queensland, National Research Centre for Environmental Toxicology (Entox), 39 Kessels Rd, Brisbane, QLD 4108, Australia; UFZ - Helmholtz Centre for Environmental Research, Cell Toxicology, Leipzig, Germany; Eberhard Karls University Tübingen, Center for Applied Geosciences, Environmental Toxicology, Tübingen, Germany; Griffith University, Smart Water Research Centre, School of Environment, Edmund Rice Dr., Southport, QLD 4222, Australia; National University of Singapore, NUS Environmental Research Institute (NERI), 5A Engineering Drive 1, T-Lab Building, #02-01117411, Singapore.

ABSTRACT: With burgeoning population and diminishing availability of freshwater resources, the world continues to expand the use of alternative water resources for drinking, and the quality of these sources has been a great concern for the public as well as public health professionals. In vitro bioassays are increasingly being used to enable rapid, relatively inexpensive toxicity screening that can be used in conjunction with analytical chemistry data to evaluate water quality and the effectiveness of water treatment. ***In this study, a comprehensive bioassay battery consisting of 36 bioassays covering 18 biological endpoints was applied to screen the bioactivity of waters of varying qualities with parallel treatments.*** Samples include wastewater effluent, ultraviolet light (UV) and/or ozone advanced oxidation processed (AOP) ***recycled water***, and infiltrated recycled groundwater. Based on assay sensitivity and detection frequency in the samples, several endpoints were highlighted in the battery, including assays for genotoxicity, mutagenicity, estrogenic activity, glucocorticoid activity, arylhydrocarbon receptor activity, oxidative stress response, and cytotoxicity. Attenuation of bioactivity was found to be dependent on the treatment process and bioassay endpoint. For instance, ozone technology significantly removed oxidative stress activity, while UV based technologies were most efficient for the attenuation of glucocorticoid activity. Chlorination partially attenuated genotoxicity and greatly decreased herbicidal activity, while groundwater infiltration efficiently attenuated most of the evaluated bioactivity with the exception of genotoxicity. ***In some cases, bioactivity (e.g., mutagenicity, genotoxicity, and arylhydrocarbon receptor) increased following water treatment, indicating that transformation products of water treatment may be a concern.*** Furthermore, several types of bioassays with the same endpoint were compared in this study, which could help guide the selection of optimized methods in future studies. Overall, ***this research indicates that a battery of bioassays can be used to support decision-making on the application of advanced water treatment processes for removal of bioactivity.*** © 2015 Elsevier Ltd.
AUTHOR KEYWORDS: Advanced oxidation process; Bioassay; In vitro; Recycled water; Toxicity; Water treatment
DOCUMENT TYPE: Article

Paranychianakis, N.V., Salgot, M., Snyder, S.A., Angelakis, A.N. Water reuse in EU states: Necessity for uniform criteria to mitigate human and environmental risks (2015) Critical Reviews in Environmental Science and Technology, 45 (13), pp. 1409-1468. Cited 39 times. DOI: 10.1080/10643389.2014.955629.

AFFILIATIONS: School of Environmental Engineering, Technical University of Crete, Chania, Greece; Soil Science Laboratory, Facultat de Farmàcia, Universitat de Barcelona, Barcelona, Spain; Department of Chemical and Environmental Engineering, University of Arizona, Tucson, AZ, United States; NUS Environmental Research Institute, National University of Singapore, Singapore; Institute of Iraklion, National Foundation for Agricultural Research (N.AG.RE.F.), Iraklion, Greece.

ABSTRACT: ***Water quality criteria are an indispensable part of water reuse projects aiming to ensure the protection of public health and the environment. In addition, criteria can affect the development, public acceptance, and economic viability of water reuse projects. Currently no uniform criteria exist, but they diverge, often greatly, between countries and states.*** The authors briefly present the evolution of reuse criteria worldwide and discuss emerging issues related to ecological and public health risks that have not addressed adequately in existing criteria. They specifically focus on European Union (EU) countries and present their water reuse status based on the published data and the existing (or nonexisting) reuse frameworks. Data gathered from public agencies reveal a high potential for water reuse in the EU that could potentially contribute to ensuring that fresh water is available for all sectors and to protect the environment, but it has not expanded at the expected rates. ***The lack of water reuse criteria was thought as the most important cause for this delay. Lasting recent years, however, several countries, particularly those located in the Mediterranean basin, established water reuse criteria.*** Similarities and differences as well as potential benefits and drawbacks of these criteria are discussed and interpreted with these of the other world. ***An important conclusion is that the criteria enacted in Greece, Italy, and Spain will probably prevent the development of water reuse projects and increase the costs. Moreover, major challenges, the future views, and the necessity for establishing common regulations for water reuse at an EU level are considered.***
AUTHOR KEYWORDS: effluent reuse; guidelines; health risks; recycled water; regulations; wastewater
DOCUMENT TYPE: Review

Anumol, T., Sgroi, M., Park, M., Roccaro, P., Snyder, S.A. Predicting trace organic compound breakthrough in granular activated carbon using fluorescence and UV absorbance as surrogates (2015) Water Research, 76, pp. 76-87. Cited 49 times. DOI: 10.1016/j.watres.2015.02.019.

AFFILIATIONS: Department of Chemical and Environmental Engineering, University of Arizona, 1133 E James E Rogers Way, Tucson, AZ 85721, United States; Department of Civil Engineering and Architecture, University of Catania, Viale A. Doria 6, Catania, 95125, Italy; National University of Singapore, NUS Environmental Research Institute (NERI), 5A Engineering Drive 1 T-Lab Building #02-01, Singapore, 117411, Singapore.

ABSTRACT: ***This study investigated the applicability of bulk organic parameters like dissolved organic carbon (DOC), UV absorbance at 254nm (UV254), and total fluorescence (TF) to act as surrogates in predicting trace organic compound (TOrC) removal by granular activated carbon in water reuse applications.*** Using rapid small-scale column testing, empirical linear correlations for 13 TOrCs were determined with DOC, UV254, and TF in four wastewater effluents. Linear correlations (R2>0.7) were obtained for eight TOrCs in each water quality in the UV254 model, while 10 TOrCs had R2>0.7 in the TF model. Conversely, DOC was shown to be a poor surrogate for TOrC breakthrough prediction. When the data from all four water qualities was combined, good linear correlations were still obtained with TF having higher R2 than UV254 especially for TOrCs with log Dow>1. Excellent linear relationship (R2>0.9) between log Dow and the removal of TOrC at 0% surrogate removal (y-intercept) were obtained for the five neutral TOrCs tested in this study. Positively charged TOrCs had enhanced removals due to electrostatic interactions with negatively charged GAC that caused them to deviate from removals that would be expected with their log Dow. Application of the empirical linear correlation models to full-scale samples provided good results for six of seven TOrCs (except meprobamate) tested when comparing predicted TOrC removal by UV254 and TF with actual removals for GAC in all the five samples tested. ***Surrogate predictions using UV254 and TF provide valuable tools for rapid or on-line monitoring of GAC performance and can result in cost savings by extended GAC run times as compared to using DOC breakthrough to trigger regeneration or replacement.*** © 2015 Elsevier Ltd.
AUTHOR KEYWORDS: Adsorption; Granular activated carbon; PFC; Pharmaceuticals; Real time

monitoring; Trace organic compounds
DOCUMENT TYPE: Article

Anumol, T., Snyder, S.A. Rapid analysis of trace organic compounds in water by automated online solid-phase extraction coupled to liquid chromatography-tandem mass spectrometry (2015) Talanta, 132, pp. 77-86. Cited 46 times. DOI: 10.1016/j.talanta.2014.08.011.

AFFILIATIONS: Department of Chemical and Environmental Engineering, University of Arizona, 1133 E James E Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States.

ABSTRACT: ***A fully automated online solid-phase extraction (SPE) with directly coupled liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for analysis of 34 trace organic compounds in diverse water matrices has been developed.*** The current method offers several advantages over traditional offline SPE methods including low sample volume (1.7 mL), decreased solvent use, higher throughput, and increased reproducibility. ***The method uses simultaneous positive and negative ESI for analysis of all compounds in one injection, which reduces cycle time (extraction+analysis) to <15 min.*** Method optimization included testing different online SPE cartridges, mobile phase compositions, and flow rates. ***The method detection limits (MDLs) ranged from 0.1 to 13.1 ng/L with 80% of the compounds having an MDL <5 ng/L.*** Matrix spike recoveries in three different water qualities were evaluated and ranged from 61.2% to145.1% with 95% of the recoveries ranging between 70-130%. As part of the method validation studies, linearity (0.9911-0.9998), intra-day variability (1.0-10.4%), inter-day variability (1.0-11.9%), and matrix effects were also assessed. ***The use of 26 isotopically-labeled standards increased the reliability of the method while retention time locking and use of two transitions for most compounds increased the specificity.*** The applicability of the method was tested on samples across treatment points from two wastewater plants, a septic tank, surface water and groundwater. © 2014 Elsevier B.V.
AUTHOR KEYWORDS: Automated online extraction; LC-MS/MS; Personal-care products; Pharmaceuticals; Tandem mass spectrometry; Water
DOCUMENT TYPE: Article

Leusch, F.D.L., Snyder, S.A. Bioanalytical tools: Half a century of application for potable reuse (2015) Environmental Science: Water Research and Technology, 1 (5), pp. 606-621. Cited 13 times. DOI: 10.1039/c5ew00115c.

AFFILIATIONS: Smart Water Research Centre, Australian Rivers Institute, School of Environment, Griffith University, Southport, QLD 4222, Australia; University of Arizona, 1133 E. James E. Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States; National University of Singapore, T-Lab Building, No02-01, NUS Environmental Research Institute (NERI), 5A Engineering Drive 1, Singapore, 117411, Singapore.

ABSTRACT: In vitro bioassays, more recently referred to as "bioanalytical tools" in an attempt to emphasize their analytical purpose rather than the uncertain relation to adverse health outcomes, are often thought of as novel tools by water stakeholders. ***They have, however, been used for over half a century in assessment of recycled water quality.*** Today, millions of chemicals and formulations are available for commercial use and most have a high propensity to enter sewage collection systems. However, traditional health risk assessment methods involving animal testing at high doses and extrapolation to environmental relevant levels are vastly overwhelmed in capacity by the innumerable chemicals and transformation products potentially present in waters. Beyond the sheer number of chemicals, the interactions of these chemicals as complex mixtures is largely unaddressed in traditional regulatory schemes. Moreover, non-human animal models are often misleading due to differences in metabolism and associated pharmacokinetics. Thus, water professionals continue to struggle with ever increasing numbers of chemicals detected at trace levels in water and the potential interactions of these

chemicals during mixture exposures. ***Bioanalytical tools offer a path forward towards more comprehensive chemical evaluations of water, which can provide greater public confidence in the ability of potable reuse schemes to produce clean and safe drinking water.*** © 2016 The Royal Society of Chemistry.
DOCUMENT TYPE: Review
ACCESS TYPE: Open Access

Anumol, T., Wu, S., Marques Dos Santos, M., Daniels, K.D., Snyder, S.A. Rapid direct injection LC-MS/MS method for analysis of prioritized indicator compounds in wastewater effluent (2015) Environmental Science: Water Research and Technology, 1 (5), pp. 632-643. Cited 14 times. DOI: 10.1039/c5ew00080g.

AFFILIATIONS: Department of Chemical and Environmental Engineering, University of Arizona, 1133 E. James E. Rogers Way, 108 Harshbarger, Tucson, AZ, United States.

ABSTRACT: ***Trace organic compounds (TOrCs) have been detected in drinking water sources for several years, raising concerns due to their potential risks to public health. The main contributor of TOrCs to drinking water is through wastewater discharges.*** However, there are several hundred TOrCs currently known with numerous new organic chemicals being released daily, making it unfeasible to monitor each one in water. ***This study used a detailed literature review and scoring system to establish a list of twenty priority indicator TOrCs in US wastewaters. Next, a rapid direct injection LC-MS/MS method for analysis of these compounds was developed without the need for an extraction step and only 80 µL sample volume while providing method reporting limits of 3-39 ng L-1 for all but one TOrC (sucralose: 302 ng L-1). The elimination of an extraction step reduced matrix effects considerably making the method suitable for wastewater analysis. Method validation including matrix spike recoveries, linearity of calibration curve and inter- and intra-day variability was successfully performed.*** Finally, the twenty indicator TOrCs were evaluated in four different wastewater treatment plant (WWTP) effluents through four sample campaigns spread across a year. The occurrence data indicated that all indicator TOrCs were detected in at least three out of the four WWTP effluents. Sucralose, iohexol, TCPP, acesulfame and gemfibrozil were detected in all samples at the four WWTPs indicating they could be used as indicators of wastewater influence in receiving waters. DEET, caffeine, triclosan, iopromide and others are effective indicators at showing seasonal variations, treatment process efficacy, and consumption patterns. ***Overall, the impact of this study will help develop more effective monitoring programs for TOrCs in water reuse schemes.*** © 2016 The Royal Society of Chemistry.
DOCUMENT TYPE: Review
ACCESS TYPE: Open Access

Vanderford, B.J., Drewes, J.E., Eaton, A., Guo, Y.C., Haghani, A., Hoppe-Jones, C., Schluesener, M.P., Snyder, S.A., Ternes, T., Wood, C.J. Results of an interlaboratory comparison of analytical methods for contaminants of emerging concern in water (2014) Analytical Chemistry, 86 (1), pp. 774-782. Cited 21 times. DOI: 10.1021/ac403274a.

AFFILIATIONS: Southern Nevada Water Authority, P.O. Box 99954, Las Vegas, NE 89193, United States; Colorado School of Mines, 1500 Illinois Street, Golden, CO 80401, United States; Eurofins Eaton Analytical, Inc., 750 Royal Oaks Drive, Monrovia, CA 91016, United States; Metropolitan Water District of Southern California, Moreno Avenue 7., La Verne, CA 91750, United States; German Federal Institute of Hydrology, Am Mainzer Tor 1, 56068 Koblenz, Germany; University of Arizona, 1133 E. James E. Rogers Way, Tucson, AZ 85721, United States; Environmental Resource Associates, 6000 W. 54th Avenue, Arvada, CO 80002, United States.

ABSTRACT: An evaluation of existing analytical methods used to measure contaminants of emerging concern (CECs) was performed through an interlaboratory comparison involving 25 research and

commercial laboratories. In total, 52 methods were used in the single-blind study to determine method accuracy and comparability for 22 target compounds, including pharmaceuticals, personal care products, and steroid hormones, all at ng/L levels in surface and drinking water. Method biases ranged from <10% to well over 100% in both matrixes, suggesting that while some methods are accurate, others can be considerably inaccurate. In addition, the number and degree of outliers identified suggest a high degree of variability may be present between methods currently in use. ***Three compounds, ciprofloxacin, 4-nonylphenol (NP), and 4-tert-octylphenol (OP), were especially difficult to measure accurately.*** While most compounds had overall false positive rates of ≤5%, bisphenol A, caffeine, NP, OP, and triclosan had false positive rates >15%. In addition, some methods reported false positives for 17β-estradiol and 17α-ethynylestradiol in unspiked drinking water and deionized water, respectively, at levels higher than published predicted no-effect concentrations for these compounds in the environment. False negative rates were also generally <5%; however, rates were higher for the steroid hormones and some of the more challenging compounds, such as ciprofloxacin. ***The elevated false positive/negative rates of some analytes emphasize the susceptibility of many current methods to blank contamination, misinterpretation of background interferences, and/or inappropriate setting of detection/quantification levels for analysis at low ng/L levels.*** The results of both comparisons were collectively assessed to identify parameters that resulted in the best overall method performance. ***Liquid chromatography-tandem mass spectrometry coupled with the calibration technique of isotope dilution were able to accurately quantify most compounds with an average bias of <10% for both matrixes. These findings suggest that this method of analysis is suitable at environmentally relevant levels for most of the compounds studied.*** This work underscores the need for robust, standardized analytical methods for CECs to improve data quality, increase comparability between studies, and help reduce false positive and false negative rates.
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Snyder, S.A. Emerging chemical contaminants: Looking for greater harmony (2014) Journal - American Water Works Association, 106 (8), pp. 38-52. Cited 34 times. DOI: 10.5942/jawwa.2014.106.0126.

AFFILIATIONS: University of Arizona's College of Engineering, United States

ABSTRACT: ***Historical and current perspectives of the methods used and policies instituted to monitor and address the increasing list of chemical contaminants in water are discussed.*** According to Chemical Abstract Services, more than 88 million organic and inorganic chemicals have been registered, more than 65 million chemicals are available commercially, and approximately 1500 new chemicals are added every day. ***The United States does not have a coordinated program that comprehensively addresses the fate and effects of chemicals in commerce entering the environment.*** The Toxic Substances Control Act (TSCA) provides the U.S. Environmental Protection Agency (U.S. EPA) with the authority to require reporting, record keeping, and testing requirements for new and existing chemicals in commerce. The Endocrine Disrupter Screening Program (EDSP) was developed by U.S. EPA to screen chemicals before they are manufactured or used in applications in which water and food may become contaminated. ***U.S. EPA uses the Contaminant Candidate List (CCL) as a mechanism to prioritize both chemical and biological contaminants.***
DOCUMENT TYPE: Article

Drewes, J.E., Anderson, P., Denslow, N., Olivieri, A., Schlenk, D., Snyder, S.A., Maruya, K.A. Designing monitoring programs for chemicals of emerging concern in potable reuse: What to include and what not to include? (2013) Water Science and Technology, 67 (2), pp. 433-439. Cited 20 times. DOI: 10.2166/wst.2012.520.

AFFILIATIONS: Colorado School of Mines, Advanced Water Technology Center (AQWATEC), Golden, CO, United States; King Abdullah University of Science and Technology, Water Desalination and Reuse Center, Thuwal, Saudi Arabia; Arcadis U.S., Inc., Chelmsford, MA, United States; University of Florida, Gainesville, FL, United States; EOA, Inc., Oakland, CA, United States; University of California-Riverside, Riverside, CA, United States; Environmental and Chemical Engineering, University of Arizona, Tucson, AZ, United States; Southern California Coastal Water Research Project, Costa Mesa, CA, United States.

ABSTRACT: ***This study discussed a proposed process to prioritize chemicals for reclaimed water monitoring programs, selection of analytical methods required for their quantification***, toxicological relevance of chemicals of emerging concern regarding human health, and related issues. Given that thousands of chemicals are potentially present in reclaimed water and that information about those chemicals is rapidly evolving, a transparent, science-based framework was developed to guide prioritization of which compounds of emerging concern (CECs) should be included in reclaimed water monitoring programs. The recommended framework includes four steps: 1) compile environmental concentrations (e.g., measured environmental concentration or MEC) of CECs in the source water for reuse projects; 2) develop a monitoring trigger level (MTL) for each of these compounds (or groups thereof) based on toxicological relevance; 3) compare the environmental concentration (e.g., MEC) to the MTL; CECs with a MEC/MTL ratio greater than one should be prioritized for monitoring, compounds with a ratio less than '1' should only be considered if they represent viable treatment process performance indicators; and 4) screen the priority list to ensure that a commercially available robust analytical method is available for that compound.
AUTHOR KEYWORDS: Chemicals of emerging concern; Monitoring programs; Potable reuse; Toxicological relevance; Water reuse
DOCUMENT TYPE: Article

Pepper, I.L., Sherchan, S.P., Miles, S.L., Clarke, B.O., Snyder, S.A. Ensuring safe water through advanced oxidation and real-time sensors (2012) 14th Water Distribution Systems Analysis Conference 2012, WDSA 2012, 2, pp. 1273-1278. Cited two times.

AFFILIATIONS: Department of Soil, Water and Environmental Science, University of Arizona, Tucson, AZ, United States; Los Angeles Department of Public Health, Los Angeles, CA, United States; Department of Chemical and Environmental Engineering, University of Arizona, Tucson, AZ, United States.

ABSTRACT: ***The overall objective of our study is to evaluate the potential for real-time monitoring of chemical and biological contaminants using in-line water quality sensors including: Safire On-line Florescence Sensor, the HACH Guardian Blue Monitoring Platform; the JMAR BioSentry unit; and the S::CAN spectro::lyser technology.*** For biological contaminants we evaluated the BioSentry sensor for the detection of Escherichia coli and Bacillus thurengiensis (a surrogate for Bacillus anthracis). The sensor was responsive to an increase in E. coli concentrations from 103 cfu/mL to 106 cfu/mL. The minimum threshold response for detection of B. thuringiensis spores was also evaluated. Specifically, spores were injected into either deionized (DI), or raw (unfiltered) tap water. The sensor responded to an increase in spore concentration over the range of 102-105 spores/ml. ***We also have proof of concept for AOP destruction of trace organics and documentation of destruction in real time.***
DOCUMENT TYPE: Conference Paper

Gerrity, D., Gamage, S., Jones, D., Korshin, G.V., Lee, Y., Pisarenko, A., Trenholm, R.A., von Gunten, U., Wert, E.C., Snyder, S.A. Development of surrogate correlation models to predict trace organic contaminant oxidation and microbial inactivation during ozonation (2012) Water Research, 46 (19), pp. 6257-6272. Cited 94 times. DOI: 10.1016/j.watres.2012.08.037.

AFFILIATIONS: Department of Civil and Environmental Engineering and Construction, University of Nevada, Las Vegas, Box 454015, 4505 S. Maryland Parkway, Las Vegas, NV 89154-4015, United States; Trussell Technologies, Inc., 232 North Lake Avenue, Suite 300, Pasadena, CA 91101, United States; Applied Research and Development Center, Southern Nevada Water Authority, River Mountain Water Treatment Facility, P.O. Box 99954, Las Vegas, NV 89193-9954, United States; Department of Chemical and Environmental Engineering, University of Arizona, 1133 E. James E. Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States; Civil and Environmental Engineering, University of Washington, 201 More Hall, Box 352700, Seattle, WA 98195-2700, United States; School of Environmental Science and Engineering, Gwangju Institute of Science and Technology (GIST), 123, Oryong-dong, Buk-gu, Gwangju 500-712, South Korea; Eawag, Swiss Federal Institute of Aquatic Science and Technology, Ueberlandstrasse 133, P.O. Box 611, 8600 Duebendorf, Switzerland; School of Architecture, Civil, and Environmental Engineering (ENAC), Ecole Polytechnique Federale de Lausanne, CH-1015 Lausanne, Switzerland

ABSTRACT: The performance of ozonation in wastewater depends on water quality and the ability to form hydroxyl radicals (OH) to meet disinfection or contaminant transformation objectives. Since there are no on-line methods to assess ozone and OH exposure in wastewater, ***many agencies are now embracing indicator frameworks and surrogate monitoring for regulatory compliance. Two of the most promising surrogate parameters for ozone-based treatment of secondary and tertiary wastewater effluents are differential UV254 absorbance (ΔUV254) and total fluorescence (ΔTF).*** In the current study, empirical correlations for ΔUV254 and ΔTF were developed for the oxidation of 18 trace organic contaminants (TOrCs), including 1,4-dioxane, atenolol, atrazine, bisphenol A, carbamazepine, diclofenac, gemfibrozil, ibuprofen, meprobamate, naproxen, N,N-diethyl-meta-toluamide (DEET), para-chlorobenzoic acid (pCBA), phenytoin, primidone, sulfamethoxazole, triclosan, trimethoprim, and tris-(2-chloroethyl)-phosphate (TCEP) (R2 = 0.50-0.83) and the inactivation of three microbial surrogates, including Escherichia coli, MS2, and Bacillus subtilis spores (R2 = 0.46-0.78). Nine wastewaters were tested in laboratory systems, and eight wastewaters were evaluated at pilot- and full-scale. ***A predictive model for OH exposure based on ΔUV254 or ΔTF was also proposed.*** © 2012 Elsevier Ltd.
AUTHOR KEYWORDS: Advanced oxidation process (AOP); Disinfection; Fluorescence; Indicator; Indirect potable reuse (IPR); Ozone; Pharmaceutical; Trace organic contaminant (TOrC); UV absorbance
DOCUMENT TYPE: Article

Pisarenko, A.N., Stanford, B.D., Yan, D., Gerrity, D., Snyder, S.A. Effects of ozone and ozone/peroxide on trace organic contaminants and NDMA in drinking water and water reuse applications (2012) Water Research, 46 (2), pp. 316-326. Cited 86 times. DOI: 10.1016/j.watres.2011.10.021.

AFFILIATIONS: Southern Nevada Water Authority, Applied Research and Development Center, Po Box 99954, Las Vegas, NV 89193, United States; Hazen and Sawyer P.C., Raleigh, NC 27607, United States; University of Arizona, Tucson, AZ, United States; Layne Christensen Company, 3804 E. Watkins Street, Phoenix, AZ 85034, United States; Trussell Technologies Inc., 6540 Lusk Blvd., Suite C274, San Diego CA 92121, United States.

ABSTRACT: An ozone and ozone/peroxide oxidation process was evaluated at pilot scale for trace organic contaminant (TOrC) mitigation and NDMA formation in both drinking water and water reuse applications. A reverse osmosis (RO) pilot was also evaluated as part of the water reuse treatment train. Ozone/peroxide showed lower electrical energy per order of removal (EEO) values for TOrCs in surface water treatment, but the addition of hydrogen peroxide increased EEO values during wastewater treatment. ***TOrC oxidation was correlated to changes in UV 254 absorbance and fluorescence offering a surrogate model for predicting contaminant removal. A decrease in N-nitrosodimethylamine (NDMA) formation potential (after chloramination) was observed after treatment with ozone and ozone/peroxide.*** However, during spiking experiments with surface water, ozone/peroxide achieved

limited destruction of NDMA, while in wastewaters net direct formation of NDMA of 6-33 ng/L was observed after either ozone or ozone/peroxide treatment. Once formed during ozonation, ***NDMA passed through the subsequent RO membranes, which highlights the significance of the potential for direct NDMA formation during oxidation in reuse applications.*** © 2011 Elsevier Ltd.
AUTHOR KEYWORDS: Advanced oxidation process (AOP); Endocrine disrupting compounds (EDCs); N-Nitrosodimethylamine (NDMA); Ozone; Ozone/H 2O 2; Ozone/hydrogen peroxide; Ozone/peroxide; Pharmaceuticals; Trace organic contaminant (TOrC)
DOCUMENT TYPE: Article

Vanderford, B.J., Mawhinney, D.B., Trenholm, R.A., Zeigler-Holady, J.C., Snyder, S.A. Assessment of sample preservation techniques for pharmaceuticals, personal care products, and steroids in surface and drinking water (2011) Analytical and Bioanalytical Chemistry, 399 (6), pp. 2227-2234. Cited 36 times. DOI: 10.1007/s00216-010-4608-5.

AFFILIATIONS: Southern Nevada Water Authority, P.O. Box 99954, Las Vegas, NV 89193-9954, United States; University of Arizona, 1133 E. James E. Rogers Way, Tucson, AZ 85721, United States.

ABSTRACT: ***Proper collection and preservation techniques are necessary to ensure sample integrity and maintain the stability of analytes until analysis.*** Data from improperly collected and preserved samples could lead to faulty conclusions and misinterpretation of the occurrence and fate of the compounds being studied. Because contaminants of emerging concern, such as pharmaceuticals and personal care products (PPCPs) and steroids, generally occur in surface and drinking water at ng/L levels, these compounds in particular require such protocols to accurately assess their concentrations. ***In this study, sample bottle types, residual oxidant quenching agents, preservation agents, and hold times were assessed for 21 PPCPs and steroids in surface water and finished drinking water. Amber glass bottles were found to have the least effect on target analyte concentrations, while high-density polyethylene bottles had the most impact. Ascorbic acid, sodium thiosulfate, and sodium sulfite were determined to be acceptable quenching agents and preservation with sodium azide at 4°C led to the stability of the most target compounds. A combination of amber glass bottles, ascorbic acid, and sodium azide preserved analyte concentrations for 28 days in the tested matrices when held at 4°C.*** Samples without a preservation agent were determined to be stable for all but two of the analytes when stored in amber glass bottles at 4°C for 72 h. Results suggest that if improper protocols are utilized, reported concentrations of target PPCPs and steroids may be inaccurate. © Springer-Verlag 2011.
AUTHOR KEYWORDS: Emerging contaminants; Endocrine disruptors; Pharmaceuticals; Preservation; Sample collection; Water
DOCUMENT TYPE: Article

Pisarenko, A.N., Stanford, B.D., Quiñones, O., Pacey, G.E., Gordon, G., Snyder, S.A. Rapid analysis of perchlorate, chlorate and bromate ions in concentrated sodium hypochlorite solutions (2010) Analytica Chimica Acta, 659 (1-2), pp. 216-223. Cited 30 times. DOI: 10.1016/j.aca.2009.11.061.

AFFILIATIONS: Sothern Nevada Water Authority, Research and Development, River Mountain Water Treatment Facility, 1299 Burkholder Blvd, Henderson, NV 89015, United States; Miami University, Department of Chemistry and Biochemistry, Oxford, OH 45056, United States; Hazen and Sawyer, 498 7th Ave, 11th Floor, New York, NY 10018, United States; Harvard University, Harvard School of Public Health, Department of Environmental Health Exposure, 401 Park Drive, Boston, MA 02215, United States.

ABSTRACT: ***A sensitive, rapid, and rugged liquid chromatography with tandem mass spectrometry (LC-MS/MS) method for measuring concentrations of perchlorate, chlorate, and bromate ions in concentrated sodium hypochlorite solutions is presented. The LC-MS/MS method offers a practical quantitation limit (PQL) of 0.05 µg L-1 for ClO4 -, 0.2 µg L-1 for BrO3 -, and 0.7 µg L-1 for ClO3 - and a***

sample analysis time of only 10 min. Additionally, an iodometric titration technique was compared with the LC-MS/MS method for measurement of chlorate ion at high concentration. The LC-MS/MS method was the most reproducible for chlorate concentrations below 0.025 M while the iodometric titration method employed was the most reproducible above 0.025 M. ***By using both methods, concentrations of chlorate can be measured over a wide range, from 0.7 µg L-1 to 210 g L-1 in hypochlorite ion solutions.*** Seven quenching agents were also evaluated for their ability to neutralize hypochlorite ion, thereby stopping formation of perchlorate ion in solution, without adversely impacting the other oxyhalide ions. Malonic acid was chosen as the quenching agent of choice, meeting all evaluation criteria outlined in this manuscript.
AUTHOR KEYWORDS: Bromate ion; Chlorate ion; Malonic acid; Perchlorate ion; Sodium hypochlorite
DOCUMENT TYPE: Article

Quiñones, O., Snyder, S.A. Occurrence of perfluoroalkyl carboxylates and sulfonates in drinking water utilities and related waters from the United States (2009) Environmental Science and Technology, 43 (24), pp. 9089-9095. Cited 85 times. DOI: 10.1021/es9024707

AFFILIATIONS: Southern Nevada Water Authority, Applied Research and Development Center, P.O. Box 99954, Las Vegas, NV 89193, United States; Harvard University, Harvard School of Public Health, Department of Environmental Health Landmark Center, 401 Park Drive, Boston, MA 02215, United States.

ABSTRACT: ***The prevalence and persistence of perfluoroalkyl compounds (PFCs) in environmental and biological systems has been well documented, and a rising number of reports suggest that certain PFCs can result in adverse health effects in mammals. As traditional water sources become increasingly impacted by waste discharge and the demand for planned potable reuse grows, there is recent interest in determining PFC occurrence in drinking water supplies.*** Here we report monitoring results from drinking water treatment facility samples collected across the United States, and from associated surface, ground, and wastewater sources. ***Using automated solid phase extraction(SPE)and isotope dilution liquid chromatography/tandem mass spectrometry (LC/ MS-MS), samples were screened for perfluorohexanoic acid (PFHxA), perfluorohexanesulfonate (PFHxS), perfluorooctanoic acid (PFOA), perfluorooctanesulfonate (PFOS), perfluorononanoic acid (PFNA) perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUdA), and perfluorododecanoic acid (PFDoA). Method reporting limits (MRLs) were established at 1.0 ng/L for all monitored PFCs except PFOA, for which the MRL was set at 5.0 ng/L given elevated procedural and instrumental background levels.*** PFOS was the only investigated PFC detected in minimally impacted surface waters, with individual site averages of 2.0 ng/L and lower. ***Conversely, wastewater treatment plant (WWTP) effluents and other highly impacted waters had almost 100% detection frequency for all PFCs except PFUdA and PFDoA, which were not detected above MRL in any samples. Of the investigated PFCs, PFOA averaged the highest overall concentration at any site at 115 ng/L.*** Substantial impacts from treated wastewater generally caused increased summed PFC concentrations at downstream drinking water facilities, although levels and distribution suggest geographical variability. No discernible differences between influent and effluent PFC levels were observed for drinking water facilities. ***Removal of PFCs, however, was observed at an indirect potable reuse facility using microfiltration and reverse osmosis for wastewater treatment, in which case all PFC levels in effluents were below the MRL.*** © 2009 American Chemical Society.
DOCUMENT TYPE: Article

Trenholm, R.A., Vanderford, B.J., Snyder, S.A. On-line solid phase extraction LC-MS/MS analysis of pharmaceutical indicators in water: A green alternative to conventional methods (2009) Talanta, 79 (5), pp. 1425-1432. Cited 69 times. DOI: 10.1016/j.talanta.2009.06.006.

AFFILIATIONS: Water Quality Research and Development Department, Southern Nevada Water Authority, 1350 Richard Bunker Road, Henderson, NV 89015, United States.

ABSTRACT: ***A method using automated on-line solid phase extraction (SPE) directly coupled to liquid chromatography/tandem mass spectrometry (LC-MS/MS) has been developed for the analysis of six pharmaceuticals by isotope dilution***. These selected pharmaceuticals were chosen as representative indicator compounds and were used to evaluate the performance of the on-line SPE method in four distinct water matrices. Method reporting limits (MRLs) ranged from 10 to 25 ng/L, based on a 1 mL extraction volume. Matrix spike recoveries ranged from 88 to 118% for all matrices investigated, including finished drinking water, surface water, wastewater effluent and septic tank influent. Precision tests were performed at 50 and 1000 ng/L with relative standard deviations (RSDs) between 1.3 and 5.7%. A variety of samples were also extracted using a traditional off-line automated SPE method for comparison. Results for both extraction methods were in good agreement; **however, on-line SPE used approximately 98% less solvent and less time. On-line SPE coupled to LC-MS/MS analysis for selected indicators offers an alternative, more environmentally friendly, method for pharmaceutical analysis in water by saving time and costs while reducing hazardous waste and potential environmental pollution as compared with off-line SPE methods.**
AUTHOR KEYWORDS: Isotope dilution; Liquid chromatography tandem mass spectrometry (LC-MS/MS); On-line solid phase extraction (SPE); Pharmaceutical
DOCUMENT TYPE: Article

Dickenson, E.R.V., Drewes, J.E., Sedlak, D.L., Wert, E.C., Snyder, S.A. Applying surrogates and indicators to assess removal efficiency of trace organic chemicals during chemical oxidation of wastewaters (2009) Environmental Science and Technology, 43 (16), pp. 6242-6247. Cited 67 times. DOI: 10.1021/es803696y.

AFFILIATIONS: Advanced Water Technology Center (AQWATEC), Environmental Science and Engineering Division, Colorado School of Mines, Golden, CO 80401, United States; Department of Civil and Environmental Engineering, University of California, Berkeley, CA 94720, United States; Applied Research and Development Center (ARDC), Water Quality Research and Development Division, Southern Nevada Water Authority, Henderson, NV 89015, United States.

ABSTRACT: To respond to concerns associated with wastewater-derived contaminants water utilities are looking for new approaches for monitoring trace organic chemicals in conventional and advanced water treatment processes. ***This study examines the use of a combination of surrogate parameters and indicator compounds tailored to monitor the removal efficiency of advanced oxidation processes employed by treatment plants engaged in indirect potable water reuse programs.*** Potential surrogate parameters and indicator compounds, identified by reviewing previous publications and classified by their structural properties, were tested in pilot- and full-scale treatment systems. ***Dilantin, DEET, meprobamate, and iopromide are good indicators to assess optimized oxidation conditions while ozonating tertiary-treated wastewaters. UVA reduction, ozone byproduct formation, such as simple organic acids, and ozone exposure correlated with "sweet spot" compounds, where ozone exposure correlated with trace organic removal across five tertiary-treated wastewaters.*** Findings indicate that the proposed framework can serve as a conservative monitoring approach for advanced oxidation processes as well as other indirect potable reuse processes to ensure proper removal of identified and unidentified wastewater-derived organic contaminants, to detect failures in system performance, and is protective of public health.
DOCUMENT TYPE: Article

Wert, E.C., Rosario-Ortiz, F.L., Snyder, S.A. Using ultraviolet absorbance and color to assess pharmaceutical oxidation during ozonation of wastewater (2009) Environmental Science and Technology, 43 (13), pp. 4858-4863. Cited 73 times. DOI: 10.1021/es803524a.

AFFILIATIONS: Southern Nevada Water Authority (SNWA), P.O. Box 99955, Las Vegas, NV 89193-9955, United States.

ABSTRACT: ***The reduction of ultraviolet (UV) absorbance at 254 nm (UV254) and true color were identified as appropriate surrogates to assess the oxidation of six pharmaceuticals (i.e., carbamazepine, meprobamate, dilantin, primidone, atenolol, and iopromide) during ozonation of wastewater.*** Three tertiary-treated wastewaters were evaluated during oxidation with ozone (O3) and O3 coupled with hydrogen peroxide (O3/H2O 2). The correlation between pharmaceutical oxidation and removal of UV254 was dependent upon the reactivity of each specific compound toward ozone, as measured by the second-order rate constant (k" O3). Oxidation of compounds with k"O3 > 10 3 M-1 s-1 correlated well (R2 > 0.73) with UV254 reduction between 0-50%. Oxidation of compounds with apparent k"O3 < 10 M-1 s-1 resulted primarily from hydroxyl radicals and correlated well (R2 > 0.80) with the UV254 reduction of 15-65%. ***The removal of true color also correlated well (R2 > 0.85) with the oxidation of pharmaceuticals during the ozonation of two wastewaters. These correlations demonstrate that UV254 reduction and true color removal may be used as surrogates to evaluate pharmaceutical oxidation in the presence or absence of dissolved ozone residual during advanced wastewater treatment with O3 or O 3/H2O2.*** The use of online UV254 measurements would allow wastewater utilities to optimize the ozone dose required to meet their specific treatment objectives. © 2009 American Chemical Society.
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Vanderford, B.J., Mawhinney, D.B., Rosario-Ortiz, F.L., Snyder, S.A. Real-time detection and identification of aqueous chlorine transformation products using QTOF MS (2008) Analytical Chemistry, 80 (11), pp. 4193-4199. Cited 12 times. DOI: 10.1021/ac8000989.

AFFILIATIONS: Southern Nevada Water Authority, P.O. Box 99954, Las Vegas, NV 89193-9954, United States.

ABSTRACT: ***A screening technique has been developed that allows the rapid, real-time detection and identification of major transformation products of organic contaminants during aqueous oxidation experiments.*** In this technique, a target contaminant is dissolved in buffered water and chlorinated by the addition of sodium hypochlorite to give a free chlorine residual of 3 mg/L. ***Solution from the reaction vessel is combined with methanol and pumped directly into the electrospray ionization source of a quadrupole time-of-flight mass spectrometer (QTOF MS).*** The realtime decay of the target contaminant and the formation/decay of transformation products are then monitored using the QTOF MS. Subsequently, accurate mass measurements with internal mass calibration (<5 ppm mass error) and product ion scans are employed to identify these transformation products. ***Unlike other techniques, it requires no liquid chromatography, derivatization, or quenching of residual chlorine, all of which can interfere with transformation product analysis.*** To validate the technique, aqueous chlorination experiments were performed on triclosan, a previously studied environmental contaminant Earlier research showing that triclosan underwent chlorine addition to form mono- and dichlorinated transformation products was successfully reproduced, demonstrating the feasibility of the technique. In addition, the technique revealed the formation of a stable oxygen radical-containing transformation product resulting from the oxidation of either mono- or dichlorinated triclosan. This triclosan transformation product was determined to have an empirical formula of C12H4O3Cl 4 with 3.9 ppm mass error. Furthermore, atorvastatin, a commonly prescribed medication and environmental contaminant, was subjected to aqueous chlorination and studied with the technique. Atorvastatin underwent hydroxylation to form two transformation products with the empirical formulas C33H34FN2O6 (1.8 ppm mass error) and C26H29O5NF (2.9 ppm mass error). © 2008 American Chemical

Society.
DOCUMENT TYPE: Article

Vanderford, B.J., Rosario-Ortiz, F.L., Snyder, S.A. Analysis of p-chlorobenzoic acid in water by liquid chromatography-tandem mass spectrometry (2007) Journal of Chromatography A, 1164 (1-2), pp. 219-223. Cited 16 times. DOI: 10.1016/j.chroma.2007.07.035.

AFFILIATIONS: Southern Nevada Water Authority, 1350 Richard Bunker Avenue, Henderson, NV 89015, United States,

ABSTRACT: ***para-Chlorobenzoic acid (p-CBA) is typically used as a probe compound to indirectly quantify hydroxyl radicals formed during advanced oxidation processes used in drinking water and wastewater treatment. A method has been developed for the sensitive analysis of p-CBA in water using liquid chromatography-tandem mass spectrometry (LC-MS/MS). A reporting limit in water of 100 ng/L was determined for the method, which is 40-fold lower than the 4.0 µg/L reporting limit of the widely used liquid chromatography with UV detection (LC-UV) method. The method was found to be robust in difficult matrices such as wastewater and highly selective, unlike LC-UV which relies on non-specific detection at 234 nm.*** The detection of p-CBA below 1 µg/L during bench-scale ozonation of wastewater after hydrogen peroxide addition was demonstrated. ***Duplicate samples were analyzed by LC-MS/MS and LC-UV and results were found to be comparable at concentrations quantifiable by both methods.***
AUTHOR KEYWORDS: LC-MS/MS; Liquid chromatography; Mass spectrometry; p-Chlorobenzoic acid (p-CBA)
DOCUMENT TYPE: Article

Vanderford, B.J., Snyder, S.A. Analysis of pharmaceuticals in water by isotope dilution liquid chromatography/tandem mass spectrometry (2006) Environmental Science and Technology, 40 (23), pp. 7312-7320. Cited 313 times. DOI: 10.1021/es0613198.

AFFILIATIONS: Southern Nevada Water Authority, 1350 Richard Bunker Avenue, Henderson, NV 89015, United States.

ABSTRACT: A method has been developed for the trace analysis of 15 pharmaceuticals, four metabolites of pharmaceuticals, three potential endocrine disruptors, and one personal care product in various waters. The method employs solid-phase extraction (SPE) and liquid chromatography/tandem mass spectrometry (LC-MS/MS), using electrospray ionization (ESI) in both positive and negative modes. ***Unlike many previous LC-MS/MS methods, which suffer from matrix suppression, this method uses isotope dilution for each compound to correct for matrix suppression, as well as SPE losses and instrument variability.*** The method was tested in five matrices, and results indicate that the method is very robust. Matrix spike recoveries for all compounds were between 88 and 106% for wastewater influent, 85 and 108% for wastewater effluent, 72 and 105% for surface water impacted by wastewater, 96 and 113% for surface water, and 91 and 116% for drinking water. ***The method reporting limits for all compounds were between 0.25 and 1.0 ng/L, based on 500 mL of sample extracted and a final extract volume of 500 µL.*** Occurrence of the compounds in all five matrices is also reported.
DOCUMENT TYPE: Article

Trenholm, R.A., Vanderford, B.J., Holady, J.C., Rexing, D.J., Snyder, S.A. Broad range analysis of endocrine disruptors and pharmaceuticals using gas chromatography and liquid chromatography tandem mass spectrometry (2006) Chemosphere, 65 (11), pp. 1990-1998. Cited 167 times. DOI: 10.1016/j.chemosphere.2006.07.004.

AFFILIATIONS: Water Quality Research and Development Department, Southern Nevada Water Authority, 1350 Richard Bunker Avenue, Henderson, NV 89015, United States.

ABSTRACT: Endocrine disrupting compounds (EDCs) and pharmaceuticals and personal care products (PPCPs) have been globally detected in impacted natural waters. The detection of trace quantities of EDCs and PPCPs in the environment is of great concern since some of these compounds have known physiological responses at low concentrations. EDCs can have a wide range of polarities, acidic and basic moieties, and exist in trace quantities, which often requires numerous complex extractions, large sample collection volumes, and multiple instrumental analyses. A comprehensive method has been developed allowing for the analysis of 58 potential EDCs in various water matrices using a single solid-phase extraction (SPE) of a 1 L sample with subsequent ***analyses using both gas chromatography and liquid chromatography, each coupled with tandem mass spectrometry (GC-MS/MS and LC-MS/MS). Instrument detection limits ranged between 0.12-7.5 pg with corresponding method reporting limits of 1-10 ng l-1 in water.*** Recoveries for most compounds were between 50% and 112% with good reproducibility (RSD 6-22%).
AUTHOR KEYWORDS: Endocrine disruptor; GC-MS/MS; LC-MS/MS; Solid-phase extraction
DOCUMENT TYPE: Article

Snyder, S.A., Vanderford, B.J., Rexing, D.J. Trace analysis of bromate, chlorate, iodate, and perchlorate in natural and bottled waters (2005) Environmental Science and Technology, 39 (12), pp. 4586-4593. Cited 123 times. DOI: 10.1021/es047935q.

AFFILIATIONS: Water Quality Research and Development Department, Southern Nevada Water Authority, 1350 Richard Bunker Avenue, Henderson, NV 89015, United States.

ABSTRACT: ***A simple and rapid method has been developed to simultaneously measure sub-µg/L quantities of the oxyhalide anions bromate, chlorate, iodate, and perchlorate in water samples. Water samples (10 mL) are passed through barium and hydronium cartridges to remove sulfate and carbonate, respectively.*** The method utilizes the direct injection of 10 µL volumes of water samples into a ***liquid chromatography-tandem triple-quadrupole mass spectrometry (LC-MS/MS) system. Ionization is accomplished using electrospray ionization in negative mode. The method detection limits were 0.021 µg/L for perchlorate, 0.045 µg/L for bromate, 0.070 µg/L for iodate, and 0.045 µg/L for chlorate anions in water.*** The LC-MS/MS method described here was compared to established EPA methods 300.1 and 317.1 for bromate analysis and EPA method 314.0 for perchlorate analysis. Samples collected from sites with known contamination were split and sent to certified laboratories utilizing EPA methods for bromate and perchlorate analysis. At concentrations above the reporting limits for EPA methods, the method described here was always within 20% of the established methods, and generally within 10%. Twenty-one commercially available bottled waters were analyzed for oxyhalides. The majority of bottled waters contained detectable levels of oxyhalides, with perchlorate ≤0.74 µg/L, bromate ≤76 µg/L, iodate ≤25 µg/ L, and chlorate ≤5.8 µg/L Perchlorate, iodate, and chlorate were detectable in nearly all natural waters tested, while bromate was only detected in treated waters. Perchlorate was found in several rivers and reservoirs where it was not found previously using EPA 314.0 (reporting limit of 4 µg/L). This method was also applied to common detergents used for cleaning laboratory glassware and equipment to evaluate the potential for sample contamination. Only chlorate appeared as a major oxyhalide in the detergents evaluated, with concentrations up to 517 µg/g. Drinking water treatment plants were also evaluated using this method. Significant formations of chlorate and bromate are demonstrated from hypochlorite generation and ozonation. From the limited data set provided here, it appears that perchlorate is a ubiquitous contaminant of natural waters at trace levels.
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Vanderford, B.J., Pearson, R.A., Cody, R.B., Rexing, D.J., Snyder, S.A. Determination of an unknown system contaminant using LC/MS/MS (2003) ACS Symposium Series, 850, pp. 96-108. Cited two times.

AFFILIATIONS: Southern Nevada Water Authority, 243 Lakeshore Road, Las Vegas, NV 89153, United States; JEOL USA Inc., 11 Dearborn Road, Peabody, MA 01960, United States.

ABSTRACT: In recent years, liquid chromatography coupled with tandem mass spectrometry (LC/MS/MS) has become an increasingly valuable tool for the study of contaminants in the environment. It has the advantage of providing structural information while simultaneously reducing background interference. ***The objective of the investigation presented here was to identify an unknown system contaminant using high resolution accurate mass measurements and LC/MS/MS***. In order to accomplish this, a reverse-geometry, double-focusing mass spectrometer equipped with linked scan capability was used. After an accurate mass measurement was performed, an elemental composition determination was carried out to generate a list of potential compounds. Once the list was narrowed down to the most likely molecular formula, linked scan MS/MS was used to provide enough structural information to confirm the chosen formula and identify the most probable constitutional isomer. ***The unknown contaminant was determined to be N-butylbenzenesulfonamide, a common plasticizer increasingly found in the environment.***
DOCUMENT TYPE: Article

Vanderford, B.J., Pearson, R.A., Rexing, D.J., Snyder, S.A. Analysis of Endocrine Disruptors, Pharmaceuticals, and Personal Care Products in Water Using Liquid Chromatography/Tandem Mass Spectrometry (2003) Analytical Chemistry, 75 (22), pp. 6265-6274. Cited 354 times. DOI: 10.1021/ac034210g.

AFFILIATIONS: Southern Nevada Water Authority, 243 Lakeshore Road, Boulder City, NV 89005, United States.

ABSTRACT: ***A method has been developed for the trace analysis of 27 compounds from a diverse group of pharmaceuticals, steroids, pesticides, and personal care products. The method employs solid-phase extraction (SPE) and liquid chromatography/tandem mass spectrometry (LC/MS/ MS), using electrospray ionization (ESI) in both positive and negative modes and atmospheric pressure chemical ionization in positive mode.*** Unlike many previous methods, a single SPE procedure using 1 L of water coupled to a simple LC method is used for all ionization modes. ***Instrument detection limits for most compounds were below 1.0 pg on column with reporting limits of 1.0 ng/L in water.*** Recoveries for most compounds in deionized water were greater than 80%. Sulfuric acid was found to be the preferred sample preservative, and structures of all MS/MS product ions are proposed. Matrix effects from waters with a high content of treated municipal effluent were observed in both ESI modes and are discussed in the paper.
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Snyder, S.A., Villeneuve, D.L., Snyder, E.M., Giesy, J.P. Identification and quantification of estrogen receptor agonists in wastewater effluents (2001) Environmental Science and Technology, 35 (18), pp. 3620-3625. Cited 274 times. DOI: 10.1021/es001254n.

AFFILIATIONS: Department of Zoology, National Food Safety and Toxicology Center, Michigan State University, East Lansing, MI 48824-1311, United States; Institute for Environmental Toxicology, Michigan State University, East Lansing, MI 48824-1311, United States.

ABSTRACT: ***Total concentrations of several known xenobiotic estrogen receptor (ER) agonists and natural and synthetic estrogen were measured in water by use of a combination of instrumental and bioanalytical approaches.*** Samples from three municipal wastewater treatment plants (WWTPs) in

south central Michigan (upstream and effluent); four point source locations on the Trenton Channel of the Detroit River, MI; and five locations in Lake Mead, NV were analyzed. ***Organic compounds were extracted from 5 L water samples using solid-phase extraction disks and separated into three fractions based on polarity. Whole extracts and fractions were tested for ER agonist potency using the MVLN in vitro bioassay. ER agonist potency was characterized by comparing the magnitude of induction elicited by the extract or fraction to the maximum induction caused by 17β-estradiol (E2).*** The greatest concentrations of ER agonists were associated with the most polar fraction (F3). Instrumental analyses and further fractionation were used to identify specific ER agonists associated with bioassay responses. Bioassay data were compared to extract concentrations in order minimize variability associated with the extraction procedure. ***Concentrations of endogenous estrogen, E2, and the synthetic estrogen ethynylestradiol (EE2) ranged from nondetectable to 14.6 ng/mL extract (nondetectable to 3.66 ng/L water) and represented from 88 to 99.5% of the total estrogen equivalents in the water samples analyzed. Concentrations of alkylphenols (APs) ranged from nondetectable to 148 μg/mL extract (nondetectable to 37 000 ng/L water). In general, alkylphenols contributed less than 0.5% of the total estrogen equivalents in the water samples.*** Both bioassay-directed fractionation results and comparison of ER agonist concentrations, adjusted for their known relative potencies, support the conclusion that E2 and EE2 were the dominant environmental estrogens in water samples from mid-Michigan and Lake Mead, NV.
DOCUMENT TYPE: Article

12/6/18 SCOPUS Search by author and keywords
AUTHOR-NAME **(*ferguson,*** AND ***p*** AND ***l*****) AND** TITLE-ABS-KEY **(*water* OR *non-target* OR *unknown* OR *suspect* OR *disinfection* OR *spectrometry*) gave 55 results.**

Hollender, J., Schymanski, E.L., Singer, H.P., Ferguson, P.L. Nontarget Screening with High Resolution Mass Spectrometry in the Environment: Ready to Go? (2017) Environmental Science and Technology, 51 (20), pp. 11505-11512. Cited 34 times. DOI: 10.1021/acs.est.7b02184.

AFFILIATIONS: Eawag, Swiss Federal Institute of Aquatic Science and Technology, Dübendorf, 8600, Switzerland; Institute of Biogeochemistry and Pollutant Dynamics, ETH Zürich, Zürich, 8092, Switzerland; Department of Civil and Environmental Engineering, Duke University, Box 90287, Durham, NC 27708, United States.

ABSTRACT: The vast, diverse universe of organic pollutants is a formidable challenge for environmental sciences, engineering, and regulation. Nontarget screening (NTS) based on high resolution mass spectrometry (HRMS) has enormous potential to help characterize this universe, but is it ready to go for real world applications? In this Feature article ***we argue that development of mass spectrometers with increasingly high resolution and novel couplings to both liquid and gas chromatography, combined with the integration of high performance computing, have significantly widened our analytical window and have enabled increasingly sophisticated data processing strategies, indicating a bright future for NTS. NTS has great potential for treatment assessment and pollutant prioritization within regulatory applications, as highlighted here by the case of real-time pollutant monitoring on the River Rhine.*** We discuss challenges for the future, including the transition from research toward solution-centered and robust, harmonized applications. © 2017 American Chemical Society.
DOCUMENT TYPE: Article

Grange, A.H., Winnik, W., Ferguson, P.L., Sovocool, G.W. Using a triple-quadrupole mass spectrometer in accurate mass mode and an ion correlation program to identify compounds (2005) Rapid Communications in Mass Spectrometry, 19 (18), pp. 2699-2715. Cited 16 times. DOI: 10.1002/rcm.2112.

AFFILIATIONS: U.S. EPA, ORD, Environmental Sciences Division, PO Box 93478, Las Vegas, NV 89193-3478, United States; U.S. EPA, ORD, Environmental Carcinogenesis Division, Research Triangle Park, NC 27111, United States.

ABSTRACT: Atomic masses and isotopic abundances are independent and complementary properties for discriminating among ion compositions. ***The number of possible ion compositions is greatly reduced by accurately measuring exact masses of monoisotopic ions and the relative isotopic abundances (RIAs) of the ions greater in mass by +1Da and +2Da. When both properties are measured, a mass error limit of 6-10 mDa (<31 ppm at 320Da) and an RIA error limit of 10% are generally adequate for determining unique ion compositions for precursor and fragment ions produced from small molecules (less than 320 Da in this study).*** 'Inherent interferences', i.e., mass peaks seen in the product ion mass spectrum of the monoisotopic [M+H]+ ion of an analyte that are -2, -1, +1, or +2 Da different in mass from monoisotopic fragment ion masses, distort measured RIAs. This problem is overcome using an ion correlation program to compare the numbers of atoms of each element in a precursor ion to the sum of those in each fragment ion and its corresponding neutral loss. Synergy occurs when accurate measurement of only one pair of +1 Da and +2 Da RIAs for the precursor ion or a fragment ion rejects all but one possible ion composition for that ion, thereby indirectly rejecting all but one fragment ion-neutral loss combination for other exact masses. ***A triple-quadrupole mass spectrometer with accurate mass capability, using atmospheric pressure chemical ionization (APCI), was used to measure masses and RIAs of precursor and fragment ions. Nine chemicals were investigated as simulated unknowns. Mass accuracy and RIA accuracy were sufficient to determine unique compositions for all precursor ions and all but two of 40 fragment ions, and the two corresponding neutral losses.*** Interrogation of the chemical literature provided between one and three possible compounds for each of the nine analytes. ***This approach for identifying compounds compensates for the lack of commercial ESI and APCI mass spectral libraries, which precludes making tentative identifications based on spectral matches.***
DOCUMENT TYPE: Article

Eichhorn, P., Ferguson, P.L., Pérez, S., Aga, D.S. Application of ion trap-MS with H/D exchange and QqTOF-MS in the identification of microbial degradates of trimethoprim in nitrifying activated sludge (2005) Analytical Chemistry, 77 (13), pp. 4176-4184. Cited 72 times. DOI: 10.1021/ac050141p.

AFFILIATIONS: Chemistry Department, State University of New York at Buffalo, 611 Natural Sciences Complex, Buffalo, NY 14260, United States; Department of Chemistry and Biochemistry, University of South Carolina, 631 Sumter Street, Columbia, SC 29208, United States.

ABSTRACT: ***In this work, the identification of two microbial degradation products of the antimicrobial trimethoprim (290 Da) is described. The structural elucidation of the metabolites, which were produced by nitrifying activated sludge bacteria in a small-scale laboratory batch reactor, was accomplished by electrospray ionization-ion trap mass spectrometry conducting consecutive fragmentation steps (MSn) combined with H/D-exchange experiments.*** Although one metabolite corresponded to α-hydroxytrimethoprim (306 Da), oxidation of the aromatic ring within the diaminopyrimidine substructure was determined for the second degradate (324 Da). ***Accurate mass measurements of the two metabolites were provided by a hybrid quadrupole time-of-flight-mass spectrometer operated in MS/MS mode. With absolute mass errors of <5 mDa, it allowed us to confirm the proposed elemental composition for the protonated precursor ions as well as for a series of fragment ions that were previously identified by ion trap mass spectrometry.*** The study emphasized the potential of nitrifying activated sludge bacteria for breaking down an environmentally relevant pharmaceutical that is otherwise poorly degradable by a bacterial community encountered in conventional activated sludge.
DOCUMENT TYPE: Article

12/6/18 SCOPUS Search by author and keywords
AUTHOR-NAME **(*young,*** AND ***t*** AND ***m*****) AND** TITLE-ABS-KEY **(*water* OR *non-target* OR *unknown* OR *suspect* OR *disinfection* OR *spectrometry*) gave 117 results.**

Moschet, C., Lew, B.M., Hasenbein, S., Anumol, T., Young, T.M. LC- and GC-QTOF-MS as Complementary Tools for a Comprehensive Micropollutant Analysis in Aquatic Systems (2017) Environmental Science and Technology, 51 (3), pp. 1553-1561. Cited 12 times. DOI: 10.1021/acs.est.6b05352.

AFFILIATIONS: Department of Civil and Environmental Engineering, University of California, One Shields Avenue, Davis, CA 95616, United States; Agilent Technologies Inc., 2850 Centerville Road, Wilmington, DE 19808, United States.

ABSTRACT: Efficient strategies are required to implement comprehensive suspect screening methods using high-resolution mass spectrometry within environmental monitoring campaigns. ***In this study, both liquid and gas chromatography time-of-flight mass spectrometry (LC-QTOF-MS and GC-QTOF-MS) were used to screen for >5000 target and suspect compounds in the Sacramento-San Joaquin River Delta in Northern California. LC-QTOF-MS data were acquired in All-Ions fragmentation mode in both positive and negative electrospray ionization (ESI). LC suspects were identified using two accurate mass LC-QTOF-MS/MS libraries containing pesticides, pharmaceuticals, and other environmental contaminants and a custom exact mass database with predicted transformation products (TPs). The additional fragment information from the All-Ions acquisition improved the confirmation of the compound identity, with a low false positive rate (9%).*** Overall, 25 targets, ***73 suspects, and 5 TPs were detected***. ***GC-QTOF-MS extracts were run in negative chemical ionization (NCI) for 21 targets (mainly pyrethroids) at sub-ng/L levels. For suspect screening, extracts were rerun in electron ionization (EI) mode with a retention time locked method using a GC-QTOF-MS pesticide library (containing exact mass fragments and retention times).*** Sixteen targets and ***42 suspects were detected***, ***of which 12 and 17, respectively, were not identified by LC-ESI-QTOF-MS. The results highlight the importance of analyzing water samples using multiple separation techniques and in multiple ionization modes to obtain a comprehensive chemical contaminant profile.*** The investigated river delta experiences significant pesticide inputs, leading to environmentally critical concentrations during rain events. © 2016 American Chemical Society.
DOCUMENT TYPE: Article

Parry, E., Young, T.M. Comparing targeted and non-targeted high-resolution mass spectrometric approaches for assessing advanced oxidation reactor performance (2016) Water Research, 104, pp. 72-81. Cited nine times. DOI: 10.1016/j.watres.2016.07.056.

AFFILIATIONS: Agricultural and Environmental Chemistry Graduate Group, University of California, One Shields Ave., Davis, CA 95616, United States; Department of Civil and Environmental Engineering, University of California, One Shields Ave., Davis, CA 95616, United States; US Environmental Protection Agency, 26 Martin Luther King Dr. W., Cincinnati, OH 45220, United States.

ABSTRACT: ***High resolution mass spectrometry (HR-MS) offers the opportunity to track large numbers of non-target analytes through water treatment processes, providing a more comprehensive view of reactor performance than targeted evaluation. Both approaches were used to evaluate the performance of a pilot scale advanced oxidation process (AOP) employing ultraviolet light and hydrogen peroxide (UV/H2O2) to treat municipal wastewater effluent.*** Twelve pharmaceuticals and personal care products were selected as target compounds and added to reactor influent. ***Target compound removal over a range of flow rates and hydrogen peroxide addition levels was assessed using a liquid chromatograph combined with a quadrupole time-of-flight mass spectrometer (LC-qTOF-MS).*** Target compound removals were used to determine hydroxyl radical concentrations and UV

fluence under pilot scale conditions. The experiments were also analyzed using a nontarget approach, which identified "molecular features" in either reactor influent or effluent. Strong correlation (r = 0.94) was observed between target compound removals calculated using the targeted and non-targeted approaches across the range of reactor conditions tested. The two approaches also produced consistent rankings of the performance of the various reactor operating conditions, ***although the distribution of compound removal efficiencies was usually less favorable with the broader, nontarget approach.*** For example, in the UV only treatment 8.3% of target compounds and 2.2% of non-target compounds exhibited removals above 50%, while 100% of target compounds and 74% of non-target compounds exhibited removals above 50% in the best condition tested. ***These results suggest that HR-MS methods can provide more holistic evaluation of reactor performance, and may reduce biases caused by selection of a limited number of target compounds. HR-MS methods also offer insights into the composition of poorly removed compounds and the formation of transformation products, which were widely detected.***
AUTHOR KEYWORDS: Advanced oxidation; LC-QTOF-MS; Non-target analysis; Pharmaceuticals and personal care products; Wastewater
DOCUMENT TYPE: Article

12/6/18 SCOPUS Search by author and keywords
AUTHOR-NAME **(*hoh,*** AND ***e*) AND** TITLE-ABS-KEY **(*water* OR *non-target* OR *unknown* OR *suspect* OR *disinfection* OR *spectrometry*) gave 32 results.**

Titaley, I.A., Ogba, O.M., Chibwe, L., Hoh, E., Cheong, P.H.-Y., Simonich, S.L.M. Automating data analysis for two-dimensional gas chromatography/time-of-flight mass spectrometry non-targeted analysis of comparative samples (2018) Journal of Chromatography A, 1541, pp. 57-62. Cited one time.
DOI: 10.1016/j.chroma.2018.02.016.

AFFILIATIONS: Department of Chemistry, Oregon State University, Corvallis, OR 97331, United States; Department of Chemistry, Pomona College, Claremont, CA 91711, United States; Graduate School of Public Health, San Diego State University, San Diego, CA 92182, United States; Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, OR 97331, United States; Man-Technology-Environment Research Centre (MTM), School of Science and Technology, Örebro University, Örebro, SE-701 82, Sweden; Canada Centre for Inland Waters, Burlington, Ontario L7S 1A1, Canada.

ABSTRACT: ***Non-targeted analysis of environmental samples, using comprehensive two-dimensional gas chromatography coupled with time-of-flight mass spectrometry (GC × GC/ToF-MS), poses significant data analysis challenges due to the large number of possible analytes.*** Non-targeted data analysis of complex mixtures is prone to human bias and is laborious, particularly for comparative environmental samples such as contaminated soil pre- and post-bioremediation. ***To address this research bottleneck, we developed OCTpy, a Python™ script that acts as a data reduction filter to automate GC × GC/ToF-MS data analysis from LECO® ChromaTOF® software and facilitates selection of analytes of interest based on peak area comparison between comparative samples.*** We used data from polycyclic aromatic hydrocarbon (PAH) contaminated soil, pre- and post-bioremediation, to assess the effectiveness of OCTpy in facilitating the selection of analytes that have formed or degraded following treatment. ***Using datasets from the soil extracts pre- and post-bioremediation, OCTpy selected, on average, 18% of the initial suggested analytes generated by the LECO® ChromaTOF® software Statistical Compare feature. Based on this list, 63-100% of the candidate analytes identified by a highly trained individual were also selected by OCTpy. This process was accomplished in several minutes per sample, whereas manual data analysis took several hours per sample. OCTpy automates the analysis of complex mixtures of comparative samples, reduces the potential for human error during heavy data handling and decreases data analysis time by at least tenfold.*** © 2018 Elsevier B.V.

AUTHOR KEYWORDS: GC × GC/ToF-MS; LECO® ChromaTOF®; Non-targeted analysis; Python™; Statistical compare
DOCUMENT TYPE: Article

Chibwe, L., Titaley, I.A., Hoh, E., Simonich, S.L.M. Integrated Framework for Identifying Toxic Transformation Products in Complex Environmental Mixtures (2017) Environmental Science and Technology Letters, 4 (2), pp. 32-43. Cited eight times. DOI: 10.1021/acs.estlett.6b00455.

AFFILIATIONS: Department of Chemistry, Oregon State University, Corvallis, Oregon 97331, United States; Graduate School of Public Health, San Diego State University, San Diego, California 92182, United States; Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, Oregon 97331, United States.

ABSTRACT: ***Complex environmental mixtures consist of hundreds to thousands of unknown and unregulated organic compounds that may have toxicological relevance, including transformation products (TPs) of anthropogenic organic pollutants. Nontargeted analysis and suspect screening analysis offer analytical approaches for potentially identifying these toxic transformation products. However, additional tools and strategies are needed to reduce the number of chemicals of interest and focus analytical efforts on chemicals that may pose risks to humans and the environment. This brief review highlights recent developments in this field and suggests an integrated framework that incorporates complementary instrumental techniques, computational chemistry, and toxicity analysis, for prioritizing and identifying toxic TPs in the environment.*** © 2017 American Chemical Society.
DOCUMENT TYPE: Review

Shaul, N.J., Dodder, N.G., Aluwihare, L.I., Mackintosh, S.A., Maruya, K.A., Chivers, S.J., Danil, K., Weller, D.W., Hoh, E. Nontargeted biomonitoring of halogenated organic compounds in two ecotypes of bottlenose dolphins (tursiops truncatus) from the Southern California bight (2015) Environmental Science and Technology, 49 (3), pp. 1328-1338. Cited 27 times. DOI: 10.1021/es505156q.

AFFILIATIONS: Center for Oceans and Human Health, Scripps Institution of Oceanography, University of California-San Diego, 9500 Gilman Drive, San Diego, CA 92037, United States; Scripps Institution of Oceanography, University of California-San Diego, 9500 Gilman Drive, San Diego, CA 92037, United States; Southern California Coastal Water Research Project Authority, 3535 Harbor Boulevard, Costa Mesa, CA 92626, United States; Graduate School of Public Health, San Diego State University, 5500 Campanile Drive, San Diego, CA 92182, United States; San Diego State University Research Foundation, 5250 Campanile Drive, San Diego, CA 92182, United States; Marine Mammal and Turtle Division, Southwest Fisheries Science Center, National Marine Fisheries Service, 8901 La Jolla Shores Drive, San Diego, CA 92037, United States.

ABSTRACT: Targeted environmental monitoring reveals contamination by known chemicals, but may exclude potentially pervasive but unknown compounds. Marine mammals are sentinels of persistent and bioaccumulative contaminants due to their longevity and high trophic position. ***Using nontargeted analysis, we constructed a mass spectral library of 327 persistent and bioaccumulative compounds identified in blubber from two ecotypes of common bottlenose dolphins (Tursiops truncatus) sampled in the Southern California Bight. This library of halogenated organic compounds (HOCs) consisted of 180 anthropogenic contaminants, 41 natural products, four with mixed sources, eight with unknown sources, and 94 with partial structural characterization and unknown sources.*** The abundance of compounds whose structures could not be fully elucidated highlights the prevalence of undiscovered HOCs accumulating in marine food webs. Eighty-six percent of the identified compounds are not currently monitored, including 133 known anthropogenic chemicals. Compounds related to dichlorodiphenyltrichloroethane (DDT) were the most abundant. Natural products were, in some cases, detected at abundances similar to anthropogenic compounds. The profile of naturally occurring HOCs

differed between ecotypes, suggesting more abundant offshore sources of these compounds. ***This nontargeted analytical framework provided a comprehensive list of HOCs that may be characteristic of the region, and its application within monitoring surveys may suggest new chemicals for evaluation.*** © 2014 American Chemical Society.
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Manzano, C., Hoh, E., Simonich, S.L.M. Quantification of complex polycyclic aromatic hydrocarbon mixtures in standard reference materials using comprehensive two-dimensional gas chromatography with time-of-flight mass spectrometry (2013) Journal of Chromatography A, 1307, pp. 172-179. Cited 24 times. DOI: 10.1016/j.chroma.2013.07.093.

AFFILIATIONS: Department of Chemistry, Oregon State University, Corvallis, OR, United States; Graduate School of Public Health, San Diego State University, San Diego, CA, United States; Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, OR, United States.

ABSTRACT: **This research is the first to quantify complex PAH mixtures in NIST SRMs using comprehensive two-dimensional gas chromatography coupled to time-of-flight mass spectrometry (GC. ×. GC/ToF-MS), with and without extract cleanup, and reports previously unidentified PAH congeners in the NIST SRMs.** We tested a novel, high orthogonality GC column combination (LC-50. ×. NSP-35), as well as with a commonly used column combination (Rtx-5ms. ×. Rxi-17) for the quantification of a complex mixture of 85 different PAHs, including parent (PAHs), alkyl- (MPAHs), nitro- (NPAHs), oxy- (OPAHs), thio- (SPAHs), bromo- (BrPAHs), and chloro-PAHs (ClPAHs) in extracts from two standard reference materials: NIST SRM1650b (diesel particulate matter), with cleanup and NIST SRM1975 (diesel particulate extract), with and without extract cleanup. The LC-50. ×. NSP-35 column combination resulted in an average absolute percent difference of 33.8%, 62.2% and 30.8% compared to the NIST certified PAH concentrations for NIST SRM1650b, NIST SRM1975 with cleanup and NIST SRM1975 without cleanup, while the Rtx-5ms. ×. Rxi-17 resulted in an absolute percent difference of 38.6%, 67.2% and 79.6% for NIST SRM1650b, NIST SRM1975 with cleanup and NIST SRM1975 without cleanup, respectively. This GC. ×. GC/ToF-MS method increases the number of PAHs detected and quantified in complex environmental extracts using a single chromatographic run. Without clean-up, seven additional compounds were detected and quantified in NIST SRM1975 using the LC-50. ×. NSP-35 column combination. ***These results suggest that the use of the LC-50. ×. NSP-35 column combination in GC. ×. GC/ToF-MS not only results in better chromatographic resolution and greater orthogonality for the separation of complex PAH mixtures, but can also be used for the accurate quantification of complex PAH mixtures in environmental extracts, such as diesel particulate matter, without silica gel cleanup.*** © 2013 Elsevier B.V.
AUTHOR KEYWORDS: Complex environmental samples; Comprehensive two-dimensional gas chromatography; PAHs; Quantitation of POPs; ToF-MS
DOCUMENT TYPE: Article

Hoh, E., Dodder, N.G., Lehotay, S.J., Pangallo, K.C., Reddy, C.M., Maruya, K.A. Nontargeted comprehensive two-dimensional gas chromatography/time-of-flight mass spectrometry method and software for inventorying persistent and bioaccumulative contaminants in marine environments (2012) Environmental Science and Technology, 46 (15), pp. 8001-8008. Cited 51 times. DOI: 10.1021/es301139q.

AFFILIATIONS: Graduate School of Public Health, San Diego State University, 5500 Campanile Drive, San Diego, CA 92182, United States; Southern California Coastal Water Research Project, 3535 Harbor Boulevard, Costa Mesa, CA 92626, United States; Eastern Regional Research Center, Agricultural Research Service, U.S. Department of Agriculture, 600 East Mermaid Lane, Wyndmoor, PA 19038,

United States; Department of Chemistry, Colgate University, 13 Oak Drive, Hamilton, NY 13446, United States; Department of Marine Chemistry and Geochemistry, Woods Hole Oceanographic Institution, Woods Hole, MA 02543, United States.

ABSTRACT: Analytical methods for contaminant monitoring are generally targeted; i.e., they measure defined lists of compounds. Routine monitoring projects using targeted methods are not usually designed to screen for unrecognized or novel contaminants and therefore miss compounds within the region or population of study that cause, or have the potential to cause, adverse biological impacts. ***We describe a nontargeted analytical method utilizing direct sample introduction coupled to comprehensive two-dimensional gas chromatography with time-of-flight mass spectrometry.*** To test the capabilities of this instrumental method within the context of marine contaminant surveys, we characterized a broad array of nonpolar, persistent, and bioaccumulative contaminants in Atlantic common dolphin (Delphinus delphis) blubber, including compounds that are not typically monitored. Compound identifications were made by searching a standard reference database, by contemporaneously analyzing mass spectra from reference standards, and by de novo interpretation. ***We identified a total of 271 compounds belonging to 24 classes; all compounds but 1 were halogenated. Anthropogenic contaminants and halogenated natural products were concurrently detected. A total of 86 compounds were anthropogenic contaminants that are not routinely targeted in environmental surveys, and 54 compounds were halogenated natural products. A total of 112 spectra were identified de novo, demonstrating that exclusive reliance on commercially available reference standards and mass spectral libraries may miss a significant fraction of identifiable compounds. We also cataloged 27 halogenated mass spectra that were not able to be identified.*** Due to the volume and complexity of the identification data, we developed custom software to organize and provide shared access to the identified mass spectra and related information. The nontargeted analytical method and data reporting system, in combination with the analysis of a high-trophic-level sentinel species, demonstrates a framework for creating an inventory of persistent and bioaccumulative contaminants in marine environments, with the future goal of suggesting new compounds for further investigation by targeted monitoring and risk assessment. © 2012 American Chemical Society.
DOCUMENT TYPE: Article

Manzano, C., Hoh, E., Simonich, S.L.M. Improved separation of complex polycyclic aromatic hydrocarbon mixtures using novel column combinations in GC × GC/ToF-MS (2012) Environmental Science and Technology, 46 (14), pp. 7677-7684. Cited 30 times. DOI: 10.1021/es301790h.

AFFILIATIONS: Department of Chemistry, Oregon State University, Corvallis, OR, United States; Graduate School of Public Health, San Diego State University, San Diego, CA, United States; Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, OR, United States

ABSTRACT: Complex mixtures of polycyclic aromatic hydrocarbons (PAHs) are difficult to resolve because of the high degree of overlap in compound vapor pressures, boiling points, and mass spectral fragmentation patterns. ***The objective of this research was to improve the separation of complex PAH mixtures (including 97 different parent, alkyl-, nitro-, oxy-, thio-, chloro-, bromo-, and high molecular weight PAHs) using GC × GC/ToF-MS by maximizing the orthogonality of different GC column combinations and improving the separation of PAHs from the sample matrix interferences, including unresolved complex mixtures (UCM).*** Four different combinations of nonpolar, polar, liquid crystal, and nanostationary phase columns were tested. Each column combination was optimized and evaluated for orthogonality using a method based on conditional entropy that considers the quantitative peak distribution in the entire 2D space. Finally, an atmospheric particulate matter with diameter <2.5 μm (PM2.5) sample from Beijing, China, a soil sample from St. Maries Creosote Superfund Site, and a sediment sample from the Portland Harbor Superfund Site were analyzed for complex mixtures of PAHs. The highest chromatographic resolution, lowest synentropy, highest orthogonality, and lowest

interference from UCM were achieved using a 10 m × 0.15 mm × 0.10 µm LC-50 liquid crystal column in the first dimension and a 1.2 m × 0.10 mm × 0.10 µm NSP-35 nanostationary phase column in the second dimension. ***In addition, the use of this column combination in GC × GC/ToF-MS resulted in significantly shorter analysis times (176 min) for complex PAH mixtures compared to 1D GC/MS (257 min), as well as potentially reduced sample preparation time.*** © 2012 American Chemical Society.
DOCUMENT TYPE: Article

Hoh, E., Mastovska, K., Lehotay, S.J. Optimization of separation and detection conditions for comprehensive two-dimensional gas chromatography-time-of-flight mass spectrometry analysis of polychlorinated dibenzo-p-dioxins and dibenzofurans (2007) Journal of Chromatography A, 1145 (1-2), pp. 210-221. Cited 34 times. DOI: 10.1016/j.chroma.2007.01.064.

AFFILIATIONS: US Department of Agriculture, Agricultural Research Service, Eastern Regional Research Center, 600 East Mermaid Lane, Wyndmoor, PA 19038, United States.

ABSTRACT: ***The 2,3,7,8-substituted polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are among the most toxic compounds known, and several sources of exposure to these chemicals should be monitored to protect human and environmental health. The current predominant method of analysis is too expensive and cumbersome, and comprehensive two-dimensional GC coupled to time-of-flight mass spectrometry (GC × GC-TOF-MS) has the potential to lower the costs and speed analysis of PCDD/Fs.*** In this study, GC × GC-TOF parameters were evaluated and optimized to yield complete separation of the 17 most important PCDD/F congeners from polychlorinated biphenyls (PCBs) interferences, and to attain the lowest detection limits. The optimization study entailed evaluation of oven temperature programs, column flow rates, ion source temperatures, electron ionization energy, data acquisition rate, and various GC × GC parameters, including modulation period, modulator temperature offset and hot pulse duration. ***After optimization, all 17 PCDD/Fs were separated in <60 min, and in particular, the critical pair of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and pentachlorobiphenyl congener CB126 did not co-elute chromatographically. Accurate identification and determination of all analytes could be made using their deconvoluted full mass spectra.*** In GC × GC, the modulation period and start time were the most important factors that affected sensitivity and selectivity for the analysis of the PCDD/Fs. The modulation period should be ≤4 s to preserve separations achieved in one-dimensional GC, and the modulation start time was important to achieve one large slice and two smaller symmetrical slices of TCDD to maximize its detection sensitivity. ***After optimization, the method could identify 0.25 pg of TCDD with standard injection from its full mass spectrum.***
AUTHOR KEYWORDS: Comprehensive gas chromatography; Polychlorinated dibenzo-p-dioxin; Polychlorinated dibenzofuran; Time-of-flight mass spectrometry
DOCUMENT TYPE: Article

12/6/18 SCOPUS Search by author and keywords
AUTHOR-NAME **(*gardinali,*** AND ***p*) AND** TITLE-ABS-KEY **(*water* OR *non-target* OR *unknown* OR *suspect* OR *disinfection* OR *spectrometry*) gave 80 results.**

Aceña, J., Heuett, N., Gardinali, P., Pérez, S. Suspect Screening of Pharmaceuticals and Related Bioactive Compounds, Their Metabolites and Their Transformation Products in the Aquatic Environment, Biota and Humans Using LC-HR-MS Techniques (2016) Comprehensive Analytical Chemistry, 71, pp. 357-378. Cited four times. DOI: 10.1016/bs.coac.2016.02.011.

AFFILIATIONS: Inst. of Environmental Assessment and Water Res. - Spanish National Research Council (IDAEA-CSIC), Barcelona, Spain; Florida International University, Miami, FL, United States.

ABSTRACT: The interdisciplinary nature of the field of high-resolution mass spectrometry (HRMS) has substantially broadened the possibilities in the environmental, forensic and clinical fields with numerous advances in each of the areas or a combination of them. ***Through a multitude of studies reported to date, presence of several hundreds of microconstituents, ranging from pesticides, drugs of abuse, pharmaceuticals and personal care products, in water and soil matrices originating from anthropogenic activities has been confirmed. This chapter presents a general overview regarding the capabilities of HRMS coupled to liquid chromatography (LC) and its applications in monitoring human pollution using a qualitative approach called suspect screening. This is the simplest form of qualitative analysis in HRMS in which some information of the suspected analytes is collected a priori.*** Three main areas are discussed in this chapter: the review focuses on many studies carried out with LC-HRMS in the field of suspect screening in wastewaters, in surface waters and biota. ***In particular the book chapter describes different workflows for the detection and identification of transformation products and metabolites applying suspect screening approaches.***
AUTHOR KEYWORDS: Fish; High-resolution mass spectrometry; Human metabolites; Plants; Polar organic compounds; Surface waters; Suspect screening; Transformation products; Wastewater
DOCUMENT TYPE: Book Chapter

Wang, J., Gardinali, P.R. Identification of phase II pharmaceutical metabolites in reclaimed water using high resolution benchtop Orbitrap mass spectrometry (2014) Chemosphere, 107, pp. 65-73. Cited 19 times. DOI: 10.1016/j.chemosphere.2014.03.021.

AFFILIATIONS: Department of Chemistry and Biochemistry, Florida International University, Miami, FL, United States; Southeast Environmental Research Center, Florida International University, Miami, FL, United States.

ABSTRACT: ***This study described an analytical method for the identification of common phase II pharmaceutical metabolites in reclaimed water using liquid chromatography high resolution Orbitrap mass spectrometry after solid phase extraction (SPE).*** Orbitrap mass spectrometer was operated at resolution of 70000 in MS mode and 35000 in data-dependent MS/MS mode, without using lock mass. ***Firstly, parent drugs and their metabolites were tentatively identified based on accurate mass using a mass tolerance of 5 ppm. A detailed examination of the extracted ion chromatograms (XICs) for all potential metabolites revealed the presence of two phase II metabolites of sulfamethoxazole, acetylsulfamethoxazole and sulfamethoxazole glucuronide in reclaimed water.*** Secondly, the high resolution data-dependent MS/MS spectra of each compound were further investigated using metabolic profiling software. After comparing characteristic ions obtained in MS/MS mode with those predicted by the software and reported in previous studies, the two phase II metabolites were positively identified in reclaimed water. Lastly, the two metabolites were detected and quantified in the reclaimed water samples collected during a period of one month. ***As a result, averaged concentrations of sulfamethoxazole, acetylsulfamethoxazole and sulfamethoxazole glucuronide were calculated at 2848±1367ngL-1, 1980±1410ngL-1, and 2859±1526ngL-1, respectively.*** The two metabolites represented 54% of the source of sulfamethoxazole in reclaimed water suggesting the importance of measuring pharmaceutical metabolites in the environment. ***To our knowledge, this is the first known report of sulfamethoxazole glucuronide surviving intact through wastewater treatment plants and occurring in environmental water samples.***
AUTHOR KEYWORDS: High resolution mass spectrometry; Metabolites; Orbitrap; Pharmaceuticals; Reclaimed water
DOCUMENT TYPE: Article

Ramirez, C.E., Wang, C., Gardinali, P.R. Fully automated trace level determination of parent and alkylated PAHs in environmental waters by online SPE-LC-APPI-MS/MS (2014) Analytical and Bioanalytical Chemistry, 406 (1), pp. 329-344. Cited 20 times. DOI: 10.1007/s00216-013-7436-6.

AFFILIATIONS: Department of Chemistry and Biochemistry, Florida International University, FIU Biscayne Bay Campus, 3000 NE 151st ST, MSB-350, North Miami Beach, FL 33181, United States; Southeast Environmental Research Center, Florida International University, FIU Biscayne Bay Campus, 3000 NE 151st ST, MSB-350, North Miami Beach, FL 33181, United States.

ABSTRACT: ***Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous compounds that enter the environment from natural and anthropogenic sources, often used as markers to determine the extent, fate, and potential effects on natural resources after a crude oil accidental release. Gas chromatography-mass spectrometry (GC-MS) after liquid-liquid extraction (LLE+GC-MS) has been extensively used to isolate and quantify both parent and alkylated PAHs. However, it requires labor-intensive extraction and cleanup steps and generates large amounts of toxic solvent waste. Therefore, there is a clear need for greener, faster techniques with enough reproducibility and sensitivity to quantify many PAHs in large numbers of water samples in a short period of time. This study combines online solid-phase extraction followed by liquid chromatography (LC) separation with dopant-assisted atmospheric pressure photoionization (APPI) and tandem MS detection, to provide a one-step protocol that detects PAHs at low nanograms per liter with almost no sample preparation and with a significantly lower consumption of toxic halogenated solvents.*** Water samples were amended with methanol, fortified with isotopically labeled PAHs, and loaded onto an online SPE column, using a large-volume sample loop with an auxiliary LC pump for sample preconcentration and salt removal. The loaded SPE column was connected to an UPLC pump and analytes were backflushed to a Thermo Hypersil Green PAH analytical column where a 20-min gradient separation was performed at a variable flow rate. Detection was performed by a triplequadrupole MS equipped with a gas-phase dopant delivery system, using 1.50 mL of chlorobenzene dopant per run. In contrast, LLE+GC-MS typically use 150 mL of organic solvents per sample, and methylene chloride is preferred because of its low boiling point. However, this solvent has a higher environmental persistence than chlorobenzene and is considered a carcinogen. The automated system is capable of performing injection, online SPE, inorganic species removal, LC separation, and MS/MS detection in 28 min. ***Selective reaction monitoring was used to detect 28 parent PAHs and 15 families of alkylated PAHs. The methodology is comparable to traditional GC-MS and was tested with surface seawater, rainwater runoff, and a wastewater treatment plant effluent. Positive detections above reporting limits are described. The virtual absence of sample preparation could be particularly advantageous for real-time monitoring of discharge events that introduce PAHs into environmental compartments, such as accidental releases of petroleumderivates and other human-related events. This work covers optimization of APPI detection and SPE extraction efficiency, a comparison with LLE+GC-MS in terms of sensitivity and chromatographic resolution, and examples of environmental applications.*** © Springer-Verlag Berlin Heidelberg 2013.

AUTHOR KEYWORDS: Alkylated PAHs; Dopant-assisted APPI; Gas-phase dopant delivery; LC-MS/MS; Online SPE; PAHs; Rainwater runoff; Reclaimed water; Seawater
DOCUMENT TYPE: Article

Aceña, J., Pérez, S., Gardinali, P., Abad, J.L., Eichhorn, P., Heuett, N., Barceló, D. Structure elucidation of phototransformation products of unapproved analogs of the erectile dysfunction drug sildenafil in artificial freshwater with UPLC-Q Exactive-MS (2014) Journal of Mass Spectrometry, 49 (12), pp. 1279-1289. Cited eight times. DOI: 10.1002/jms.3461.

AFFILIATIONS: IDAEA-CSIC, Water and Soil Quality Research Group, Jordi Girona 18-26, Barcelona, 08034, Spain; Florida International University, 11200 SW 8th Street, Miami, FL 33199-0001, United States; IQAC-CSIC, Department of Biomedicinal Chemistry, Jordi Girona 18-26, Barcelona, 08034, Spain; Catalan Institute of Water Research, ICRA Catalan Institute for Water Research-ICRA, Parc Científic i Tecnològic de la Universitat de Girona, C/Emili Grahit, 101, Girona, E-17003, Spain.

ABSTRACT: ***In this study, four unapproved analogues of Sildenafil (SDF) were photodegraded under synthetic sunlight in artificial freshwater. Homosildenafil (H-SDF), hydroxyhomo-sildenafil (HH-SDF), norneosildenafil (NR-SDF) and thiosildenafil (T-SDF) were selected because they are frequently detected as adulterants in natural herbal products. Using UPLC-Orbitrap (QExactive)-MS, six photoproducts common to H-SDF, HH-SDF and T-SDF and nine unique transformation products of different molecular weights were identified based on their high-resolution (+)ESI product ion spectra***. Mass spectral analysis of deuterated H-SDF, labeled on the N-ethyl group, allowed to gain mechanistic insight into the fragmentation pathway of the substituted piperazine ring and to support the postulated photoproduct structures. The mass spectral fragmentation confirmed the stepwise destruction of the piperazine ring eventually producing a sulfonic acid derivative (C<inf>17</inf>H<inf>20</inf>N<inf>4</inf>O<inf>5</inf>S: 392.1151Da). In contrast, the photodegradation of NR-SDF, which lacks a piperazine ring in its structure, formed only two prominent photoproducts originating from N,Ndealkylation of the sulfonamide followed by hydrolysis. ***The current work constitutes the first study on the photodegradation of analogs of erectile dysfunction drugs and the first detection of two transformation products (m/z 449 and 489) in environmental samples.***

AUTHOR KEYWORDS: Analogs of erectile dysfunction drugs; High-resolution mass spectrometry; Photolysis; Transformation products
DOCUMENT TYPE: Article

Batchu, S.R., Quinete, N., Panditi, V.R., Gardinali, P.R. Online solid phase extraction liquid chromatography tandem mass spectrometry (SPE-LC-MS/MS) method for the determination of sucralose in reclaimed and drinking waters and its photo degradation in natural waters from South Florida (2013) Chemistry Central Journal, 7 (1), art. no. 141. Cited 16 times. DOI: 10.1186/1752-153X-7-141.

AFFILIATIONS: Department of Chemistry and Biochemistry, Florida International University, 3000 NE 151st ST, FIU Biscayne Bay Campus, MSB-356, North Miami, FL 33181, United States; Southeast Environmental Research Center (SERC), Florida International University, Miami, FL, United States.

ABSTRACT: Background: Sucralose has gained popularity as a low calorie artificial sweetener worldwide. Due to its high stability and persistence, sucralose has shown widespread occurrence in environmental waters, at concentrations that could reach up to several μg/L. Previous studies have used time consuming sample preparation methods (offline solid phase extraction/derivatization) or methods with rather high detection limits (direct injection) for sucralose analysis. ***This study described a faster and sensitive analytical method for the determination of sucralose in environmental samples. Results: An online SPE-LC-MS/MS method was developed, being capable to quantify sucralose in 12 minutes using only 10 mL of sample, with method detection limits (MDLs) of 4.5 ng/L, 8.5 ng/L and 45 ng/L for deionized water, drinking and reclaimed waters (1:10 diluted with deionized water), respectively. Sucralose was detected in 82% of the reclaimed water samples at concentrations reaching up to 18 μg/L. The monthly average for a period of one year was 9.1 ± 2.9 μg/L. The calculated mass loads per capita of sucralose discharged through WWTP effluents based on the concentrations detected in wastewaters in the U. S. is 5.0 mg/day/person*. As expected, the concentrations observed in drinking water were much lower but still relevant reaching as high as 465 ng/L.** In order to evaluate the stability of sucralose, photodegradation experiments were performed in natural waters. Significant photodegradation of sucralose was observed only in freshwater at 254 nm. Minimal degradation (<20%) was observed for all matrices under more natural conditions (350 nm or solar simulator). The only photolysis product of sucralose identified by high resolution mass spectrometry was a de-chlorinated molecule at m/z 362.0535, with molecular formula C12H20Cl2O8. ***Conclusions: Online SPE LC-APCI/MS/MS developed in the study was applied to more than 100 environmental samples.***

Sucralose was frequently detected (>80%) indicating that the conventional treatment process employed in the sewage treatment plants is not efficient for its removal. Detection of sucralose in drinking waters suggests potential contamination of surface and ground waters sources with anthropogenic wastewater streams. Its high resistance to photodegradation, minimal sorption and high solubility indicate that sucralose could be a good tracer of anthropogenic wastewater intrusion into the environment. © 2013 Batchu et al.; licensee Chemistry Central Ltd.
AUTHOR KEYWORDS: Artificial sweetener; Degradation products; Drinking water; High resolution mass spectrometry; Online SPE; Photo degradation; Reclaimed waters; Sucralose
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Wang, C., Gardinali, P.R. Detection and occurrence of microconstituents in reclaimed water used for irrigation - A potentially overlooked source (2013) Analytical and Bioanalytical Chemistry, 405 (18), pp. 5925-5935. Cited eight times. DOI: 10.1007/s00216-013-6799-z.

AFFILIATIONS: Department of Chemistry and Biochemistry, Florida International University, 3000 NE 151st Street, North Miami, FL 33181, United States.

ABSTRACT: ***An online SPE-HPLC-HESI-MS/MS method and an online SPE-HPLC-APPI-MS/MS method were developed to analyze 72 microconstituents in reclaimed water. In this study, 55 reclaimed water samples were collected from the sprinkler system for a year-long period at Florida International University Biscayne Bay Campus, where reclaimed water was reused for daily irrigation.*** Analysis results showed that several analytes were continuously detected in all reclaimed water samples and others will show rather transient signal increases. ***Coprostanol, bisphenol A, and DEET's maximum concentration exceeded 10,000 ng/L. The four most frequently detected compounds were diphenhydramine (100%), DEET (98%), atenolol (98%) and carbamazepine (96%).*** © 2013 Springer-Verlag Berlin Heidelberg.
AUTHOR KEYWORDS: APPI; HESI; Irrigation; LC-MS/MS; Microconstituents; Reclaimed water
DOCUMENT TYPE: Conference Paper

Panditi, V.R., Batchu, S.R., Gardinali, P.R. Online solid-phase extraction-liquid chromatography-electrospray-tandem mass spectrometry determination of multiple classes of antibiotics in environmental and treated waters

(2013) Analytical and Bioanalytical Chemistry, 405 (18), pp. 5953-5964. Cited 27 times. DOI: 10.1007/s00216-013-6863-8.

AFFILIATIONS: Department of Chemistry and Biochemistry, Florida International University, Biscayne Bay Campus, 3000 NE 151 Street, North Miami, FL 33181, United States; Southeast Environmental Research Center, Florida International University, 11200 SW 8th Street, Miami, FL 33199, United States.

ABSTRACT: ***An online solid-phase extraction and liquid chromatography in combination with tandem mass spectrometry method was developed for the simultaneous determination of 31 antibiotics in drinking water, surface water and reclaimed waters. The developed methodology requires small sample volume (10 mL), very little sample preparation and total sample run time was 20 min.*** An Ion Max API heated electrospray ionization source operated in the positive mode with two selected reaction monitoring transitions was used per antibiotic for positive identity and quantification performed by the internal standard approach, to correct for matrix effects and any losses in the online extraction step. ***Method detection limits were in the range of 1.2-9.7, 2.2-15, 5.5-63 ng/L in drinking water, surface water and reclaimed waters, respectively.*** The method accuracy in matrix spiked samples ranged from 50-150% for the studied antibiotics. The applicability of the method was demonstrated using various environmental and reclaimed water matrices. Erythromycin was detected in more than 85% of the

samples in all matrices (28-414, n.d.-199, n.d.-66 ng/L in reclaimed, river and drinking waters respectively). The other frequently detected antibiotics in reclaimed waters were nalidixic acid, clarithromycin, azithromycin, trimethoprim, and sulfamethoxazole. © 2013 Springer-Verlag Berlin Heidelberg.
AUTHOR KEYWORDS: Antibiotics; Drinking water; Online SPE; Reclaimed water; Surface water; Tandem mass spectrometry
DOCUMENT TYPE: Conference Paper

Wang, C., Gardinali, P.R. Comparison of multiple API techniques for the simultaneous detection of microconstituents in water by on-line SPE-LC-MS/MS

(2012) Journal of Mass Spectrometry, 47 (10), pp. 1255-1268. Cited 24 times. DOI: 10.1002/jms.3051.

AFFILIATIONS: Florida International University, Department of Chemistry and Biochemistry, Miami, FL, United States; Florida International University, Department of Chemistry and Biochemistry, Southeast Environmental Research Center, 3000 NE 151st Street, North Miami, FL 33181, United States.

ABSTRACT: ***This study described a fully automated method using on-line solid phase extraction of large volume injections coupled with high performance liquid chromatography (HPLC) and tandem mass spectrometry (MS/MS) to simultaneously detect a group of recalcitrant microconstituents (pharmaceuticals and personal care products, steroid hormones and sterols) in aqueous matrices.*** Samples (1 mL to 20 mL) were loaded to the preconcentration column at 1 mL/min, and the column was washed with 1000 µL of 25% methanol in LC/MS water to remove polar and ionic interferences before LC-MS/MS analysis. ***Three different atmospheric pressure ionization (API) techniques, including photoionization (APPI) with four different dopants (acetone, anisole, chlorobenzene and toluene), heated electrospray ionization (HESI) and atmospheric pressure chemical ionization (APCI), were evaluated on the basis of method detection limits (MDLs) and recoveries from different aqueous matrixes. Results indicated that APPI with toluene as dopant was the most sensitive ionization method for the majority of the analytes. When using 5 mL of sample, MDLs for pharmaceuticals and personal care products, including carbamazepine, DEET, caffeine, naproxen, acetaminophen and primidone, were between 0.3 ng/L and 15 ng/L. MDLs of hormones, including testosterone, equilenin, progesterone, equilin, 17β-estradiol, 17α-ethynylestradiol, estrone, androsterone, mestranol and estriol, were between 1.2 ng/L and 37 ng/L. The combination of APPI with dopant allowed the detection of two difficult to ionize fecal related sterols, such as coprostan-3-ol and coprostan-3-one with MDLs of 5.4 ng/L and 11 ng/L, respectively. Calculated MDLs are more than adequate for analysis of wastewater using 1 to 5 mL sample size and for surface waters using up to 20 mL sample size.***

AUTHOR KEYWORDS: APCI; APPI; HESI; hormones; on-line SPE; PPCPs
DOCUMENT TYPE: Article

Gardinali, P.R., Zhao, X. Trace determination of caffeine in surface water samples by liquid chromatography - Atmospheric pressure chemical ionization - Mass spectrometry (LC-APCI-MS) (2002) Environment International, 28 (6), pp. 521-528. Cited 74 times. DOI: 10.1016/S0160-4120(02)00080-6.

AFFILIATIONS: Southeast Environ. Research Center, Florida International University, University Park Campus, Miami, FL 33199, United States; Department of Chemistry, Florida International University, University Park Campus, Miami, FL 33199, United States.

ABSTRACT: ***A new method based on liquid-liquid extraction (LLE) coupled to reverse phase liquid chromatography and atmospheric pressure chemical ionization mass spectrometry (LC-APCI-MS) has been applied to determine trace amounts of caffeine (1,3,7-trimethylxanthine) in surface water samples from a near coastal ecosystem such as Biscayne Bay, Florida***. The rationale behind the

development of such method will be to evaluate the use of unmetabolized caffeine as a potential dissolved phase tracer of human waste contamination. ***The method allows for the determination of caffeine at levels as low as 4.0 ng/l (ppt) in both salt and freshwater by extracting and concentrating a 1-1 water sample to a final volume of 500 µl and using HPLC separation coupled to an atmospheric pressure chemical ionization mass spectrometry (APCI-MS) system operated in selected ion monitoring (SIM) for the protonated molecular ions (M+H+)***. Samples from different portions of Biscayne Bay and the Miami River, one of its major tributaries, were analyzed and caffeine was detected in those areas previously identified for consistently exceeding the water quality criteria for fecal coliform bacteria contamination. The caffeine concentration in the samples with positive detection was generally low at levels equal or lower than 41 ng/l. However, there is a marked difference between samples collected in open bay areas and those collected from the Miami River.
AUTHOR KEYWORDS: Caffeine; Dissolved phase tracers; LC-APCI-MS; Wastewater
DOCUMENT TYPE: Review

12/10/18 SCOPUS Search by author and keywords
AUTHOR-NAME **(*schymanski,*** AND ***e*) AND** TITLE-ABS-KEY **(*water* OR *non-target* OR *unknown* OR *suspect* OR *disinfection* OR *spectrometry*) gave 44 results.**

McEachran, A.D., Mansouri, K., Grulke, C., Schymanski, E.L., Ruttkies, C., Williams, A.J. "MS-Ready" structures for non-targeted high-resolution mass spectrometry screening studies (2018) Journal of Cheminformatics, 10 (1), art. no. 45,. DOI: 10.1186/s13321-018-0299-2.

AFFILIATIONS: U.S. Environmental Protection Agency, Oak Ridge Institute for Science and Education (ORISE) Research Participation Program, 109 T.W. Alexander Dr., Research Triangle Park, NC 27711, United States; U.S. Environmental Protection Agency, National Center for Computational Toxicology, Office of Research and Development, 109 T.W. Alexander Dr., Mail Drop D143-02, Research Triangle Park, NC 27711, United States; Integrated Laboratory Systems, Inc., 601 Keystone Dr., Morrisville, NC 27650, United States; University of Luxembourg, Luxembourg Centre for Systems Biomedicine (LCSB), 6, avenue du Swing, Belvaux, 4367, Luxembourg; Leibniz Institute of Plant Biochemistry (IPB), Department of Stress and Development Biology, Weinberg 3, Halle (Saale), 06120, Germany.

ABSTRACT: ***Chemical database searching has become a fixture in many non-targeted identification workflows based on high-resolution mass spectrometry (HRMS). However, the form of a chemical structure observed in HRMS does not always match the form stored in a database (e.g., the neutral form versus a salt; one component of a mixture rather than the mixture form used in a consumer product). Linking the form of a structure observed via HRMS to its related form(s) within a database will enable the return of all relevant variants of a structure, as well as the related metadata, in a single query. A Konstanz Information Miner(KNIME) workflow has been developed to produce structural representations observed using HRMS ("MS-Ready structures") and links them to those stored in a database. These MS-Ready structures, and associated mappings to the full chemical representations, are surfaced via the US EPA's Chemistry Dashboard (https://comptox.epa.gov/dashboard/). This article describes the workflow for the generation and linking of ~700,000 MS-Ready structures (derived from ~760,000 original structures) as well as download, search and export capabilities to serve structure identification using HRMS.*** The importance of this form of structural representation for HRMS is demonstrated with several examples, including integration with the in silico fragmentation software application MetFrag. The structures, search, download and export functionality are all available through the CompTox Chemistry Dashboard, while the MetFrag implementation can be viewed at https://msbi.ipb-halle.de/MetFragBeta/. © 2018 The Author(s).
AUTHOR KEYWORDS: Database searching; High-resolution mass spectrometry (HRMS); Structure

curation; Structure identification
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Alygizakis, N.A., Samanipour, S., Hollender, J., Ibáñez, M., Kaserzon, S., Kokkali, V., Van Leerdam, J.A., Mueller, J.F., Pijnappels, M., Reid, M.J., Schymanski, E.L., Slobodnik, J., Thomaidis, N.S., Thomas, K.V. Exploring the Potential of a Global Emerging Contaminant Early Warning Network through the Use of Retrospective Suspect Screening with High-Resolution Mass Spectrometry (2018) Environmental Science and Technology, 52 (9), pp. 5135-5144. Cited three times. DOI: 10.1021/acs.est.8b00365.

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ABSTRACT: A key challenge in the environmental and exposure sciences is to establish experimental evidence of the role of chemical exposure in human and environmental systems. ***High resolution and accurate tandem mass spectrometry (HRMS) is increasingly being used for the analysis of environmental samples. One lauded benefit of HRMS is the possibility to retrospectively process data for (previously omitted) compounds that has led to the archiving of HRMS data. Archived HRMS data affords the possibility of exploiting historical data to rapidly and effectively establish the temporal and spatial occurrence of newly identified contaminants through retrospective suspect screening. We propose to establish a global emerging contaminant early warning network to rapidly assess the spatial and temporal distribution of contaminants of emerging concern in environmental samples through performing retrospective analysis on HRMS data. The effectiveness of such a network is demonstrated through a pilot study, where eight reference laboratories with available archived HRMS data retrospectively screened data acquired from aqueous environmental samples collected in 14 countries on three different continents. The widespread spatial occurrence of several surfactants (e.g., polyethylene glycols (PEGs) and C12AEO-PEGs), transformation products of selected drugs (e.g., gabapentin-lactam, metoprolol-acid, carbamazepine-10-hydroxy, omeprazole-4-hydroxy-sulfide, and 2-benzothiazole-sulfonic-acid), and industrial chemicals (3-nitrobenzenesulfonate and bisphenol-S) was revealed.*** Obtaining identifications of increased reliability through retrospective suspect screening is challenging, and recommendations for dealing with issues such as broad chromatographic peaks, data acquisition, and sensitivity are provided. © 2018 American Chemical Society.
DOCUMENT TYPE: Article

Hu, M., Müller, E., Schymanski, E.L., Ruttkies, C., Schulze, T., Brack, W., Krauss, M. Performance of combined fragmentation and retention prediction for the identification of organic micropollutants by LC-HRMS (2018) Analytical and Bioanalytical Chemistry, 410 (7), pp. 1931-1941. Cited four times. DOI: 10.1007/s00216-018-0857-5.

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ABSTRACT: ***In nontarget screening, structure elucidation of small molecules from high resolution mass spectrometry (HRMS) data is challenging, particularly the selection of the most likely candidate structure among the many retrieved from compound databases.*** Several fragmentation and retention prediction methods have been developed to improve this candidate selection. ***In order to evaluate their performance, we compared two in silico fragmenters (MetFrag and CFM-ID) and two retention time prediction models (based on the chromatographic hydrophobicity index (CHI) and on log D). A set of 78 known organic micropollutants was analyzed by liquid chromatography coupled to a LTQ Orbitrap HRMS with electrospray ionization (ESI) in positive and negative mode using two fragmentation techniques with different collision energies. Both fragmenters (MetFrag and CFM-ID) performed well for most compounds***, with average ranking the correct candidate structure within the top 25% and 22 to 37% for ESI+ and ESI− mode, respectively. The rank of the correct candidate structure slightly improved when MetFrag and CFM-ID were combined. ***For unknown compounds detected in both ESI+ and ESI–, generally positive mode mass spectra were better for further structure elucidation. Both retention prediction models performed reasonably well for more hydrophobic compounds but not for early eluting hydrophilic substances.*** The log D prediction showed a better accuracy than the CHI model. ***Although the two fragmentation prediction methods are more diagnostic and sensitive for candidate selection, the inclusion of retention prediction by calculating a consensus score with optimized weighting can improve the ranking of correct candidates as compared to the individual methods.*** [Figure not available: see full text.]. © 2018, Springer-Verlag GmbH Germany, part of Springer Nature.
AUTHOR KEYWORDS: Environmental contaminants; Fragmentation prediction; LC-HRMS; Micropollutants; Retention prediction; Structure elucidation
DOCUMENT TYPE: Article

Schollée, J.E., Schymanski, E.L., Stravs, M.A., Gulde, R., Thomaidis, N.S., Hollender, J. Similarity of High-Resolution Tandem Mass Spectrometry Spectra of Structurally Related Micropollutants and Transformation Products (2017) Journal of the American Society for Mass Spectrometry, 28 (12), pp. 2692-2704. Cited four times. DOI: 10.1007/s13361-017-1797-6.

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ABSTRACT: High-resolution tandem mass spectrometry (HRMS2) with electrospray ionization is frequently applied to study polar organic molecules such as micropollutants. Fragmentation provides structural information to confirm structures of known compounds or propose structures of unknown compounds. Similarity of HRMS2 spectra between structurally related compounds has been suggested to facilitate identification of unknown compounds. To test this hypothesis, the similarity of reference standard HRMS2 spectra was calculated for 243 pairs of micropollutants and their structurally related transformation products (TPs); for comparison, spectral similarity was also calculated for 219 pairs of unrelated compounds. ***Spectra were measured on Orbitrap and QTOF mass spectrometers and similarity was calculated with the dot product.*** The influence of different factors on spectral similarity [e.g., normalized collision energy (NCE), merging fragments from all NCEs, and shifting fragments by the

mass difference of the pair] was considered. ***Spectral similarity increased at higher NCEs and highest similarity scores for related pairs were obtained with merged spectra including measured fragments and shifted fragments.*** Removal of the monoisotopic peak was critical to reduce false positives. Using a spectral similarity score threshold of 0.52, 40% of related pairs and 0% of unrelated pairs were above this value. Structural similarity was estimated with the Tanimoto coefficient and pairs with higher structural similarity generally had higher spectral similarity. Pairs where one or both compounds contained heteroatoms such as sulfur often resulted in dissimilar spectra. ***This work demonstrates that HRMS2 spectral similarity may indicate structural similarity and that spectral similarity can be used in the future to screen complex samples for related compounds such as micropollutants and TPs, assisting in the prioritization of non-target compounds.*** [Figure not available: see full text.].
AUTHOR KEYWORDS: High-resolution tandem mass spectrometry; Micropollutants; Non-target screening; Spectral similarity; Transformation products
DOCUMENT TYPE: Article

Schymanski, E.L., Williams, A.J. Open Science for Identifying "Known Unknown" Chemicals (2017) Environmental Science and Technology, 51 (10), pp. 5357-5359. Cited nine times. DOI: 10.1021/acs.est.7b01908.

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DOCUMENT TYPE: Review

Schymanski, E.L., Ruttkies, C., Krauss, M., Brouard, C., Kind, T., Dührkop, K., Allen, F., Vaniya, A., Verdegem, D., Böcker, S., Rousu, J., Shen, H., Tsugawa, H., Sajed, T., Fiehn, O., Ghesquière, B., Neumann, S. Critical Assessment of Small Molecule Identification 2016: automated methods (2017) Journal of Cheminformatics, 9 (1), art. no. 22. DOI: 10.1186/s13321-017-0207-1.

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ABSTRACT: Background: ***The fourth round of the Critical Assessment of Small Molecule Identification (CASMI) Contest (www.casmi-contest.org) was held in 2016, with two new categories for automated methods.*** This article covers the 208 challenges in Categories 2 and 3, without and with metadata, from organization, participation, results and post-contest evaluation of CASMI 2016 through to perspectives for future contests and small molecule annotation/identification. Results: ***The Input Output Kernel Regression (CSI:IOKR) machine learning approach performed best in "Category 2***: Best Automatic Structural Identification - In Silico Fragmentation Only", won by Team Brouard with 41% challenge wins.

The winner of "Category 3: Best Automatic Structural Identification - Full Information" was Team Kind (MS-FINDER), with 76% challenge wins. The best methods were able to achieve over 30% Top 1 ranks in Category 2, with all methods ranking the correct candidate in the Top 10 in around 50% of challenges. This success rate rose to 70% Top 1 ranks in Category 3, with candidates in the Top 10 in over 80% of the challenges. ***The machine learning and chemistry-based approaches are shown to perform in complementary ways. Conclusions: The improvement in (semi-)automated fragmentation methods for small molecule identification has been substantial. The achieved high rates of correct candidates in the Top 1 and Top 10, despite large candidate numbers, open up great possibilities for high-throughput annotation of untargeted analysis for "known unknowns".*** As more high quality training data becomes available, the improvements in machine learning methods will likely continue, but the alternative approaches still provide valuable complementary information. Improved integration of experimental context will also improve identification success further for "real life" annotations. The true "unknown unknowns" remain to be evaluated in future CASMI contests. Graphical abstract. © 2017 The Author(s).
AUTHOR KEYWORDS: Compound identification; High resolution mass spectrometry; In silico fragmentation; Metabolomics; Structure elucidation
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Metz, T.O., Baker, E.S., Schymanski, E.L., Renslow, R.S., Thomas, D.G., Causon, T.J., Webb, I.K., Hann, S., Smith, R.D., Teeguarden, J.G. Integrating ion mobility spectrometry into mass spectrometry-based exposome measurements: What can it add and how far can it go? (2017) Bioanalysis, 9 (1), pp. 81-98. Cited 19 times. DOI: 10.4155/bio-2016-0244.

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ABSTRACT: Measuring the exposome remains a challenge due to the range and number of anthropogenic molecules that are encountered in our daily lives, as well as the complex systemic responses to these exposures. ***One option for improving the coverage, dynamic range and throughput of measurements is to incorporate ion mobility spectrometry (IMS) into current MS-based analytical methods. The implementation of IMS in exposomics studies will lead to more frequent observations of previously undetected chemicals and metabolites. LC-IMS-MS will provide increased overall measurement dynamic range, resulting in detections of lower abundance molecules.*** Alternatively, the throughput of IMS-MS alone will provide the opportunity to analyze many thousands of longitudinal samples over lifetimes of exposure, capturing evidence of transitory accumulations of chemicals or metabolites. The volume of data corresponding to these new chemical observations will almost certainly outpace the generation of reference data to enable their confident identification. ***In this perspective, we briefly review the state-of-the-art in measuring the exposome, and discuss the potential use for IMS-MS and the physico-chemical property of collisional cross section in both exposure assessment and molecular identification.*** © 2017 Future Science Ltd.
AUTHOR KEYWORDS: collision cross section; exposome; ion mobility spectrometry; mass spectrometry; metabolome
DOCUMENT TYPE: Article
ACCESS TYPE: Open Access

Vinaixa, M., Schymanski, E.L., Neumann, S., Navarro, M., Salek, R.M., Yanes, O. Mass spectral databases for LC/MS- and GC/MS-based metabolomics: State of the field and future prospects (2016) TrAC - Trends in Analytical Chemistry, 78, pp. 23-35. Cited 105 times. DOI: 10.1016/j.trac.2015.09.005

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ABSTRACT: At present, mass spectrometry (MS)-based metabolomics has been widely used to obtain new insights into human, plant, and microbial biochemistry; drug and biomarker discovery; nutrition research; and food control. Despite the high research interest, identifying and characterizing the structure of metabolites has become a major drawback for converting raw MS data into biological knowledge. ***Comprehensive and well-annotated MS-based spectral databases play a key role in serving this purpose via the formation of metabolite annotations. The main characteristics of the mass spectral databases currently used in MS-based metabolomics are reviewed in this study, underlining their advantages and limitations.*** In addition, the overlap of compounds with MSn (n ≥ 2) spectra from authentic chemical standards in most public and commercial databases has been calculated for the first time. ***Finally, future prospects of mass spectral databases are discussed in terms of the needs posed by novel applications and instrumental advancements***. © 2015 Elsevier B.V.
AUTHOR KEYWORDS: Databases; Gas chromatography; Identification; Liquid chromatography; Mass spectral databases; Mass spectrometry; Metabolomics
DOCUMENT TYPE: Review
ACCESS TYPE: Open Access

Brack, W., Ait-Aissa, S., Burgess, R.M., Busch, W., Creusot, N., Di Paolo, C., Escher, B.I., Mark Hewitt, L., Hilscherova, K., Hollender, J., Hollert, H., Jonker, W., Kool, J., Lamoree, M., Muschket, M., Neumann, S., Rostkowski, P., Ruttkies, C., Schollee, J., Schymanski, E.L., Schulze, T., Seiler, T.-B., Tindall, A.J., De Aragão Umbuzeiro, G., Vrana, B., Krauss, M. Effect-directed analysis supporting monitoring of aquatic environments - An in-depth overview (2016) Science of the Total Environment, 544, pp. 1073-1118. Cited 82 times. DOI: 10.1016/j.scitotenv.2015.11.102.

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ABSTRACT: ***Aquatic environments are often contaminated with complex mixtures of chemicals that may pose a risk to ecosystems and human health. This contamination cannot be addressed with target analysis alone but tools are required to reduce this complexity and identify those chemicals that might cause adverse effects. Effect-directed analysis (EDA) is designed to meet this challenge and faces increasing interest in water and sediment quality monitoring. Thus, the present paper summarizes current experience with the EDA approach and the tools required, and provides practical advice on their application.*** The paper highlights the need for proper problem formulation and gives general advice for study design. As the EDA approach is directed by toxicity, ***basic principles for the selection of bioassays are given as well as a comprehensive compilation of appropriate assays, including their strengths and weaknesses. A specific focus is given to strategies for sampling, extraction and bioassay dosing since they strongly impact prioritization of toxicants in EDA.*** Reduction of sample complexity mainly relies on fractionation procedures, which are discussed in this paper, including quality assurance and quality control. Automated combinations of fractionation, biotesting and chemical analysis using so-called hyphenated tools can enhance the throughput and might reduce the risk of artifacts in laboratory work. The key to determining the chemical structures causing effects is analytical toxicant identification. ***The latest approaches, tools, software and databases for target-, suspect and non-target screening as well as unknown identification are discussed together with analytical and toxicological confirmation approaches.*** A better understanding of optimal use and combination of EDA tools will help to design efficient and successful toxicant identification studies in the context of quality monitoring in multiply stressed environments. © 2015 Elsevier B.V.
AUTHOR KEYWORDS: Bioassay; Dosing; Enrichment; Fractionation; Non-target analysis; Toxicant identification
DOCUMENT TYPE: Review

Schollée, J.E., Schymanski, E.L., Hollender, J. Statistical Approaches for LC-HRMS Data to Characterize, Prioritize, and Identify Transformation Products from Water Treatment Processes (2016) ACS Symposium Series, 1241, pp. 45-65. Cited one time. DOI: 10.1021/bk-2016-1241.ch004.

AFFILIATIONS: Eawag Swiss Federal Institute of Aquatic Science and Technology, Dübendorf, 8600, Switzerland; Institute of Biogeochemistry and Pollutant Dynamics, ETH Zürich, Zürich, 8092, Switzerland.

ABSTRACT: Studying the formation of unknown transformation products (TPs) from water treatment processes can be a daunting task due to the high volume of information generated with modern analytics such as non-targeted liquid chromatrography high-resolution mass spectrometry. ***To disentangle and select those unknown compounds, including TPs, a variety of statistical methods can be applied. Significance testing and fold changes can provide an overview of those non-target features in post-treatment samples that are both statistically significant and large in magnitude. Time trend analysis can select non-target features that follow expected intensity trends. Finally, multivariate analysis such as principal component analysis, hierarchical clustering, and partial least squares can cope with co-varying features to help characterize and group unknown non-targets.*** With proper sampling and pre-processing, these tools can help to prioritize and identify potential TPs that may be relevant in the environment. In this review, different approaches are presented using examples from the literature and our own research. © 2016 American Chemical Society.
DOCUMENT TYPE: Book Chapter

Gago-Ferrero, P., Schymanski, E.L., Hollender, J., Thomaidis, N.S. Nontarget Analysis of Environmental Samples Based on Liquid Chromatography Coupled to High Resolution Mass Spectrometry (LC-HRMS) (2016) Comprehensive Analytical Chemistry, 71, pp. 381-403. Cited eight times. DOI: 10.1016/bs.coac.2016.01.012.

AFFILIATIONS: National and Kapodistrian University of Athens, Athens, Greece; Eawag: Swiss Federal Institute of Aquatic Science and Technology, Dübendorf, Switzerland; Institute of Biogeochemistry and Pollutant Dynamics, Zürich, Switzerland.

ABSTRACT: The existing target analytical methods described in the literature only cover a tiny fraction of the large number of compounds present in environmental samples. As a result, many potential chemical stressors are systematically omitted and there is an urgent need of analytical methodologies capable of detecting and identifying compounds using nontarget methods. ***In this regard, high resolution mass spectrometry coupled to liquid chromatography (LC-HRMS) has opened up new windows of opportunity for the detection of polar organic contaminants in complex samples. The objective of this chapter is to provide a critical overview of the state-of-the-art of the application of LC-HRMS to the nontarget analysis of organic contaminants in environmental samples.*** The existing methodologies and the different prioritization strategies as well as workflows to characterize unknown organic pollutants are evaluated. © 2016 Elsevier B.V.
AUTHOR KEYWORDS: Emerging pollutants; LC-HRMS; Nontarget analysis; Prioritization strategies; Tentative identification
DOCUMENT TYPE: Book Chapter

Schollée, J.E., Schymanski, E.L., Avak, S.E., Loos, M., Hollender, J. Prioritizing Unknown Transformation Products from Biologically-Treated Wastewater Using High-Resolution Mass Spectrometry, Multivariate Statistics, and Metabolic Logic (2015) Analytical Chemistry, 87 (24), pp. 12121-12129. Cited 21 times. DOI: 10.1021/acs.analchem.5b02905.

AFFILIATIONS: Eawag, Swiss Federal Institute of Aquatic Science and Technology, Dübendorf, 8600, Switzerland; Institute of Biogeochemistry and Pollutant Dynamics, ETH Zürich, Zürich, 8092, Switzerland; Department of Chemistry, University of Zürich, Zürich, 8057, Switzerland.

ABSTRACT: Incomplete micropollutant elimination in wastewater treatment plants (WWTPs) results in transformation products (TPs) that are released into the environment. ***Improvements in analytical technologies have allowed researchers to identify several TPs from specific micropollutants but an overall picture of nontarget TPs is missing. In this study, we addressed this challenge by applying multivariate statistics to data collected with liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS) and subsequent tandem HRMS (MS/MS) in order to characterize peaks detected in the influent and effluent of a WWTP.*** Known biotransformation reactions were used to link potential parent compounds and TPs, while the structural similarity of these pairs hypothesized by MS/MS similarity was used for further prioritization. ***The methodology was validated with a set of spiked compounds, which included 25 parent/TP pairs for which analytical standards were available.*** This procedure was then applied to nontarget data, and 20 potential parent and TP pairs were selected for identification. In summary, primarily a surfactant homologue series, with associated TPs, was detected. ***Some obstacles still remain, including spectral interferences from coeluting compounds and identification of TPs, whose structures are less likely to be present in compound databases.*** The workflow was developed using openly accessible tools and, after parameter adjustment, could be applied to any data set with before and after information about various biological or chemical processes. © 2015 American Chemical Society.
DOCUMENT TYPE: Article

Schymanski, E.L., Singer, H.P., Slobodnik, J., Ipolyi, I.M., Oswald, P., Krauss, M., Schulze, T., Haglund, P., Letzel, T., Grosse, S., Thomaidis, N.S., Bletsou, A., Zwiener, C., Ibáñez, M., Portolés, T., De Boer, R., Reid, M.J., Onghena, M., Kunkel, U., Schulz, W., Guillon, A., Noyon, N., Leroy, G., Bados, P., Bogialli, S., Stipaničev, D., Rostkowski, P., Hollender, J. Non-target screening with high-resolution mass

spectrometry: Critical review using a collaborative trial on water analysis (2015) Analytical and Bioanalytical Chemistry, 407 (21), pp. 6237-6255. Cited 121 times. DOI: 10.1007/s00216-015-8681-7.

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ABSTRACT: In this article, ***a dataset from a collaborative nontarget screening trial organized by the NORMAN Association is used to review the state-of-the-art and discuss future perspectives of non-target screening using high-resolution mass spectrometry in water analysis***. ***A total of 18 institutes from 12 European countries analyzed an extract of the same water sample collected from the River Danube with either one or both of liquid and gas chromatography coupled with mass spectrometry detection.*** This article focuses mainly on the use of high resolution screening techniques with target, suspect, and ***non-target workflows to identify substances in environmental samples.*** Specific examples are given to emphasize major challenges including isobaric and co-eluting substances, dependence on target and suspect lists, formula assignment, the use of retention information, and the confidence of identification. Approaches and methods applicable to unit resolution data are also discussed. ***Although most substances were identified using high resolution data with target and suspect-screening approaches,*** **some participants proposed tentative non-target identifications.** This comprehensive dataset revealed that non-target analytical techniques are already substantially harmonized between the participants, but the ***data processing remains time-consuming.*** Although the objective of a "fully-automated identification workflow" remains elusive in the short term, important steps in this direction have been taken, exemplified by the growing popularity of suspect screening approaches. ***Major recommendations to improve non-target screening include better integration and connection of desired features into software packages, the exchange of target and suspect lists, and the contribution of more spectra from standard substances into (openly accessible) databases.*** © Springer-Verlag Berlin Heidelberg 2015.

AUTHOR KEYWORDS: GC-MS; High resolution mass spectrometry; LC-MS; Non-target screening; Surface water; Suspect screening
DOCUMENT TYPE: Article

Altenburger, R., Ait-Aissa, S., Antczak, P., Backhaus, T., Barceló, D., Seiler, T.-B., Brion, F., Busch, W., Chipman, K., de Alda, M.L., de Aragão Umbuzeiro, G., Escher, B.I., Falciani, F., Faust, M., Focks, A., Hilscherova, K., Hollender, J., Hollert, H., Jäger, F., Jahnke, A., Kortenkamp, A., Krauss, M., Lemkine, G.F., Munthe, J., Neumann, S., Schymanski, E.L., Scrimshaw, M., Segner, H., Slobodnik, J., Smedes, F., Kughathas, S., Teodorovic, I., Tindall, A.J., Tollefsen, K.E., Walz, K.-H., Williams, T.D., Van den Brink, P.J., van Gils, J., Vrana, B., Zhang, X., Brack, W. Future water quality monitoring - Adapting tools to deal with mixtures of pollutants in water resource management (2015) Science of the Total Environment, 512-513, pp. 540-551. Cited 102 times. DOI: 10.1016/j.scitotenv.2014.12.057.

AFFILIATIONS: UFZ - Helmholtz Centre for Environmental Research, Permoserstr. 15, Leipzig, 04318, Germany; RWTH Aachen University, Aachen, Germany; Institut National de l'Environnement Industriel et des Risques INERIS, BP2, Verneuil-en-Halatte, 60550, France; Centre for Computational Biology and Modelling, University of LiverpoolL69 7ZB, United Kingdom; Department of Biological and Environmental Sciences, University of Gothenburg, Carl Skottbergs Gata 22b, Gothenburg, 40530, Sweden; Water and Soil Quality Research Group, Institute of Environmental Assessment and Water Research (IDAEA-CSIC), Jordi Girona 18-26, Barcelona, 08034, Spain; School of Biosciences, The University of Birmingham, Birmingham, B15 2TT, United Kingdom; University of Campinas, Limeira, Brazil; National Research Centre for Environmental Toxicology (Entox), The University of Queensland, Brisbane, Australia; Faust and Backhaus Environmental Consulting, Fahrenheitstr. 1, Bremen, 28359, Germany; Alterra, Wageningen University and Research Centre, P.O. Box 47, Wageningen, 6700 AA, Netherlands; Masaryk University, Research Centre for Toxic Compounds in the Environment (RECETOX), Masaryk University, Kamenice 753/5, Brno, 625 00, Czech Republic; Eawag, Swiss Federal Institute of Aquatic Science and Technology, Dübendorf, 8600, Switzerland; Synchem UG and Co. KG, Am Kies 2, Felsberg-Altenburg, 34587, Germany; Brunel University, Institute of Environment, Health and Societies, Uxbridge, UB8 3PH, United Kingdom; WatchFrog, Bâtiment Genavenir 3, 1 rue Pierre Fontaine, Evry, 91000, France; IVL Swedish Environmental Research Institute, P.O. Box 53021, Göteborg, 400 14, Sweden; Leibniz Institute of Plant Biochemistry, Weinberg 3, Halle, 06120, Germany; University of Bern, Centre for Fish and Wildlife Health, PO Box 8466, Bern, CH-3001, Switzerland; Environmental Institute, Okruzna 784/42, Kos, 97241, Slovakia; University of Novi Sad, Faculty of Scienceş Trg Dositeja Obradovića, Novi Sad, 321000, Serbia; Norwegian Institute for Water Research NIVA, Gaustadalléen 21, Oslo, N-0349, Norway; MAXX Mess- und Probenahmetechnik GmbH, Hechinger Straße 41, Rangendingen, D-72414, Germany; Foundation Deltares, Potbus 177, Delft, 277 MH, Netherlands; State Key Laboratory of Pollution Control and Resource Reuse, School of the Environment, Collaborative Innovation Center for Regional Environmental Quality, Nanjing University, Nanjing, 210023, China.

ABSTRACT: Environmental quality monitoring of water resources is challenged with providing the basis for safeguarding the environment against adverse biological effects of anthropogenic chemical contamination from diffuse and point sources. While current regulatory efforts focus on monitoring and assessing a few legacy chemicals, many more anthropogenic chemicals can be detected simultaneously in our aquatic resources. However, exposure to chemical mixtures does not necessarily translate into adverse biological effects nor clearly shows whether mitigation measures are needed. ***Thus, the question which mixtures are present and which have associated combined effects becomes central for defining adequate monitoring and assessment strategies.*** Here we describe the vision of the international, EU-funded project SOLUTIONS, where three routes are explored to link the occurrence of chemical mixtures at specific sites to the assessment of adverse biological combination effects. ***First of all, multi-residue target and non-target screening techniques covering a broader range of anticipated chemicals co-occurring in the environment are being developed. By improving sensitivity and detection limits for known bioactive compounds of concern, new analytical chemistry data for multiple components can be obtained and used to characterize priority mixtures. This information on chemical***

occurrence will be used to predict mixture toxicity and to derive combined effect estimates suitable for advancing environmental quality standards. Secondly, bioanalytical tools will be explored to provide aggregate bioactivity measures integrating all components that produce common (adverse) outcomes even for mixtures of varying compositions. The ambition is to provide comprehensive arrays of effect-based tools and trait-based field observations that link multiple chemical exposures to various environmental protection goals more directly and to provide improved in situ observations for impact assessment of mixtures. Thirdly, effect-directed analysis (EDA) will be applied to identify major drivers of mixture toxicity. Refinements of EDA include the use of statistical approaches with monitoring information for guidance of experimental EDA studies. These three approaches will be explored using case studies at the Danube and Rhine river basins as well as rivers of the Iberian Peninsula. The synthesis of findings will be organized to provide guidance for future solution-oriented environmental monitoring and explore more systematic ways to assess mixture exposures and combination effects in future water quality monitoring. © 2015 Elsevier B.V.
AUTHOR KEYWORDS: Chemical status; Ecological status; Effect-based tools; Mixture toxicity; Priority chemicals; Water quality; WFD
DOCUMENT TYPE: Note

Hollender, J., Bourgin, M., Fenner, K.B., Longrée, P., McArdell, C.S., Moschet, C., Ruff, M., Schymanski, E.L., Singer, H.P. Exploring the behaviour of emerging contaminants in the water cycle using the capabilities of high resolution mass spectrometry (2014) Chimia, 68 (11), pp. 793-798. Cited three times. DOI: 10.2533/chimia.2014.793.

AFFILIATIONS: Eawag, Swiss Federal Institute of Aquatic Science and Technology, Überlandstrasse 133, Dübendorf, CH-8600, Germany; Institute of Biogeochemistry and Pollutant Dynamics, ETH Zürich, Zürich, CH-8092, Switzerland.

ABSTRACT: To characterize a broad range of organic contaminants and their transformation products (TPs) as well as their loads, input pathways and fate in the water cycle, the Department of Environmental Chemistry (Uchem) at Eawag applies and develops high-performance liquid chromatography (LC) methods combined with high-resolution tandem mass spectrometry (HRMS/MS). ***In this article, the background and state-of-the-art of LC-HRMS/MS for detection of i) known targets, ii) suspected compounds like TPs, and iii) unknown emerging compounds are introduced briefly.*** Examples for each approach are taken from recent research projects conducted within the department. These include the detection of trace organic contaminants and their TPs in wastewater, pesticides and their TPs in surface water, ***identification of new TPs in laboratory degradation studies and ozonation experiments and finally the screening for unknown compounds in the catchment of the river Rhine.*** © Schweizerische Chemische Gesellschaft.
AUTHOR KEYWORDS: Emerging contaminants; High-resolution mass spectrometry; Non-target screening; Transformation products; Water cycle
DOCUMENT TYPE: Article

Huntscha, S., Hofstetter, T.B., Schymanski, E.L., Spahr, S., Hollender, J. Biotransformation of benzotriazoles: Insights from transformation product identification and compound-specific isotope analysis (2014) Environmental Science and Technology, 48 (8), pp. 4435-4443. Cited 49 times. DOI: 10.1021/es405694z.

AFFILIATIONS: Eawag, Swiss Federal Institute of Aquatic Science and Technology, 8600 Dübendorf, Switzerland; Institute of Biogeochemistry and Pollutant Dynamics (IBP), ETH Zurich, 8092 Zurich, Switzerland.

ABSTRACT: ***Benzotriazoles are widely used domestic and industrial corrosion inhibitors and have become omnipresent organic micropollutants in the aquatic environment.*** Here, the range of aerobic

biological degradation mechanisms of benzotriazoles in activated sludge was investigated. ***Degradation pathways were elucidated by identifying transient and persistent transformation products in batch experiments using liquid chromatography-high-resolution tandem mass spectrometry (LC-HR-MS/MS).*** In addition, initial reactions were studied using compound-specific isotope analysis (CSIA). Biodegradation half-lives of 1.0 days for 1H-benzotriazole, 8.5 days for 4-methyl-1H-benzotriazole, and 0.9 days for 5-methyl-1H-benzotriazole with activated sludge confirmed their known partial persistence in conventional wastewater treatment. Major transformation products were identified as 4- and 5-hydroxy-1H-benzotriazole for the degradation of 1H-benzotriazole, and 1H-benzotriazole-5-carboxylic acid for the degradation of 5-methyl-1H-benzotriazole. These transformation products were found in wastewater effluents, showing their environmental relevance. Many other candidate transformation products, tentatively identified by interpretation of HR-MS/MS spectra, showed the broad range of possible reaction pathways including oxidation, alkylation, hydroxylation and indicate the significance of cometabolic processes for micropollutant degradation in biological wastewater treatment in general. The combination of evidence from product analysis with the significant carbon and nitrogen isotope fractionation suggests that aromatic monohydroxylation is the predominant step during the biotransformation of 1H-benzotriazole. © 2014 American Chemical Society.
DOCUMENT TYPE: Article

Schymanski, E.L., Jeon, J., Gulde, R., Fenner, K., Ruff, M., Singer, H.P., Hollender, J. Identifying small molecules via high resolution mass spectrometry: Communicating confidence (2014) Environmental Science and Technology, 48 (4), pp. 2097-2098. Cited 308 times. DOI: 10.1021/es5002105.

AFFILIATIONS: Eawag: Swiss Federal Institute of Aquatic Science and Technology, Überlandstrasse 133, 8600 Dübendorf, Switzerland; Institute of Biogeochemistry and Pollutant Dynamics, ETH Zurich, 8092, Zurich, Switzerland
DOCUMENT TYPE: Short Survey

Gallampois, C.M.J., Schymanski, E.L., Bataineh, M., Buchinger, S., Krauss, M., Reifferscheid, G., Brack, W. Integrated biological-chemical approach for the isolation and selection of polyaromatic mutagens in surface waters (2013) Analytical and Bioanalytical Chemistry, 405 (28), pp. 9101-9112. Cited 19 times. DOI: 10.1007/s00216-013-7349-4.

AFFILIATIONS: Department of Chemistry, Umeå University, 901 87 Umeå, Sweden; Department of Effect-Directed Analysis, UFZ - Helmholtz Centre for Environmental Research, Permoserstr. 15, 04318 Leipzig, Germany; Eawag - Swiss Federal Institute of Aquatic Science and Technology, Überlandstrasse 133, 8600 Dübendorf, Switzerland; Abu Dhabi Men's College, P.O. Box 25035, Abu Dhabi, United Arab Emirates; BfG - German Federal Institute of Hydrology, Am Mainzer Tor 1, 56068 Koblenz, Germany.

ABSTRACT: Many environmental mutagens, including polyaromatic compounds are present in surface waters, often in complex mixtures and at low concentrations. The present study provides and applies a novel, integrated approach to isolate polyaromatic mutagens in river water using a sample from the River Elbe. ***The sample was taken downstream of industrial discharges using blue rayon (BR) as a passive sampler that selectively adsorbs polyaromatic compounds and was subjected to effect-directed fractionation in order to characterize the compounds causing the detected effect(s).*** The procedure relies on three complementary fractionation steps, the Ames fluctuation assay with strains TA98, YG1024 and YG1041 with and without S9 activation and analytical screening. Several mutagenic fractions were isolated by combining mutagenicity testing with fractionation. The enhanced mutagenicity in the nitroreductase and/or O-acetyltransferase overexpressing strains YG1024 and YG1041 strains suggested amino- and/or nitro-compounds causing mutagenicity in several fractions. ***Analytical screening of mutagenic fractions with LC-HRMS/MS provided a list of molecular formulas typically containing one to 10 nitrogen and at least two oxygen atoms supporting the presence of***

amino and nitro-compounds in the mutagenic fractions. [Figure not available: see fulltext.] © 2013 Springer-Verlag Berlin Heidelberg.
AUTHOR KEYWORDS: Blue rayon; Liquid-chromatography- high resolution MS/MS; Multi-dimensional fractionation; Multi-strains Ames fluctuation assay; Polyaromatic compounds; Reversed-phase HPLC
DOCUMENT TYPE: Article

Schymanski, E.L., Meringer, M., Brack, W. Automated strategies to identify compounds on the basis of GC/EI-MS and calculated properties (2011) Analytical Chemistry, 83 (3), pp. 903-912. Cited 28 times. DOI: 10.1021/ac102574h.

AFFILIATIONS: Department of Effect-Directed Analysis, UFZ Helmholtz Centre for Environmental Research, Permoser Strasse 15, D-04103 Leipzig, Germany; Remote Sensing Technology Institute, DLR, German Aerospace Centre, Münchner Strasse 20, D-82234 Oberpfaffenhofen-Wessling, Germany.

ABSTRACT: ***The identification of unknown compounds based on GC/EI-MS spectrum and structure generation techniques has been improved by combining a number of strategies into a programmed sequence.*** The program MOLGEN-MS is used to determine the molecular formula and incorporate substructural information to generate all structures matching the mass spectral information. Mass spectral fragments are then predicted for each structure and compared with the experimental spectrum using a match value. Additional data are then calculated automatically for each candidate to allow exclusion of candidates that did not match other analytical information. The effectiveness of these "exclusion criteria", as well as the programming sequence, was tested using a case study of 29 isomers of formula C12H10O2. The default classifier precision resulted in the generation of too many structures in some cases, which was improved by up to several orders of magnitude by including additional classifiers or restrictions. Combining this with the exclusion of candidates based on a Lee retention index/boiling point correlation, octanol-water partitioning coefficients, steric energies, and finally spectral match values limited the number of candidate structures further from over one billion without any restrictions down to less than six structures in 10 cases and below 35 in all but three cases. ***This method can be used in the absence of matching database spectra and brings unknown identification based on MS interpretation and structure generation techniques a step closer to practical reality.*** © 2011 American Chemical Society.
DOCUMENT TYPE: Article

Meinert, C., Schymanski, E., Küster, E., Kühne, R., Schüürmann, G., Brack, W. Application of preparative capillary gas chromatography (pcGC), automated structure generation and mutagenicity prediction to improve effect-directed analysis of genotoxicants in a contaminated groundwater (2010) Environmental Science and Pollution Research, 17 (4), pp. 885-897. Cited 24 times. DOI: 10.1007/s11356-009-0286-2.

AFFILIATIONS: Department of Effect-Directed Analysis, UFZ, Helmholtz Centre for Environmental Research, Permoserstraße 15, 04318 Leipzig, Germany; Department of Bioanalytical Ecotoxicology, UFZ, Helmholtz Centre for Environmental Research, Permoserstraße 15, 04318 Leipzig, Germany; Department of Ecological Chemistry, UFZ, Helmholtz Centre for Environmental Research, Permoserstraße 15, 04318 Leipzig, Germany.

ABSTRACT: Background, aim and scope: The importance of groundwater for human life cannot be overemphasized. Besides fulfilling essential ecological functions, it is a major source of drinking water. However, in the industrial area of Bitterfeld, it is contaminated with a multitude of harmful chemicals, including genotoxicants. ***Therefore, recently developed methodologies including preparative capillary gas chromatography (pcGC), MOLGEN-MS structure generation and mutagenicity prediction were applied within effect-directed analysis (EDA) to reduce sample complexity and to identify candidate mutagens in the samples.*** A major focus was put on the added value of these tools compared to

conventional EDA combining reversed-phase liquid chromatography (RP-LC) followed by GC/MS analysis and MS library search. Materials and methods: We combined genotoxicity testing with umuC and RP-LC with pcGC fractionation to isolate genotoxic compounds from a contaminated groundwater sample. Spectral library information from the NIST05 database was combined with a computer-based structure generation tool called MOLGEN-MS for structure elucidation of unknowns. ***Finally, we applied a computer model for mutagenicity prediction (ChemProp) to identify candidate mutagens and genotoxicants.*** Results and discussion: A total of 62 components were tentatively identified in genotoxic fractions. Ten of these components were predicted to be potentially mutagenic, ***whilst 2,4,6-trichlorophenol, 2,4-dichloro-6-methylphenol and 4-chlorobenzoic acid were confirmed as genotoxicants.*** Conclusions and perspectives: The results suggest pcGC as a high-resolution fractionation tool and MOLGEN-MS to improve structure elucidation, ***whilst mutagenicity prediction failed in our study to predict identified genotoxicants. Genotoxicity, mutagenicity and carcinogenicity caused by chemicals are complex processes, and prediction from chemical structure still appears to be quite difficult.*** Progress in this field would significantly support EDA and risk assessment of environmental mixtures. © 2010 Springer-Verlag.
AUTHOR KEYWORDS: EDA; Identification of unknowns; MODELKEY; QSAR; UmuC
DOCUMENT TYPE: Article

Schymanski, E.L., Meinert, C., Meringer, M., Brack, W. The use of MS classifiers and structure generation to assist in the identification of unknowns in effect-directed analysis (2008) Analytica Chimica Acta, 615 (2), pp. 136-147. Cited 43 times. DOI: 10.1016/j.aca.2008.03.060.

AFFILIATIONS: UFZ, Helmholtz Centre for Environmental Research - UFZ, Department of Effect-Directed Analysis, Permoserstr. 15, D-04318 Leipzig, Germany; DLR - German Aerospace Centre, Remote Sensing Technology Institute, Munchner Straße 20, D-82234 Oberpfaffenhofen, Wessling, Germany.

ABSTRACT: Structure generation and mass spectral classifiers have been incorporated into a new method to gain further information from low-resolution GC-MS spectra and subsequently assist in the identification of toxic compounds isolated using effect-directed fractionation. The method has been developed for the case where little analytical information other than the mass spectrum is available, common, for example, in effect-directed analysis (EDA), where further interpretation of the mass spectra is necessary to gain additional information about unknown peaks in the chromatogram. Structure generation from a molecular formula alone rapidly leads to enormous numbers of structures; hence reduction of these numbers is necessary to focus identification or confirmation efforts. ***The mass spectral classifiers and structure generation procedure in the program MOLGEN-MS was enhanced by including additional classifier information available from the NIST05 database and incorporation of post-generation 'filtering criteria'.*** The presented method can reduce the number of possible structures matching a spectrum by several orders of magnitude, creating much more manageable data sets and increasing the chance of identification. Examples are presented to show how the method can be used to provide 'lines of evidence' for the identity of an unknown compound. ***This method is an alternative to library search of mass spectra and is especially valuable for unknowns where no clear library match is available.***
AUTHOR KEYWORDS: Confirmation; Effect-directed analysis; Mass spectral classifiers; MODELKEY; Structure generation
DOCUMENT TYPE: Article

Brack, W., Schmitt-Jansen, M., MacHala, M., Brix, R., Barceló, D., Schymanski, E., Streck, G., Schulze, T. How to confirm identified toxicants in effect-directed analysis (2008) Analytical and Bioanalytical Chemistry, 390 (8), pp. 1959-1973. Cited 70 times. DOI: 10.1007/s00216-007-1808-8.

AFFILIATIONS: Department Effect-Directed Analysis, UFZ Helmholtz Centre for Environmental Research, Permoserstraße 15, 04318 Leipzig, Germany; Department Bioanalytical Ecotoxicology, UFZ Helmholtz Centre for Environmental Research, Permoserstraße 15, 04318 Leipzig, Germany; Veterinary Research Institute, Hudcova 70, Brno 62132, Czech Republic; Department of Environmental Chemistry, IIQAB-CSIC, Jordi Girona 18-26, Barcelona 08034, Spain.

ABSTRACT: Due to the production and use of a multitude of chemicals in modern society, waters, sediments, soils and biota may be contaminated with numerous known and unknown chemicals that may cause adverse effects on ecosystems and human health. ***Effect-directed analysis (EDA), combining biotesting, fractionation and chemical analysis, helps to identify hazardous compounds in complex environmental mixtures.*** Confirmation of tentatively identified toxicants will help to avoid artefacts and to establish reliable cause-effect relationships. A tiered approach to confirmation is suggested in the present paper. ***The first tier focuses on the analytical confirmation of tentatively identified structures. If straightforward confirmation with neat standards for GC-MS or LC-MS is not available, it is suggested that a lines-of-evidence approach is used that combines spectral library information with computer-based structure generation and prediction of retention behaviour in different chromatographic systems using quantitative structure-retention relationships (QSRR).*** In the second tier, the identified toxicants need to be confirmed as being the cause of the measured effects. Candidate components of toxic fractions may be selected based, for example, on structural alerts. ***Quantitative effect confirmation is based on joint effect models.*** Joint effect prediction on the basis of full concentration-response plots and careful selection of the appropriate model are suggested as a means to improve confirmation quality. Confirmation according to the Toxicity Identification Evaluation (TIE) concept of the US EPA and novel tools of hazard identification help to confirm the relevance of identified compounds to populations and communities under realistic exposure conditions. Promising tools include bioavailability-directed extraction and dosing techniques, biomarker approaches and the concept of pollution-induced community tolerance (PICT). © 2007 Springer-Verlag.
AUTHOR KEYWORDS: Effect-directed analysis; Hazard; Mixture toxicity; Structural analysis; Toxicity confirmation; Toxicity identification evaluation
DOCUMENT TYPE: Article

12/10/18 SCOPUS Search by author and keywords
AUTHOR-NAME **(*richardson,*** AND ***s*** AND ***d*****) AND** TITLE-ABS-KEY **(*water* OR *non-target* OR *unknown* OR *suspect* OR *disinfection* OR *spectrometry*) gave 173 results.**

Ackerson, N.O.B., Machek, E.J., Killinger, A.H., Crafton, E.A., Kumkum, P., Liberatore, H.K., Plewa, M.J., Richardson, S.D., Ternes, T.A., Duirk, S.E. Formation of DBPs and halogen-specific TOX in the presence of iopamidol and chlorinated oxidants (2018) Chemosphere, 202, pp. 349-357. Cited two times. DOI: 10.1016/j.chemosphere.2018.03.102.

AFFILIATIONS: Department of Civil Engineering, University of Akron, Akron, OH 44325, United States; Department of Chemistry and Biochemistry, University of South Carolina, 631 Sumter St., Columbia, SC 29208, United States; Department of Crop Sciences and Safe Global Water Institute and NSF Science and Technology Center of Advanced Materials for the Purification of Water with Systems, University of Illinois at Urbana-Champaign, 1101 West Peabody Drive, Urbana, IL 61801, United States; Federal Institute of Hydrology (BfG), Am Mainzer Tor 1, Koblenz, D-56068, Germany.

ABSTRACT: Iopamidol is a known direct precursor to iodinated and chlorinated DBP formation; however, the influence of iopamidol on both iodo/chloro-DBP formation has yet to be fully investigated. ***This study investigated the effect of iopamidol on the formation and speciation of halogen-specific total organic halogen (TOX)***, as well as iodo/chloro-DBPs, in the presence of three source waters (SWs) from Northeast Ohio and chlorinated oxidants. Chlorination and chloramination of SWs were carried out at

pH 6.5-9.0 and, different iopamidol and dissolved organic carbon (DOC) concentrations. ***Total organic iodine (TOI) loss was approximately equal (22-35%) regardless of SW. Total organic chlorine (TOCl) increased in all SWs and was substantially higher in the higher SUVA254 SWs.*** Iopamidol was a direct precursor to chloroform (CHCl3), trichloroacetic acid (TCAA), and dichloroiodomethane (CHCl2I) formation. While CHCl3 and TCAA exhibited different formation trends with varying iopamidol concentrations, CHCl2I increased with increasing iopamidol and DOC concentrations. Low concentrations of iodo-acids were detected without discernible trends. ***Total trihalomethanes (THMs), total haloacetic acids (HAAs), TOCl, and unknown TOCl (UTOCl) were correlated with fluorescence regional volumes and SUVA254.*** The yields of all these species showed a strong positive correlation with fulvic, humic, and combined humic and fulvic regions, as well as SUVA254. Iopamidol was then compared to the three SWs with respect to DBP yield. Although the SUVA254 of iopamidol was relatively high, it did not produce high yields of THMs and HAAs compared to the three SWs. ***However, chlorination of iopamidol did result in high yields of TOCl and UTOCl.*** © 2018 Elsevier Ltd
AUTHOR KEYWORDS: Aqueous chlorine; Disinfection byproducts; Iopamidol; Monochloramine; Natural organic matter; Total organic halogen
DOCUMENT TYPE: Article

Richardson, S.D., Ternes, T.A. Water Analysis: Emerging Contaminants and Current Issues (2018) Analytical Chemistry, 90 (1), pp. 398-428. Cited 29 times. DOI: 10.1021/acs.analchem.7b04577.

AFFILIATIONS: Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC 29205, United States;

Federal Institute of Hydrology, KoblenzD-56068, Germany
DOCUMENT TYPE: Review

Liberatore, H.K., Plewa, M.J., Wagner, E.D., Vanbriesen, J.M., Burnett, D.B., Cizmas, L.H., Richardson, S.D. Identification and Comparative Mammalian Cell Cytotoxicity of New Iodo-Phenolic Disinfection Byproducts in Chloraminated Oil and Gas Wastewaters (2017) Environmental Science and Technology Letters, 4 (11), pp. 475-480. Cited six times. DOI: 10.1021/acs.estlett.7b00468.

AFFILIATIONS: Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC 29208, United States; Department of Crop Sciences, University of Illinois at Urbana-Champaign, Urbana, IL 61801, United States; Safe Global Water Institute, University of Illinois at Urbana-Champaign, Urbana, IL 61801, United States; Department of Civil and Environmental Engineering, Carnegie Mellon University, Pittsburgh, PA 15213, United States; Department of Petroleum Engineering, Texas AandM University, College Station, TX 77843, United States; Department of Environmental and Occupational Health, School of Public Health, Texas AandM University, College Station, TX 77843, United States.

ABSTRACT: Hydraulic fracturing wastewaters discharged to surface water have led to elevated bromide and iodide levels, as well as enhanced formation of brominated trihalomethanes, haloacetic acids, haloacetonitriles, and iodo-trihalomethanes at downstream drinking water treatment plants, in chlorinated effluent from wastewater treatment plants, and in controlled laboratory studies. This enhanced formation of brominated and iodinated disinfection byproducts (DBPs) raises concerns regarding human health, because they are much more toxic than chlorinated DBPs. ***This study represents the first nontarget, comprehensive analysis of iodinated DBPs formed in chloraminated produced waters associated with hydraulic fracturing of shale and conventional gas formations. Fifty-six iodo-phenolics were identified, comprising three homologous series of mono-, di-, and tri-iodinated phenols, along with two new classes of DBPs: iodomethylphenols and iododimethylphenols. Four iodo-phenolics (2-iodophenol, 4-iodophenol, 2,4,6-triiodophenol, and 4-iodo-2-methylphenol) were investigated for mammalian cell cytotoxicity. All were cytotoxic, especially 2,4,6-triiodophenol, which was more cytotoxic than all trihalomethanes and most haloacetic acids.*** In addition, geogenic organic

compounds present in the oil and gas produced waters, including methylphenol and dimethylphenol, were found to be potential precursors to these iodo-DBPs. © 2017 American Chemical Society.
DOCUMENT TYPE: Article

Richardson, S.D., Kimura, S.Y. Emerging environmental contaminants: Challenges facing our next generation and potential engineering solutions (2017) Environmental Technology and Innovation, 8, pp. 40-56. Cited 20 times. DOI: 10.1016/j.eti.2017.04.002.

AFFILIATIONS: Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC 29208, United States.

ABSTRACT: While our current generation continues to make efforts to remediate and minimize traditional pollutants in the environment, other "emerging" environmental contaminants are now warranting attention. These include perfluorinated compounds, nanomaterials, pharmaceuticals, illicit drugs, antibacterials, hormones, flame retardants, disinfection by-products (DBPs), artificial sweeteners, benzotriazoles, 1,4-dioxane, and algal toxins, as well as emerging contaminants on the horizon: prions and ionic liquids. ***Wastewater effluents are a major source for many of these emerging contaminants, due to their use in products we use in our households, from pharmaceuticals, detergents, fabric coatings, foam cushions, lotions, sunscreens, cosmetics, hair products, foods and beverages, and food packaging.*** After use, these chemicals are released in wastewater, and because many are incompletely removed in wastewater treatment, they enter our rivers and drinking water supplies. Surface run-off and agricultural run-off can also be important sources of their entry into the environment. ***Moreover, many of these contaminants can transform in the environment, from such processes as microbial degradation, photolysis, and hydrolysis, and they can also react with disinfectants in drinking water or wastewater treatment to form disinfection by-products.*** Issues surrounding these emerging contaminants, include widespread occurrence, bioaccumulation, persistence, and toxicity. Climate change can also serve to exasperate their effects by concentrating them in rivers during times of drought and by causing resuspension of some (like nanomaterials) during floods. ***This review will discuss these issues surrounding emerging contaminants and also propose some engineering solutions for the future.*** © 2017 Elsevier B.V.
DOCUMENT TYPE: Article

Plewa, M.J., Wagner, E.D., Richardson, S.D. TIC-Tox: A preliminary discussion on identifying the forcing agents of DBP-mediated toxicity of disinfected water (2017) Journal of Environmental Sciences (China), 58, pp. 208-216. DOI: 10.1016/j.jes.2017.04.014.

AFFILIATIONS: Safe Global Water Institute, the Department of Crop Sciences, University of Illinois at Urbana-ChampaignIL 61801, United States; Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC 29208, United States.

ABSTRACT: ***The disinfection of drinking water is a major public health achievement; however, an unintended consequence of disinfection is the generation of disinfection by-products (DBPs). Many of the identified DBPs exhibit in vitro and in vivo toxicity, generate a diversity of adverse biological effects, and may be hazards to the public health and the environment.*** Only a few DBPs are regulated by several national and international agencies and it is not clear if these regulated DBPs are the forcing agents that drive the observed toxicity and their associated health effects. ***In this study, we combine analytical chemical and biological data to resolve the forcing agents associated with mammalian cell cytotoxicity of drinking water samples from three cities.*** These data suggest that the trihalomethanes (THMs) and haloacetic acids may be a small component of the overall cytotoxicity of the organic material isolated from disinfected drinking water. ***Chemical classes of nitrogen-containing DBPs, such as the haloacetonitriles and haloacetamides, appear to be the major forcing agents of toxicity in these samples.*** These findings may have important implications for the design of epidemiological studies that

primarily rely on the levels of THMs to define DBP exposure among populations. The TIC-Tox approach constitutes a beginning step in the process of identifying the forcing agents of toxicity in disinfected water. © 2017
AUTHOR KEYWORDS: Additivity; CHO cell cytotoxicity; DBPs; Toxicity
DOCUMENT TYPE: Article

Postigo, C., Cojocariu, C.I., Richardson, S.D., Silcock, P.J., Barcelo, D. Erratum to: Characterization of iodinated disinfection by-products in chlorinated and chloraminated waters using Orbitrap based gas chromatography-mass spectrometry (Anal Bioanal Chem, 10.1007/s00216-016-9435-x) (2016) Analytical and Bioanalytical Chemistry, 408 (24), pp. 6869-6870. DOI: 10.1007/s00216-016-9794-3.

AFFILIATIONS: Department of Environmental Chemistry, Institute of Environmental Assessment and Water Research, (IDAEA-CSIC) Water and Soil Quality Research Group, Jordi Girona 18-26, Barcelona, 08034, Spain; Thermo Fisher Scientific, Tudor Road, Manor Park, Runcorn, Cheshire WA7 1TA, United Kingdom; Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC, United States; Catalan Institute for Water Research (ICRA), Parc Científic i Tecnològic de la Universitat de Girona, Edifici H2O, Emili Grahit 101, Girona, 17003, Spain.

ABSTRACT: ***In the original version of this article, one of the chromatographic peaks found in NL NOM extracts was identified as iodoethene. However, the molecular structure proposed was not correct. Following Professor Albert T. Lebedev's suggestion, this peak may correspond to ethyl β-iodopropionate (C5IO2H9). The authors completely agree with this suggestion***, based on the following facts: – The retention time for iodoethene should be shorter than that observed for ethyl iodoacetate (tR = 8.07). On the other hand, ethyl β-iodopropionate should be retained in the column longer as compared to ethyl iodoacetate. – The other ions in the mass spectrum, i.e., 87.04409 (C4H7O2, 0.4 ppm), 154.93519 (C2H4I, -0.2 ppm), and 140.91956 (CH2I, 0.04 ppm) also support the structural assignment as ethyl β-iodopropionate. The authors would like to highlight that this peak misidentification is attributed only to the manual interpretation of the HRMS data and not to the GC-Orbitrap MS instrument performance. Figure 3b has been also changed accordingly, and ethyl β-iodopropionate should read throughout the text instead of iodoethene. In order to confirm that this compound was a disinfection byproduct and not formed during an extraction process based on ethyl acetate, an additional blank of the chloramination process with purified water spiked with 500 ppb of bromide and 50 ppb of iodide (as KBr and KI, respectively) was performed. Both, ethyl iodoacetate and ethyl β-iodopropionate were found in this blank extract; however, the peak areas in chloraminated and chlorinated extracts were comparatively much higher than in the blank (10 times and five times, respectively). Therefore, it was concluded that these compounds also were generated during the disinfection process. © 2016, Springer-Verlag Berlin Heidelberg.
DOCUMENT TYPE: Erratum
ACCESS TYPE: Open Access

Postigo, C., Cojocariu, C.I., Richardson, S.D., Silcock, P.J., Barcelo, D. Characterization of iodinated disinfection by-products in chlorinated and chloraminated waters using Orbitrap based gas chromatography-mass spectrometry (2016) Analytical and Bioanalytical Chemistry, 408 (13), pp. 3401-3411. Cited 18 times. DOI: 10.1007/s00216-016-9435-x.

AFFILIATIONS: Water and Soil Quality Research Group, Department of Environmental Chemistry, Institute of Environmental Assessment and Water Research - Spanish National Research Council (IDAEA-CSIC), Jordi Girona 18-26, Barcelona, 08034, Spain; Thermo Fisher Scientific, Tudor Road, Manor Park, Runcorn, Cheshire, WA7 1TA, United Kingdom; Department of Chemistry and Biochemistry, University of South Carolina, 631 Sumter St., Columbia, SC 29208, United States; Catalan Institute for Water Research

(ICRA), Parc Científic i Tecnològic de la Universitat de Girona, Edifici H2O, Emili Grahit 101, Girona, 17003, Spain.

ABSTRACT: Recent developments in gas chromatography (GC)-mass spectrometry (MS) have opened up the possibility to use the high resolution-accurate mass (HRAM) Orbitrap mass analyzer to further characterize the volatile and semivolatile fractions of environmental samples. ***This work describes the utilization of GC Orbitrap MS technology to characterize iodine-containing disinfection by-products (iodo-DBPs) in chlorinated and chloraminated DBP mixture concentrates.*** These DBP mixtures were generated in lab-scale disinfection reactions using Llobregat river water and solutions containing Nordic Lake natural organic matter (NOM). ***The DBPs generated were concentrated using XAD resins, and extracts obtained were analyzed in full scan mode with the GC Orbitrap MS.*** Integration of high resolution accurate mass information and fragment rationalization allowed the characterization of up to 11 different iodo-DBPs in the water extracts analyzed, including one new iodo-DBP reported for the first time. ***Overall, formation of iodo-DBPs was enhanced during chloramination reactions. As expected, NOM characteristics and iodide and bromide content of the tested waters affected the amount and type of iodo-DBPs generated.*** [Figure not available: see fulltext.] © 2016, Springer-Verlag Berlin Heidelberg.
AUTHOR KEYWORDS: Chloramination; Chlorination; Gas chromatography; High resolution mass spectrometry; Iodinated disinfection by-products; Orbitrap GC
DOCUMENT TYPE: Article

Richardson, S.D., Postigo, C. Discovery of New Emerging DBPs by High-Resolution Mass Spectrometry (2016) Comprehensive Analytical Chemistry, 71, pp. 335-356. Cited five times. DOI: 10.1016/bs.coac.2016.01.008.

AFFILIATIONS: University of South Carolina, Columbia, SC, United States; Inst. for Environmental Assessment and Water Res. - Spanish National Research Council (IDAEA-CSIC), Barcelona, Spain.

ABSTRACT: ***More than 50% of the halogenated disinfection by-products (DBPs) formed during disinfection treatments are still unknown, and they may be relevant for the potential toxicity exerted by DBP mixtures of disinfected waters.*** High-resolution mass spectrometry (HR-MS) technology has contributed to reduce the amount of unknown DBPs. ***This chapter discusses the role of magnetic sectors, time-of-flight, Orbitrap and Fourier transform ion cyclotron resonance (FT-ICR) instruments in the comprehensive identification of DBPs in disinfected waters (including drinking water, swimming pool water, disinfected ballast water and disinfected wastewater-impacted waters) and reviews the most relevant DBP discoveries found in the peer-reviewed literature, in terms of novel DBP chemical classes or highly toxic compounds.*** Furthermore, the use of HR-MS analyzers to quantify target DBPs in biological samples is also briefly discussed. © 2016 Elsevier B.V.
AUTHOR KEYWORDS: DBPs; Disinfection by-products; Drinking water; Emerging contaminants; High-resolution mass spectrometry; Structure elucidation
DOCUMENT TYPE: Book Chapter

Postigo, C., Jeong, C.H., Richardson, S.D., Wagner, E.D., Plewa, M.J., Simmons, J.E., Barcelo, D. Analysis, occurrence, and toxicity of haloacetaldehydes in drinking waters: Iodoacetaldehyde as an emerging disinfection by-product (2015) ACS Symposium Series, 1190, pp. 25-43. Cited one time. DOI: 10.1021/bk-2015-1190.ch002.

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Columbia, SC 29208, United States; National Health and Environmental Effects Research Laboratory (NHEERL-U.S. EPA), 109 T.W. Alexander Drive, Research Triangle Park, NC 27709, United States; Catalan Institute for Water Research (ICRA), Parc Cientific i Tecnologic de la Universitat de Girona, Edifici H2O, Carrer d'Emili Grahit, 101, Girona, 17003, Spain.

ABSTRACT: ***Chlorinated and brominated haloacetaldehydes (HALs) are considered the 3rd largest class of disinfection by-products (DBPs) by weight. The iodinated HAL, iodoacetaldehyde, has been recently reported as an emerging DBP in finished drinking waters. Overall, iodinated DBPs, e.g., iodoacetic acids, iodoacetamides, and iodonitriles, are among the most genotoxic of all DBPs identified. In this context, this chapter reviews the analytical methods available to date to determine HALs in water, and the concentrations at which they are present in finished drinking waters.*** Since systematic toxicological effects have been only investigated for selected chloro- and bromo- HALs, a comparative study of the genotoxicity and cytotoxicity of this DBP class to mammalian cells is also presented. © 2015 American Chemical Society.
AUTHOR KEYWORDS: Chloral hydrate; Cytotoxicity; Disinfection by-products; Drinking waters; Genotoxicity; Halogenated aldehydes; Mammalian cells; Occurrence
DOCUMENT TYPE: Book Chapter

Wendel, F.M., Lütke Eversloh, C., Machek, E.J., Duirk, S.E., Plewa, M.J., Richardson, S.D., Ternes, T.A. Transformation of iopamidol during chlorination (2014) Environmental Science and Technology, 48 (21), pp. 12689-12697. Cited 44 times. DOI: 10.1021/es503609s.

AFFILIATIONS: Water Chemistry Department, Federal Institute of Hydrology (BfG), Am Mainzer Tor 1, Koblenz, D-56068, Germany; Department of Civil Engineering, University of Akron, Akron, OH 44325, United States; Department of Crop Sciences and Safe Global Water Institute, NSF Science and Technology Center of Advanced Materials for the Purification of Water with Systems, University of Illinois at Urbana-Champaign, 1101 West Peabody Drive, Urbana, IL 61801, United States; Department of Chemistry and Biochemistry, University of South Carolina, 631 Sumter St., Columbia, SC 29208, United States.

ABSTRACT: The transformation of the iodinated X-ray contrast media (ICM) iopamidol, iopromide, iohexol, iomeprol, and diatrizoate was examined in purified water over the pH range from 6.5 to 8.5 in the presence of sodium hypochlorite, monochloramine, and chlorine dioxide. ***In the presence of aqueous chlorine, only iopamidol was transformed. All other ICM did not show significant reactivity, regardless of the oxidant used.*** Chlorination of iopamidol followed a second order reaction, with an observed rate constant of up to 0.87 M-1 s-1 (±0.021 M-1 s-1) at pH 8.5. The hypochlorite anion was identified to be the reactive chlorine species. ***Iodine was released during the transformation of iopamidol, and was mainly oxidized to iodate. Only a small percentage (less than 2% after 24 h) was transformed to known organic iodinated disinfection byproducts (DBPs) of low molecular weight. Some of the iodine was still present in high-molecular weight DBPs.*** The chemical structures of these DBPs were elucidated via MSn fragmentation and NMR. Side chain cleavage was observed as well as the exchange of iodine by chlorine. ***An overall transformation pathway was proposed for the degradation of iopamidol. CHO cell chronic cytotoxicity tests indicate that chlorination of iopamidol generates a toxic mixture of high molecular weight DBPs (LC50 332 ng/µL).*** © 2014 American Chemical Society.
DOCUMENT TYPE: Article

Postigo, C., Richardson, S.D. Transformation of pharmaceuticals during oxidation/disinfection processes in drinking water treatment (2014) Journal of Hazardous Materials, 279, pp. 461-475. Cited 90 times. DOI: 10.1016/j.jhazmat.2014.07.029.

AFFILIATIONS: Inst. for Environmental Assessment and Water Research (IDAEA), Spanish National Research Council (CID-CSIC), Barcelona, Spain; Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC, United States.

ABSTRACT: Pharmaceuticals are emerging contaminants of concern and are widespread in the environment. While the levels of these substances in finished drinking waters are generally considered too low for human health concern, ***there are now concerns about their disinfection by-products (DBPs) that can form during drinking water treatment, which in some cases have been proven to be more toxic than the parent compounds. The present manuscript reviews the transformation products of pharmaceuticals generated in water during different disinfection processes, i.e., chlorination, ozonation, chloramination, chlorine dioxide, UV, and UV/hydrogen peroxide, and the main reaction pathways taking place.*** Most of the findings considered for this review come from controlled laboratory studies involving reactions of pharmaceuticals with these oxidants used in drinking water treatment. © 2014 Elsevier B.V.
AUTHOR KEYWORDS: Chlorination; DBPs; Disinfection by-products; Drinking water; Pharmaceuticals; Transformation pathways
DOCUMENT TYPE: Review

Jeong, C.H., Wagner, E.D., Siebert, V.R., Anduri, S., Richardson, S.D., Daiber, E.J., McKague, A.B., Kogevinas, M., Villanueva, C.M., Goslan, E.H., Luo, W., Isabelle, L.M., Pankow, J.F., Grazuleviciene, R., Cordier, S., Edwards, S.C., Righi, E., Nieuwenhuijsen, M.J., Plewa, M.J. Occurrence and toxicity of disinfection byproducts in European drinking waters in relation with the HIWATE epidemiology study (2012) Environmental Science and Technology, 46 (21), pp. 12120-12128. Cited 70 times. DOI: 10.1021/es3024226.

AFFILIATIONS: College of Agricultural, Consumer and Environmental Sciences, University of Illinois at Urbana-Champaign, Urbana, IL, United States; National Exposure Research Laboratory, U.S. Environmental Protection Agency, Athens, GA, United States; CanSyn Chem. Corp., Toronto, ON, Canada; Center for Research in Environmental Epidemiology (CREAL), Barcelona, Spain; Cranfield Water Science Institute, Cranfield University, Cranfield, Bedford, United Kingdom; Portland State University, Portland, OR, United States; Department of Environmental Sciences, Vytautas Magnus University, Kaunas, Lithuania; National Institute for Health and Medical Research (INSERM), U1085-IRSET, University of Rennes i, Rennes, France; MRC-HPA Centre for Environment and Health, Imperial College, London, United Kingdom; Department of Public Health Sciences, University of Modena and Reggio Emilia, Modena, Italy; Hospital Del Mar Research Institute (IMIM), CIBER Epidemiologia y Salud Publica (CIBERESP), Spain.

ABSTRACT: ***The HIWATE (Health Impacts of long-term exposure to disinfection byproducts in drinking WATEr) project was a systematic analysis that combined the epidemiology on adverse pregnancy outcomes and other health effects with long-term exposure to low levels of drinking water disinfection byproducts (DBPs) in the European Union.*** The present study focused on the relationship of the occurrence and concentration of DBPs with in vitro mammalian cell toxicity. Eleven drinking water samples were collected from five European countries. Each sampling location corresponded with an epidemiological study for the HIWATE program. ***Over 90 DBPs were identified; the range in the number of DBPs and their levels reflected the diverse collection sites, different disinfection processes, and the different characteristics of the source waters.*** For each sampling site, chronic mammalian cell cytotoxicity correlated highly with the numbers of DBPs identified and the levels of DBP chemical classes. ***Although there was a clear difference in the genotoxic responses among the drinking waters, these data did not correlate as well with the chemical analyses. Thus, the agents responsible for the genomic DNA damage observed in the HIWATE samples may be due to unresolved associations of combinations of identified DBPs, unknown emerging DBPs that were not identified, or other toxic***

water contaminants. This study represents the first to integrate quantitative in vitro toxicological data with analytical chemistry and human epidemiologic outcomes for drinking water DBPs. © 2012 American Chemical Society.
DOCUMENT TYPE: Article

Boyd, J.M., Hrudey, S.E., Li, X.-F., Richardson, S.D. Solid-phase extraction and high-performance liquid chromatography mass spectrometry analysis of nitrosamines in treated drinking water and wastewater (2011) TrAC - Trends in Analytical Chemistry, 30 (9), pp. 1410-1421. Cited 57 times. DOI: 10.1016/j.trac.2011.06.009.

AFFILIATIONS: Division of Analytical and Environmental Toxicology, Department of Laboratory Medicine and Pathology, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB T6G 2G3, Canada; National Exposure Research Laboratory, US Environmental Protection Agency, Athens, GA 30605, United States.

ABSTRACT: ***N-Nitrosamines, including N-nitrosodimethylamine (NDMA), were identified as chlorination byproducts in drinking water in 1989. Nitrosamines are known rodent carcinogens and probable human carcinogens, and so they are considered disinfection byproducts (DBPs) of public health concern.*** Epidemiological studies show a potential association of consumption of chlorinated drinking water with an increased risk of bladder cancer. ***As small, relatively polar DBPs that often occur at low-ng/L concentrations in water, nitrosamines pose analytical challenges for accurate determination. Sample preparation (e.g., the commonly used solid-phase extraction) plays a critical role in achieving reliable determination of nitrosamines at ng/L concentrations. Historically, gas chromatography (GC)-based techniques have been used for nitrosamine analysis. Recently, newly developed liquid chromatography-tandem mass spectrometry (LC-MS2) methods have shown potential advantages in determining polar DBPs. This review focuses on the sample preconcentration methods and LC-MS2 determination of nitrosamines in drinking water and wastewater. It also provides a historical perspective on nitrosamines and their occurrence in drinking water.*** © 2011 Elsevier Ltd.
AUTHOR KEYWORDS: Chlorinated; Disinfection byproduct; Drinking water; Gas chromatography; Liquid chromatography; Nitrosamine; Sample preconcentration; Solid-phase extraction; Tandem mass spectrometry; Wastewater
DOCUMENT TYPE: Review

Pressman, J.G., Richardson, S.D., Speth, T.F., Miltner, R.J., Narotsky, M.G., Hunter III, E.S., Rice, G.E., Teuschler, L.K., McDonald, A., Parvez, S., Krasner, S.W., Weinberg, H.S., McKague, A.B., Parrett, C.J., Bodin, N., Chinn, R., Lee, C.-F.T., Simmons, J.E. Concentration, chlorination, and chemical analysis of drinking water for disinfection byproduct mixtures health effects research: U.S. EPAs four lab study (2010) Environmental Science and Technology, 44 (19), pp. 7184-7192. Cited 83 times. DOI: 10.1021/es9039314.

AFFILIATIONS: National Risk Management Research Laboratory, U.S. EPA, Cincinnati, OH 45268, United States; National Exposure Research Laboratory, U.S. EPA, Athens, GA 30605, United States; National Health and Environmental Effects Research Laboratory, U.S. EPA, Research Triangle Park, NC 27711, United States; National Center for Environmental Risk Assessment, U.S. EPA, Cincinnati, OH 45268, United States; Metropolitan Water District of Southern California, La Verne, CA 91750, United States; Gillings School of Global Public Health, Department of Environmental Sciences and Engineering, University of North Carolina, Chapel Hill, NC 27599-7431, United States; CanSyn Chem. Corp., Toronto M5S 3E5, Canada; Centre de Recherche Halieutique Mé Diterranéenne et Tropicale, Institut de Recherche et de Développement, Sète Cedex, France.

ABSTRACT: ***The U.S. Environmental Protection Agency's "Four Lab Study" involved participation of researchers from four national Laboratories and Centers of the Office of Research and Development along with collaborators from the water industry and academia.*** The study evaluated toxicological effects of complex disinfection byproduct (DBP) mixtures, with an emphasis on reproductive and developmental effects that have been associated with DBP exposures in some human epidemiologic studies. This paper describes a new procedure for producing chlorinated drinking water concentrate for animal toxicology experiments, comprehensive identification of >100 DBPs, and quantification of 75 priority and regulated DBPs. In the research reported herein, complex mixtures of DBPs were produced by concentrating a natural source water with reverse osmosis membranes, followed by addition of bromide and treatment with chlorine. By concentrating natural organic matter in the source water first and disinfecting with chlorine afterward, DBPs (including volatiles and semivolatiles) were formed and maintained in a water matrix suitable for animal studies. DBP levels in the chlorinated concentrate compared well to those from EPAs Information Collection Rule (ICR) and a nationwide study of priority unregulated DBPs when normalized by total organic carbon (TOC). ***DBPs were relatively stable over the course of the animal studies (125 days) with multiple chlorination events (every five-14 days), and a significant portion of total organic halogen was accounted for through a comprehensive identification approach. DBPs quantified included regulated DBPs, priority unregulated DBPs, and additional DBPs targeted by the ICR. Many DBPs are reported for the first time, including previously undetected and unreported haloacids and haloamides.*** The new concentration procedure not only produced a concentrated drinking water suitable for animal experiments, but also provided a greater TOC concentration factor (136 -), enhancing the detection of trace DBPs that are often below detection using conventional approaches. © 2010 American Chemical Society.
DOCUMENT TYPE: Article

Vincenti, M., Fasano, F., Valsania, M.C., Guarda, P., Richardson, S.D. Application of the novel 5-chloro-2,2,3,3,4,4,5,5-octafluoro-1-pentyl chloroformate derivatizing agent for the direct determination of highly polar water disinfection byproducts (2010) Analytical and Bioanalytical Chemistry, 397 (1), pp. 43-54. Cited 20 times. DOI: 10.1007/s00216-010-3477-2

AFFILIATIONS: Dipartimento di Chimica Analitica, Università Degli Studi di Torino, Via Pietro Giuria 5, Torino 10125, Italy; Dipartimento di Traumatologia, Ortopedia e Medicina Del Lavoro, Università Degli Studi di Torino, Via Zuretti 29, Torino 10126, Italy; Solvay Solexis S.p.A., Viale Lombardia, 20, Bollate, Milan 20021, Italy; National Exposure Research Laboratory, U.S. Environmental Protection Agency, Athens, GA 30605, United States.

ABSTRACT: ***A novel derivatizing agent, 5-chloro-2,2,3,3,4,4,5,5-octafluoropentyl chloroformate (ClOFPCF), was synthesized and tested as a reagent for direct water derivatization of highly polar and hydrophilic analytes. Its analytical performance satisfactorily compared to a perfluorinated chloroformate previously described, namely 2,2,3,3,4,4,5,5-octafluoropentyl chloroformate (OFPCF).*** The chemical properties (reactivity, selectivity, derivatization products, and their chromatographic and spectral features) for ClOFPCF were investigated using a set of 39 highly polar standard analytes, including, among others, hydroxylamine, malic and succinic acids, resorcinol, hydroxybenzaldehyde, and dihydroxybenzoic acid. Upon derivatization, the analytes were extracted from the aqueous solvent and analyzed by gas chromatography (GC)-mass spectrometry (MS) in the electron-capture negative ionization (ECNI) mode. Positive chemical ionization (PCI)-MS was used for confirming the molecular ions, which were virtually absent in the ECNI mass spectra. ClOFPCF showed good reaction efficiency, good chromatographic and spectroscopic properties (better than with OFPCF), good linearity in calibration curves, and low detection limits (0.3-1µg/L). A unique feature of the derivatizations with ClOFPCF, and, in general, highly fluorinated chloroformates, is their effectiveness in reacting with carboxylic, hydroxylic, and aminic groups at once, forming multiply-substituted non-polar derivatives

that can be easily extracted from the aqueous phase and determined by GC-ECNI-MS. ***The entire procedure from raw aqueous sample to ready-to-inject hexane solution of the derivatives requires less than 10 min. Another benefit of this procedure is that it produced stable derivatives, with optimal volatility for GC separation, and high electron affinity, which allows their detection as negative ions at trace level. In addition, their mass spectra exhibits chlorine isotopic patterns that clearly indicate how many polar hydrogens of the analyte undergo derivatization. Finally, derivatization with ClOFPCF was used successfully to identify 13 unknown highly polar disinfection byproducts (DBPs) in ozonated fulvic and humic acid aqueous solutions and in real ozonated drinking water.***
AUTHOR KEYWORDS: Chloroformate; Derivatization; ECNI; Humic substances; Hydrophilic compounds; Water disinfection byproducts
DOCUMENT TYPE: Conference Paper

Richardson, S.D., Thruston Jr., A.D., Krasner, S.W., Weinberg, H.S., Miltner, R.J., Schenck, K.M., Narotsky, M.G., McKague, A.B., Simmons, J.E. Integrated disinfection by-products mixtures research: Comprehensive characterization of water concentrates prepared from chlorinated and ozonated/postchlorinated drinking water (2008) Journal of Toxicology and Environmental Health - Part A: Current Issues, 71 (17), pp. 1165-1186. Cited 75 times. DOI: 10.1080/15287390802182417.

AFFILIATIONS: National Exposure Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Athens, GA, United States; Metropolitan Water District of Southern California, LaVerne, CA, United States; Department of Environmental Sciences and Engineering, University of North Carolina, Chapel Hill, NC, United States; National Risk Management Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Cincinnati, OH, United States; National Health and Environmental Effects Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC, United States; CanSyn Chem. Corp., Toronto, ON, Canada; U.S. EPA, National Exposure Research Laboratory, 960 College Station Rd., Athens, GA 30605, United States.

ABSTRACT: ***This article describes the disinfection by-product (DBP) characterization portion of a series of experiments designed for comprehensive chemical and toxicological evaluation of two drinking-water concentrates containing highly complex mixtures of DBPs.*** This project, called the Four Lab Study, involved the participation of scientists from four laboratories and centers of the U.S. Environmental Protection Agency (EPA) Office of Research and Development, along with collaborators from the water industry and academia, and addressed toxicologic effects of complex DBP mixtures, with an emphasis on reproductive and developmental effects that are associated with DBP exposures in epidemiologic studies. Complex mixtures of DBPs from two different disinfection schemes (chlorination and ozonation/postchlorination) were concentrated successfully, while maintaining a water matrix suitable for animal studies. ***An array of chlorinated/brominated/iodinated DBPs was created.*** The DBPs were relatively stable over the course of the animal experiments, ***and a significant portion of the halogenated DBPs formed in the drinking water was accounted for through a comprehensive qualitative and quantitative identification approach.*** DBPs quantified included priority DBPs that are not regulated but have been predicted to produce adverse health effects, as well as those currently regulated in the United States and those targeted during implementation of the Information Collection Rule. ***New by-products were also reported for the first time. These included previously undetected and unreported bromo- and chloroacids, iodinated compounds, bromo- and iodophenols, and bromoalkyltins.*** Copyright © Taylor & Francis Group, LLC.
DOCUMENT TYPE: Article

Bodin, N., Weinberg, H.S., Krasner, S.W., Richardson, S.D., Pressman, J.G., Speth, T.F., Miltner, R.J., Simmons, J.E. Methods for the analysis of priority dbps in ro-concentrated drinking water (2007) American Water Works Association - Water Quality Technology Conference and Exposition 2007: Fast

Tracks to Water Quality, pp. 3775-3780.
DOCUMENT TYPE: Conference Paper

Richardson, S.D., Plewa, M.J., Wagner, E.D., Schoeny, R., DeMarini, D.M. Occurrence, genotoxicity, and carcinogenicity of regulated and emerging disinfection by-products in drinking water: A review and roadmap for research (2007) Mutation Research - Reviews in Mutation Research, 636 (1-3), pp. 178-242. Cited 1395 times. DOI: 10.1016/j.mrrev.2007.09.001.

AFFILIATIONS: National Exposure Research Laboratory, U.S. Environmental Protection Agency, Athens, GA 30605, United States; Department of Crop Sciences, College of Agricultural, Consumer, and Environmental Sciences, University of Illinois at Urbana-Champaign, Urbana, IL 61801, United States; Office of Water, U.S. Environmental Protection Agency, 1200 Pennsylvania Avenue NW, Washington, DC 20460, United States; National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, United States.

ABSTRACT: Disinfection by-products (DBPs) are formed when disinfectants (chlorine, ozone, chlorine dioxide, or chloramines) react with naturally occurring organic matter, anthropogenic contaminants, bromide, and iodide during the production of drinking water. ***Here we review 30 years of research on the occurrence, genotoxicity, and carcinogenicity of 85 DBPs, 11 of which are currently regulated by the U.S., and 74 of which are considered emerging DBPs due to their moderate occurrence levels and/or toxicological properties.*** These 74 include halonitromethanes, iodo-acids and other unregulated halo-acids, iodo-trihalomethanes (THMs), and other unregulated halomethanes, halofuranones (MX [3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone] and brominated MX DBPs), haloamides, haloacetonitriles, tribromopyrrole, aldehydes, and N-nitrosodimethylamine (NDMA) and other nitrosamines. Alternative disinfection practices result in drinking water from which extracted organic material is less mutagenic than extracts of chlorinated water. However, the levels of many emerging DBPs are increased by alternative disinfectants (primarily ozone or chloramines) compared to chlorination, and many emerging DBPs are more genotoxic than some of the regulated DBPs. Our analysis identified three categories of DBPs of particular interest. Category 1 contains eight DBPs with some or all of the toxicologic characteristics of human carcinogens: four regulated (bromodichloromethane, dichloroacetic acid, dibromoacetic acid, and bromate) and four unregulated DBPs (formaldehyde, acetaldehyde, MX, and NDMA). Categories 2 and 3 contain 43 emerging DBPs that are present at moderate levels (sub- to low-μg/L): category 2 contains 29 of these that are genotoxic (including chloral hydrate and chloroacetaldehyde, which are also a rodent carcinogens); category 3 contains the remaining 14 for which little or no toxicological data are available. In general, the brominated DBPs are both more genotoxic and carcinogenic than are chlorinated compounds, and iodinated DBPs were the most genotoxic of all but have not been tested for carcinogenicity. ***There were toxicological data gaps for even some of the 11 regulated DBPs, as well as for most of the 74 emerging DBPs.*** A systematic assessment of DBPs for genotoxicity has been performed for ~60 DBPs for DNA damage in mammalian cells and 16 for mutagenicity in Salmonella. A recent epidemiologic study found that much of the risk for bladder cancer associated with drinking water was associated with three factors: THM levels, showering/bathing/swimming (i.e., dermal/inhalation exposure), and genotype (having the GSTT1-1 gene). This finding, along with mechanistic studies, highlights the emerging importance of dermal/inhalation exposure to the THMs, or possibly other DBPs, and the role of genotype for risk for drinking-water-associated bladder cancer. ***More than 50% of the total organic halogen (TOX) formed by chlorination and more than 50% of the assimilable organic carbon (AOC) formed by ozonation has not been identified chemically.*** The potential interactions among the 600 identified DBPs in the complex mixture of drinking water to which we are exposed by various routes is not reflected in any of the toxicology studies of individual DBPs. The categories of DBPs described here, the identified data gaps, and the emerging role of dermal/inhalation exposure provide guidance for

drinking water and public health research. © 2007 Elsevier B.V. All rights reserved.
AUTHOR KEYWORDS: N-Nitrosodimethylamine; Regulated and unregulated DBPs; Total organic carbon; Total organic halogen
DOCUMENT TYPE: Review

Krasner, S.W., Weinberg, H.S., Richardson, S.D., Pastor, S.J., Chinn, R., Sclimenti, M.J., Onstad, G.D., Thruston Jr., A.D. Occurrence of a new generation of disinfection byproducts (2006) Environmental Science and Technology, 40 (23), pp. 7175-7185. Cited 865 times. DOI: 10.1021/es060353j.

AFFILIATIONS: Metropolitan Water District of Southern California, 700 Moreno Avenue, La Verne, CA 91750-3399, United States; Department of Environmental Sciences and Engineering, University of North Carolina, Chapel Hill, NC 27599-7431, United States; National Exposure Research Laboratory, U.S. Environmental Protection Agency, 960 College Station Road, Athens, GA 30605, United States.

ABSTRACT: A survey of disinfection byproduct (DBP) occurrence in the United States was conducted at 12 drinking water treatment plants. ***In addition to currently regulated DBPs, more than 50 DBPs that rated a high priority for potential toxicity were studied. These priority DBPs included iodinated trihalomethanes (THMs), other halomethanes, a nonregulated haloacid, haloacetonitriles, haloketones, halonitromethanes, haloaldehydes, halogenated furanones, haloamides, and nonhalogenated carbonyls.*** The purpose of this study was to obtain quantitative occurrence information for new DBPs (beyond those currently regulated and/or studied) for prioritizing future health effects studies. An effort was made to select plants treating water that was high in total organic carbon and/or bromide to enable the detection of priority DBPs that contained bromine and/or iodine. THMs and haloacetic acids (HAAs) represented the two major classes of halogenated DBPs formed on a weight basis. Haloacetaldehydes represented the third major class formed in many of the waters. In addition to obtaining quantitative occurrence data, important new information was discovered or confirmed at full-scale plants on the formation and control of DBPs with alternative disinfectants to chlorine. Although the use of alternative disinfectants (ozone, chlorine dioxide, and chloramines) minimized the formation of the four regulated THMs, trihalogenated HAAs, and total organic halogen (TOX), several priority DBPs were formed at higher levels with the alternative disinfectants as compared with chlorine. For example, the highest levels of iodinated THMs - which are not part of the four regulated THMs - were found at a plant that used chloramination with no prechlorination. The highest concentration of dichloroacetaldehyde was at a plant that used chloramines and ozone; however, this disinfection scheme reduced the formation of trichloroacetaldehyde. Preozonation was found to increase the formation of trihalonitromethanes. In addition to the chlorinated furanones that have been measured previously, brominated furanones - which have seldom been analyzed - were detected, especially in high-bromide waters. The presence of bromide resulted in a shift to the formation of other bromine-containing DBPs not normally measured (e.g., brominated ketones, acetaldehydes, nitromethanes, acetamides). ***Collectively, ~30 and 39% of the TOX and total organic bromine, respectively, were accounted for (on a median basis) by the sum of the measured halogenated DBPs. In addition, 28 new, previously unidentified DBPs were detected. These included brominated and iodinated haloacids, a brominated ketone, and chlorinated and iodinated aldehydes.*** © 2006 American Chemical Society.
DOCUMENT TYPE: Article

Richardson, S.D. Disinfection by-products and other emerging contaminants in drinking water (2003) TrAC - Trends in Analytical Chemistry, 22 (10), pp. 666-684. Cited 425 times. DOI: 10.1016/S0165-9936(03)01003-3.

AFFILIATIONS: US Environmental Protection Agency, Office of Research and Development, Natl. Exposure Research Laboratory, Athens, GA 30605, United States.

ABSTRACT: Although drinking-water disinfection by-products (DBPs) have been studied for the last 30 years, significant, new concerns have arisen. These concerns include adverse reproductive and developmental effects recently observed in human populations, concerns that the types of cancer observed in laboratory animals (for regulated DBPs) do not correlate with the cancers observed in human populations (indicating that other DBPs may be important), and concerns arising from human-exposure studies that show that other routes besides ingestion (i.e., inhalation and dermal adsorption) are also significant sources of DBP exposures. In addition, many drinking-water utilities are changing their primary disinfectant from chlorine to alternative disinfectants (e.g., ozone, chlorine dioxide, and chloramines), which generally reduce regulated trihalomethane and haloacetic acid levels, but can increase the levels of other potentially toxicologically important DBPs. ***For example, results of a new US Nationwide DBP Occurrence Study (discussed in this review) demonstrated that bromo-trihalonitromethanes, iodo-trihalomethanes, dihaloaldehydes, MX (3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone), and brominated forms of MX were formed at higher levels when alternative disinfectants were used to treat drinking water.*** Specific DBPs of emerging toxicological interest include brominated and iodinated compounds - including bromonitromethanes, iodo-trihalomethanes, iodo-acids, and brominated forms of MX - as well as nitrosodimethylamine (NDMA). In addition to concerns about DBPs, there are also new concerns about the presence of pharmaceuticals, organotins, methyl-tert-butyl ether (MTBE), perchlorate, and algal toxins in drinking water. ***This article will discuss these drinking-water contaminants of emerging concern and the analytical methods currently being used for their determination.*** © 2003 Published by Elsevier B.V.
DOCUMENT TYPE: Review

Vincenti, M., Davit, P., Richardson, S.D. Comparison of perfluorinated chloroformates as direct aqueous sample derivatizing agents for highly hydrophilic analytes (2002) Proceedings 50th ASMS Conference on Mass Spectrometry and Allied Topics, pp. 69-70.

AFFILIATIONS: Dipartimento di Chimica Analitica, Università di Torino, Torino, Italy; Dipartimento di Chimica, I.F.M., Università di Torino, Torino, Italy; U.S. Environmental Protection Agency, Athens, GA, United States.

ABSTRACT: ***The synthesis of perfluoroalkyl and perfluoroaryl chloroformates was investigated which achieved high sensitivity and selectivity by electron capture negative ionization MS detection.*** 2 mL aliqout of aqueous sample was basified with 150 µl of NaOH 3 M which was added to 150 µl of chloroformate acetonic solution. The introduction of substituents in analyte structure and reaction efficiency strongly depended on specific derivatizing agent used. ***The positive ion Cl spectra provided molecular ion information while detection limits in positive ion mode proved 23 orders-of-magnitude higher than in negative ion mode.***
DOCUMENT TYPE: Conference Paper

Richardson, S.D., Thruston Jr., A.D., McKague, B., Rav-Acha, C., Glezer, V. Identification of new brominated acids in drinking water (2002) Proceedings 50th ASMS Conference on Mass Spectrometry and Allied Topics, pp. 669-670.

AFFILIATIONS: U.S. Environmental Protection Agency, Athens, GA 30605, United States; CanSyn Chem. Corp., Toronto, Canada; Israel Ministry of Health, Tel-Aviv, Israel.

ABSTRACT: ***The identification of new brominated acids in drinking water by using has chromatography/mass spectrometry (MS) was discussed.*** Drinking water samples from full-scale plants were acidified and extracted with XAD resins. ***The bromine-containing acids were identified as the derivatized methyl esters. The high resolution MS was used to confirm empirical formula assignments for the molecular ions and the fragments. The identity of nine of the 18 bromo-acids was confirmed by***

analysis of authentic chemical standards.
DOCUMENT TYPE: Conference Paper

Simmons, J.E., Richardson, S.D., Speth, T.F., Miltner, R.J., Rice, G., Schenck, K.M., Hunter III, E.S., Teuschler, L.K. Development of a research strategy for integrated technology-based toxicological and chemical evaluation of complex mixtures of drinking water disinfection byproducts (2002) Environmental Health Perspectives, 110 (SUPPL. 6), pp. 1013-1024. Cited 60 times.

AFFILIATIONS: Natl. Hlth./Envir. Effects Res. Lab., Office of Research and Development, U.S. Environmental Protection Agency, 109 T.W. Alexander Dr., Research Triangle Park, NC 27711, United States; National Exposure Research Lab., Office of Research and Development, U.S. Environmental Protection Agency, Athens, GA, United States; Natl. Risk Management Research Lab., Office of Research and Development, U.S. Environmental Protection Agency, Cincinnati, OH, United States; Natl. Ctr. for Environ. Assessment, Office of Research and Development, U.S. Environmental Protection Agency, Cincinnati, OH, United States.

ABSTRACT: Chemical disinfection of water is a major public health triumph of the 20th century. Dramatic decreases in both morbidity and mortality of waterborne diseases are a direct result of water disinfection. ***With these important public health benefits comes low-level, chronic exposure to a very large number of disinfection byproducts (DBPs), chemicals formed through reaction of the chemical disinfectant with naturally occurring inorganic and organic material in the source water. This article provides an overview of joint research planning by scientists residing within the various organizations of the U.S. Environmental Protection Agency Office of Research and Development.*** The purpose is to address concerns related to potential health effects from exposure to DBPs that cannot be addressed directly from toxicological studies of individual DBPs or simple DBP mixtures. Two factors motivate the need for such an investigation of complex mixtures of DBPs: a***) a significant amount of the material that makes up the total organic halide and total organic carbon portions of the DBPs has not been identified***; and b) epidemiologic data, although not conclusive, are suggestive of potential development, reproductive, or carcinogenic health effects in humans exposed to DBPs. The plan is being developed and the experiments necessary to determine the feasibility of its implementation are being conducted by scientists from the National Health and Environmental Effects Research Laboratory, the National Risk Management Research Laboratory, the National Exposure Research Laboratory, and the National Center for Environmental Assessment.
AUTHOR KEYWORDS: Analytical chemistry; Complex mixtures; Disinfection byproducts; Drinking water; Reverse osmosis; Toxicology
DOCUMENT TYPE: Review

Richardson, S.D. The role of GC-MS and LC-MS in the discovery of drinking water disinfection by-products (2002) Journal of Environmental Monitoring, 4 (1), pp. 1-9. Cited 85 times. DOI: 10.1039/b105578j.

AFFILIATIONS: United States Envtl. Protect. Agcy., Natl. Exposure Research Laboratory, Ecosystems Research Division, 960 College Station Rd., Athens, GA 30605, United States.

ABSTRACT: ***Gas chromatography-mass spectrometry (GC-MS) has played a pivotal role in the discovery of disinfection by-products (DBPs) in drinking water. DBPs are formed when disinfectants, such as chlorine, ozone, chlorine dioxide or chloramine, react with natural organic matter in the water. The first DBP known - chloroform - was identified by Rook in 1974 using GC-MS. Soon thereafter, chloroform and other trihalomethanes were found to be ubiquitous in chlorinated drinking water. In 1976, the National Cancer Institute published results linking chloroform to cancer in laboratory animals, and an important public health issue was born. Mass spectrometry and, specifically, GC-MS became the key tool used for measuring these DBPs in water and for discovering other DBPs that were***

formed. Over the last 25 years, hundreds of DBPs have been identified, mostly through the use of GC-MS, which has spawned additional health effects studies and regulations. Early on, GC with low resolution electron ionization (EI)-MS was used, together with confirmation with chemical standards, for identification work. Later, researchers utilized chemical ionization (CI)-MS to provide molecular weight information and high resolution EI-MS to aid in the determination of empirical formulae for the molecular ions and fragments. More recently, liquid chromatography-mass spectrometry (LC-MS) With either electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) has been used to try to uncover highly polar DBPs that most experts believe have been missed by earlier GC-MS studies. Despite 25 years of research in the identification of new DBPs, new ones are being discovered every year, even for chlorine which has been the most extensively studied.
DOCUMENT TYPE: Review

Richardson, S.D. Emerging contaminants: The need for elegant analytical chemistry solutions for the new environmental pollutants of concern (2001) ACS Division of Environmental Chemistry, Preprints, 41 (2), p. 598.

AFFILIATIONS: U.S. Environmental Protection Agency, National Exposure Research Laboratory, Athens, GA 30605, United States.

ABSTRACT: Chemical and microbial contaminants that the EPA and other agencies are concerned about are presented. In this group of contaminants are endocrine disrupting chemicals, emerging drinking water pollutants (MTBE), new drinking water disinfection by-products, and other water pollutants (e.g., nitrobenzene). Many of these contaminants have been proposed for consideration under the Unregulated Monitoring Rule, which requires EPA to select five or more contaminants every five years to consider for regulation. ***Methods are available for many of the proposed contaminants; however, several contaminants do not have rugged, reliable methods. Elegant analytical chemistry solutions are needed for many of these emerging environmental contaminants.*** This is an abstract of a paper presented at the 222nd ACS National Meeting (Chicago, IL 8/26-30/2001).
DOCUMENT TYPE: Note

Richardson, S.D., Caughran, T.V., Poiger, T., Guo, Y., Crumley, F.G. Identification of polar drinking water disinfection by-products using liquid chromatography-math spectrometry (2000) ACS Symposium Series, 761, pp. 374-388. Cited two times.

AFFILIATIONS: Natl. Exposure Research Laboratory, U.S. Environmental Protection Agency, Athens, GA 30605, United States; Swiss Fed. Inst. for Fruit Growing, Horticulture and Viticulture Schloss, CH-8820 Wädenswil, Switzerland; Metropol. Water Dist. S. California, La Verne, CA 91750-3399, United States.

ABSTRACT: ***A qualitative method using 2,4-dinitrophenylhydrazine (DNPH) derivatization followed by analysis with liquid chromatography (LC)/negative ion-electrospray mass spectrometry (MS) was developed for identifying polar aldehydes and ketones in ozonated drinking water. This method offers advantages over the currently accepted method using pentafluorobenzylhydroxylamine (PFBHA) derivatization and gas chromatography/mass spectrometry (GC/MS) analysis, in that it allows for the detection of highly polar carbonyl compounds (with multiple polar substituents) and produces mass spectra and chromatographic behavior that can be used to distinguish between aldehydes and ketones in ozonated water.*** Results for many polar-substituted aldehyde and ketone standards are presented, as well as the identification of polar disinfection by-products (DBFs) in ozonated drinking water from full-scale plants and laboratory-scale ozonations of humic acid.
DOCUMENT TYPE: Article

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