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Direct injection analysis of polar micropollutants in natural drinking water sources with biphenyl liquid chromatography coupled to high-resolution time-of-flight mass spectrometry

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ABSTRACT

A method for the trace analysis of polar micropollutants (MPs) by direct injection of surface water and groundwater was validated with ultrahigh-performance liquid chromatography using a core-shell biphenyl stationary phase coupled to time-of-flight high-resolution mass spectrometry. The validation was successfully conducted with 33 polar MPs representative for several classes of emerging contaminants. Identification and quantification were achieved by semi-automated processing of full-scan and data-independent acquisition MS/MS spectra. In most cases good linearity ($R^2 \geq 0.99$), recovery (75% to 125%) and intra-day (RSD < 20%) and inter-day precision (RSD < 10%) values were observed. Detection limits of 9 to 83 ng/L and 9 to 93 ng/L could be achieved in riverbank filtrate and surface water, respectively. A solid-phase extraction was additionally validated to screen samples from full-scale reverse osmosis drinking water treatment at sub-ng/L levels and overall satisfactory analytical performance parameters were observed for RBF and reverse osmosis permeate. Applicability of the direct injection method is shown for surface water and riverbank filtrate samples from an actual drinking water source. Several targets linkable to incomplete removal in wastewater treatment and farming activities were detected and quantified in concentrations between 28 ng/L for saccharine in riverbank filtrate and up to 1 μg/L for acesulfame in surface water. The solid phase extraction method applied to samples from full-scale reverse osmosis drinking water treatment plant led to quantification of 8 targets between 6 and 57 ng/L in the feed water, whereas only diglyme was detected and quantified in reverse osmosis permeate. Our study shows that combining the chromatographic resolution of biphenyl stationary phase with the performance of time-of-flight high-resolution tandem mass spectrometry resulted in a fast, accurate and robust method to monitor polar MPs in source waters by direct injection with high efficiency.

1. Introduction

Anthropogenic organic micropollutants (MPs) and their transformation products are ubiquitously detected in the aquatic environment [1–3]. MPs can preferentially remain in the water phase during environmental and water treatment processes based on their polarity and degree of persistency to (a)biotic degradation. These chemicals can reach drinking water, possibly triggering adverse effects on human health [4,5]. In the European Union, regulation to protect natural waters from hazardous substances is implemented, e.g. the Water Framework Directive [6]. However, most polar MPs known to occur in the aquatic environment are currently overlooked by these regulatory actions [7], resulting in the need for accurate, sensitive and robust analytical tools to efficiently monitor source waters.

Hybrid high-resolution mass analyzers (HRMS) such as linear ion trap (LTQ) Orbitrap and quadrupole time-of-flight (q-ToF) coupled to either liquid (LC) or gas chromatography (GC) are being increasingly applied to environmental samples [8–10]. HRMS has dramatically improved the potential for identification of small organic molecules, providing a resolving power, typically defined at full width at half maximum (FWHM), of 500,000 (at *m/z* 200) and 80,000 (at *m/z* 400) for modern Orbitrap and ToF detectors, respectively, and a mass deviation lower than 5 ppm for both precursors

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and product ions [10]. HRMS can provide sensitivity comparable to that of low-resolution MS [10,11] and greater selectivity in full-scan acquisitions [12]. LC-HRMS/MS represents the obvious tool to screen for polar MPs in water samples in most cases, holding a pivotal role in the elucidation of unknowns [13,14] and offering robust quantitative performance [10].

So far, reversed-phase high-performance LC (RP-HPLC) with octadecyl carbon chain-bonded silica stationary phase (C18) and coupled to hybrid Orbitrap MS equipped with electrospray ionization (ESI) has been the most used setup to quantify small polar MPs in water samples [15–18]. The improved sensitivity and dynamic range of more recent q-ToF technology have widened the possibilities for quantitative applications with hyphenated HRMS [8,19,20]. Recent q-ToFs can be a tremendous asset when coupled to ultrahigh-performance liquid chromatography (UHPLC) [10], for its additional benefits in terms of throughput and chromatographic resolution [21]. Greater efficiency can be achieved by carrying chromatographic separation on core-shell stationary phases [22].

In this context, we explored the capabilities of UHPLC-ESI-q-ToF/MS to screen qualitatively and quantitatively for polar MPs in natural raw waters. The main objective of this study was to optimize and validate a high-efficiency target screening method to analyze polar MPs in drinking water sources at environmentally relevant concentrations by direct injection analysis. A second objective was to validate a generic solid-phase extraction (SPE) with hydrophilic-lipophilic balance (HLB) for applications requiring sub-ng/L detection limits. To the best of our knowledge we introduce the first accurate-mass screening method for polar MPs in source waters which conjugates LC-HRMS analysis by direct injection, UHPLC separation on a novel core-shell biphenyl analytical column, and semi-automated identification with high confidence and quantification from full-scan HRMS data and MS/MS data recorded in a data-independent acquisition (DIA). Direct injection analysis with UHPLC-ESI-q-ToF/MS should deliver satisfactory performance to detect trace concentrations of MPs with high efficiency thanks to minimum sample preparation, high chromatographic resolution with core-shell technology [22] and semi-automated identification and quantification. Furthermore hybrid ToF analyses result in identification with confidence higher than low-resolution MS thanks to full-scan MS and DIA MS/MS data [23], offering the advantages of posing no hard limits on full-scan acquisition, the possibility to analyze target and non-target compounds retrospectively, and to apply diverse data mining strategies.

The direct injection analysis method presented in this manuscript was validated for surface water and riverbank filtrate (RBF) with a set of 33 target analytes previously chosen to investigate the efficiency of removal of polar MPs by pilot-scale reverse osmosis (RO) treatment [24]. The compounds were selected from scientific literature data and included chemicals regarded as critical for RO and for the quality of source waters. RP chromatography was chosen not to overlook moderately polar MPs when investigating RO filtration, as hydrophobicity can result in incomplete chemical removal [25]. The biphenyl column was chosen for its aqueous stability, enhanced selectivity compared to phenyl stationary phases, higher selectivity than C18 for aromatic compounds and a larger electron cloud that promotes dipole-dipole interactions with polar analytes [26]. Shape selectivity and polarizability have been identified as the main factors affecting the retention and selectivity with biphenyl stationary phases, with π-π and polar-π being the main interactions involved [27]. The applicability of our screening method was demonstrated by (i) direct injection analysis of field samples from two drinking water sources consisting of river water and RBF and (ii) SPE followed by analysis of samples from a drinking water treatment plant where anaerobic RBF is treated by standalone RO.

2. Materials and methods

2.1. Standards, chemicals and stock solutions

Details are provided in the Supplementary material section S-1.

2.2. Sample matrices

RBF, surface water and RO permeate were provided by the drinking water company Oasen (Gouda, The Netherlands) and sampled at different production locations in the Dutch river Rhine basin. RBF and RO permeate grab samples were taken from a full-scale RO treatment plant fed with freshly abstracted bank filtrate from a site located in the province of Utrecht. The surface water grab samples were taken from the river Lek in the village of Lekkerkerk, The Netherlands. All samples were collected in 5 L polyethylene bottles and stored in the dark at 2 °C for not more than three months before any procedure was applied. Procedural blanks consisting of ultrapure water were prepared for each batch and treated as samples.

2.3. Sample preparation

For analysis of RBF and surface water by direct injection, 990 μL aliquots were transferred to a 2 mL luer polypropylene (PP) syringe fitted with a 0.22 μm disk filter (Nantong FilterBio Membrane Co., Ltd, Nantong, China) and spiked with 10 μL isotope-labeled standards to obtain a concentration of 2 μg/L. The filtrate was collected in 1.5 mL PP LC vials and analyzed. A generic solid-phase extraction method was validated for RBF and RO permeate by using Oasis HLB (150 mg) from Waters (Etten-Leur, The Netherlands). The cartridges were placed on a vacuum manifold, conditioned with 5 mL of MeOH and equilibrated with 5 mL of ultrapure water. Samples and procedural blanks, 100 mL (n = 4) were transferred to a 250 mL PP bottle, spiked to 50 ng/L with the working isotope-labeled stock mixture and loaded onto the cartridges with the aid of a vacuum pump. After loading, the cartridges were washed with 2 mL of ultrapure water and dried under vacuum for 15 min. The cartridges were then eluted with 4 × 2.5 mL of MeOH by gravity whenever possible or by means of vacuum. The extracts filtered with 0.22 μm PP filters (Filter-Bio, Jiangsu, China) and collected in 15 mL PP falcon tubes before evaporation to 0.5 mL under a gentle nitrogen flow. After evaporation, the extracts were transferred to 1.5 mL PP LC vials and stored in the dark at 2 °C. Prior to UHPLC-q-ToF/MS analysis the extracts were diluted 5 times in ultrapure water to be more compatible with the aqueous mobile phase used for chromatographic separation (see Section 2.4). The procedure resulted in an enrichment factor of 40 and a concentration of internal standards equal to 2 μg/L to match that of the standards used for the calibration series (see Section 2.5).

2.4. LC conditions and HRMS settings

The analyses were conducted with a UHPLC system (Nexera, Shimadzu, Den Bosch, The Netherlands) coupled to a Bruker Daltonics maXis 4G high resolution q-ToF/MS upgraded with HD collision cell and equipped with a ESI source (Wormer, The Netherlands). Before MS detection the analytes were separated along a reversed-phase core–shell Kinetex biphenyl LC column, having 2.6 μm particle size, pore size of 100 Å and dimensions of 100 × 2.1 mm (Phenomenex, Utrecht, The Netherlands). The mobile phases considered for this study were ultrapure water (eluent A) and MeOH (eluent B). The effects of including acetic acid or formic acid in eluent A were evaluated in terms of number of detectable analytes. The LC gradient expressed as B percentage was 0% at 0 min, 50% at 2.5 min, 100% at 5 and until 7 min. The total flow rate was 0.3 mL/min. The initial

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