Anal Bioanal Chem (2015) 407:3717–3725
DOI 10.1007/s00216-015-8593-6

RESEARCH PAPER

Rapid ultra-trace analysis of sucralose in multiple-origin aqueous samples by online solid-phase extraction coupled to high-resolution mass spectrometry

Sudha Rani Batchu · Cesar E. Ramirez · Piero R. Gardinali

Received: 1 November 2014 / Revised: 10 February 2015 / Accepted: 24 February 2015 / Published online: 14 March 2015

Abstract Because of its widespread consumption and its persistence during wastewater treatment, the artificial sweetener sucralose has gained considerable interest as a proxy to detect wastewater intrusion into usable water resources. The molecular resilience of this compound dictates that coastal and oceanic waters are the final recipient of this compound with unknown effects on ecosystems. Furthermore, no suitable methodologies have been reported for routine, ultra-trace detection of sucralose in seawater as the sensitivity of traditional liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis is limited by a low yield of product ions upon collision-induced dissociation (CID). In this work, we report the development and field test of an alternative analysis tool for sucralose in environmental waters, with enough sensitivity for the proper quantitation and confirmation of this analyte in seawater. The methodology is based on automated online solid-phase extraction (SPE) and high-resolving-power orbitrap MS detection. Operating in full scan (no CID), detection of the unique isotopic pattern (100:96:31 for $[M-H]^-$, $[M-H+2]^-$, and $[M-H+4]^-$, respectively) was used for ultra-trace quantitation and analyte identification. The method offers fast analysis (14 min per run) and low sample consumption (10 mL per sample) with method detection and confirmation limits (MDLs and MCLs) of 1.4 and 5.7 ng/L in seawater, respectively. The methodology involves low operating costs due to virtually no sample preparation steps or consumables. As an application example, samples were collected from 17 oceanic and estuarine sites in Broward County, FL, with varying salinity (6–40 PSU). Samples included the ocean outfall of the Southern Regional Wastewater Treatment Plant (WWTP) that serves Hollywood, FL. Sucralose was detected above MCL in 78 % of the samples at concentrations ranging from 8 to 148 ng/L, with the exception of the WWTP ocean outfall (at pipe end, 28 m below the surface) where the measured concentration was 8418±3813 ng/L. These results demonstrate the applicability of this monitoring tool for the trace-level detection of this wastewater marker in very dilute environmental waters.

Keywords Sucralose · Online SPE · Orbitrap · HRMS · Seawater

Introduction

The artificial sweetener sucralose (4-chloro-4-deoxy-α,D-galactopyranosyl-1,6-dichloro-1,6-didexoy-β,D-fructofuranoside, CAS Number 56038-13-2, Fig. 1) is a popular low-calorie replacement of sucrose, with an estimated global consumption of ca. 2000 t/year [1]. The consumption of sucralose in virtually all human populations combined with its documented resilience against body metabolism and wastewater treatment has caused a ubiquitous occurrence of this compound in treatment plant effluents [2–4]; therefore, the compound has been proposed as a good analytical marker for sewage pollution of usable water resources [5–7]. Furthermore, sucralose has negligible bioconcentration, biodegradation, volatilization, or soil/particulate matter adsorption rates, remaining

Electronic supplementary material The online version of this article (doi:10.1007/s00216-015-8593-6) contains supplementary material, which is available to authorized users.

C. E. Ramirez · P. R. Gardinali
Department of Chemistry and Biochemistry, Florida International University, Miami, FL 33199, USA

S. R. Batchu · C. E. Ramirez (✉) · P. R. Gardinali
Southeast Environmental Research Center, Florida International University, 3000 NE 151 ST, MSB 350, North Miami Beach, FL 33181, USA
e-mail: crami023@fiu.edu

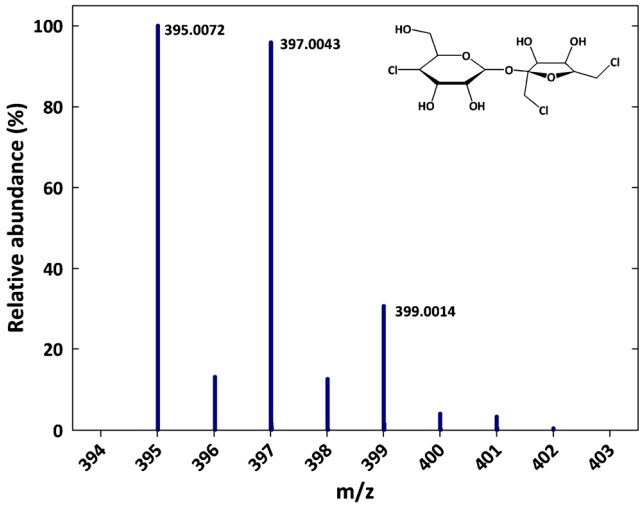

Fig. 1 Isotopic pattern of sucralose anion (from molecular calculation). *Inset*: structure of sucralose

in solution after introduction into surface waters, with oceans considered its ultimate environmental recipient [2]. However, the long-term effects of this compound in coastal and estuarine aquatic ecosystems are still largely unknown. Therefore, there is a pressing need for simple-yet-sensitive analytical methodologies for constant monitoring of sucralose in many types of aqueous matrices, including source (highly concentrated wastewaters), transport (rivers and estuaries), and recipient waters.

Ultra-trace analysis of sucralose is challenging as current analytical methods do not offer enough sensitivity, simplicity, or cost-effectiveness for successful employment in large-scale monitoring efforts. Currently, the only available report of analysis of sucralose in seawater and estuarine waters [8] detected concentrations as low as 1 ng/L in oceanic sites after solid-phase extraction (SPE) of large volumes of seawater (up to 34 L) followed by derivatization and GC-MS analysis. Although simple and effective, low sample throughput and sample economics make this procedure impractical for large-scale monitoring efforts. Other methods employing SPE in combination with liquid chromatography-tandem mass spectrometry (LC-MS/MS) detection have been reported in the literature for sucralose analysis in freshwater, drinking water, and wastewater (see Table 1), including our previous communication of a highly automated methodology that performs fast, trace-level detection of sucralose in short periods of time [14]. Most of those previous works relied on MS/MS after the formation of the anionic form of sucralose using electrospray ionization (ESI) or APCI, which is favorable and yields large quantities of the ionized analyte [9]. However, negative-mode MS/MS detection is hindered as the tri-chlorinated anion is resistant towards collision-induced dissociation (CID) which translates into a poor yield of product ions and therefore low quantitation signals [9, 16].

An unexplored alternative is the avoidance of MS/MS using other means to achieve simultaneous analyte quantitation and confirmation, such as the use of high-resolving-power mass spectrometers to detect the intact anion. The bench-top orbitrap high-resolution mass spectrometry (HRMS) instruments combine very low maintenance costs (relative to other HRMS machines such as FT-ICRs which require cryogenic gases) with the high resolving power and virtually background-free detection associated with Fourier-transform mass spectrometers [19]. It also offers comparable quantitative performance than those offered by triple-quadrupole (QqQ) machines because of its high ion transmission [19], and thus has been considered a viable alternative to MS/MS for the routine quantitation of environmental pollutants [20, 21, 22]. In the case of sucralose, unequivocal identification in negative-mode electrospray has been previously demonstrated by measuring the accurate masses of the anions forming its unique isotopic pattern, derived from the presence of three chlorine atoms of the molecule (see Fig. 1) [16, 18].

In this work, the use of an orbitrap HRMS in combination with a fast and robust online SPE preconcentration methodology that does not require sample pre-treatment is proposed as an alternative for ultra-trace quantitation of sucralose in almost all types of environmental aqueous samples. This is the first report (to the best of our knowledge) of the combination of automated online preconcentration and a high-resolving-power HRMS, enabling the analysis of many low-concentration samples with complex matrices such as seawater or drinking water in short periods of time.

Experimental section

Materials and reagents

Sucralose analytical standard was purchased from Sigma-Aldrich (St. Louis, MO, USA). Sucralose-D6 (98 % purity) was used as internal standard and was obtained from Santa Cruz Biotechnology Inc. (Santa Cruz, CA, USA). Stock solutions were prepared in acetonitrile and stored at or below 4 °C until needed. Acetonitrile, water, methanol, and ammonium formate (all LC/MS grade) were purchased from Fisher Scientific (Fair Lawn, NJ, USA). Ammonium hydroxide (Optima grade) was also purchased from Fisher Scientific. Artificial seawater (3.5 % *w*/*v*) was prepared using the commercially available Instant Ocean® salt. Fresh mobile phases were prepared every analysis day. Online preconcentration was performed using an EQuan MAX Plus online SPE system (Thermo Scientific, Waltham, MA, USA), consisting of an HTC-PAL autosampler equipped with a 5-mL glass syringe, an Accela™ 1250 as analytical HPLC pump, and an Accela™ 600 as SPE loading pump. The stainless steel sample loop (model CSL10K, 10 mL) was obtained from

Table 1 Summary of available methodologies for analysis of sucralose in water

Year, reference	Water type	Preconcentration	ESI	Scan type	Inst. type	LOD/MDL (ng/L)[a]	Sample size (mL)[b]
2009 [9]	S	SPE	−	MS/MS	QqQ	10	400
2009 [8]	SW	SPE	n.a.	GC-MS	Ion trap	n.a.	34,000
2010 [10]	E, S, G	SPE	+	MS	TOF	50	200
2011 [7]	E, S	Online SPE	−	MS/MS	QqQ	100	2.5
2011 [5]	D	SPE	−	MS/MS	QTrap	10	1000
2011 [11]	E, S	SPE	+	SIM	QqQ	20	1000
2012 [12]	G, S, E	Online SPE	−	MS/MS	QqQ	12.2	20
2013 [13]	W	SPE	−	MS/MS	QqQ	500	50
2013 [14]	D, E	Online SPE	−, +	MS/MS	QqQ	8.5	10
2013 [15]	E	SPE	−	MS/MS	QqQ	100	500
2013 [16]	E, S	SPE	−, +	MS/MS	QqQ	15	100
2014 [17]	S	SPE	−	MS/MS	QqQ	20	100
2014 [18]	G	None	−	MS/MS	QTrap	5	0.500

S surface waters, *D* drinking water, *G* groundwater, *SW* seawater, *E* wastewater treatment plant effluents, *W* wastewater (raw sewage), *n.a.* not available

[a] Reported method detection limits (MDLs)

[b] Volume of sample analyzed for the reported detection and quantitation/confirmation limits

Valco Instruments (Houston, TX, USA). The online SPE column was a Hypersep Retain PEP® (20 mm×3 mm, 12 μm) and analytical separations were carried out using a Hypersil Gold® column (50×2.1 mm, 3 μm), protected by a Hypersil Gold® guard column (10×2.1 mm, 3 μm). Detection was performed on a Q Exactive™ hybrid quadrupole-orbitrap mass spectrometer, equipped with an Ion Max API ionization source with a heated electrospray (HESI) interface. The analytical system was controlled using the Xcalibur 2.1 data acquisition software. All columns and instruments, the ionization source, and controlling software were also obtained from Thermo Scientific.

Sample collection

Field samples were collected in 500-mL PET bottles and transported to the laboratory on ice. Upon arrival, salinity was measured and samples were stored at 4 °C if analysis was to be performed no more than 14 days later. For longer-term storage, samples were frozen and kept at or below −20 °C.

Analytical methodology

Sample preparation

Working solutions were prepared each analysis day in water from stock solutions. Refrigerated samples were allowed to reach room temperature before preparation. Samples were vigorously shaken for at least 20 s, and 10.98-mL aliquots of raw water samples were transferred directly from the sampling containers into 11-mL LC vials; sucralose-D6 internal standard was added to obtain 140 ng/L. Solutions were capped, thoroughly mixed, and loaded into the online SPE system without further treatment.

Online SPE-LC-HRMS procedure

Analysis steps are a modification of a seawater analysis methodology previously released by our group [23]. Valve turning events are presented and described in the Electronic Supplementary Material (ESM). The HRMS instrument was operated with a HESI source in the negative mode using the following parameters, optimized by infusing aqueous sucralose-D6 (2 mg/L at 10 μL/min): sheath gas (N_2), 25 arb. units; auxiliary gas (N_2), 2 arb. units; capillary temperature, 350 °C; vaporizer temperature, 250 °C; S-lens RF level=90; auto gain control (AGC)=$1*10^6$; maximum injection time=100 ms; scan range, 350–465 *m*/*z*; and resolving power=140,000. Instrument mass calibration was performed weekly.

Calibration and quality control

Calibration curves were obtained by injecting 10-mL solutions of known concentrations (0.5–500 ng/L) of sucralose in deionized water using the same online SPE method that was used for the samples, plotting the response factor of the sucralose and sucralose-D6 anions (RF=$[M-H]^-/[D6-H]^-$) against concentrations in nanograms per liter. A 7-point set of calibration solutions was freshly prepared for each analysis batch. Linearity was observed in the range used (R^2>0.99).

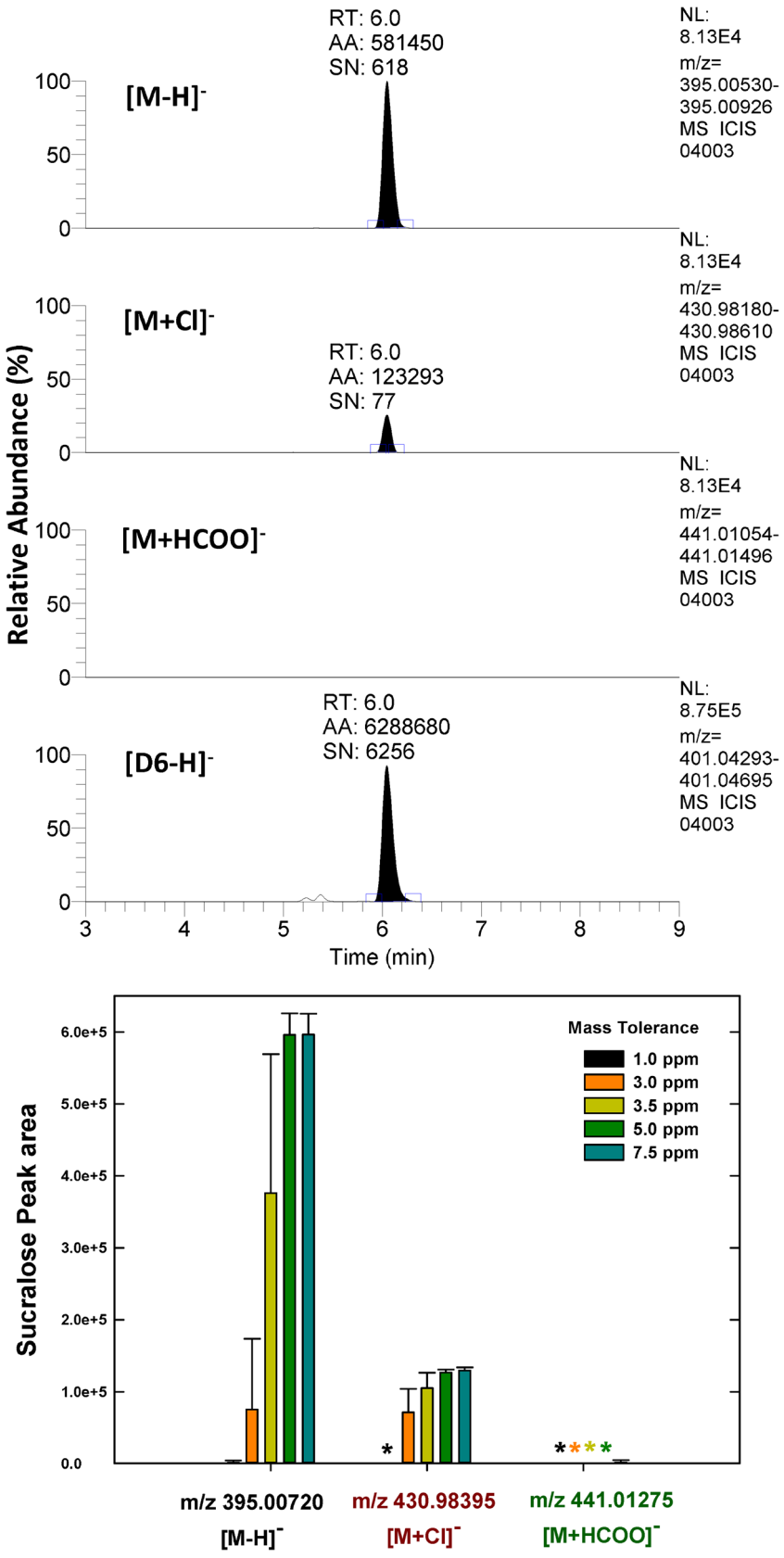

Fig. 2 (*Top*) Chromatograms of natural seawater fortified with 10 ng/L of sucralose and 140 ng/L of sucralose-D6, comparing peak areas of the accurate masses of deprotonated sucralose ($[M-H]^-$) and the chloride ($[M+Cl]^-$) and formate ($[M+HCOO]^-$) adducts (mass tolerance window=5 ppm). (*Bottom*) Comparison of peak areas vs. mass tolerance window used for peak integration (averages of seven seawater samples fortified to 10 ng/L). No gain in sensitivity was obtained above 5 ppm, and this value was used for quantitation (*asterisk* denotes non-detections)

Calibration stability was evaluated every 10 runs by injecting DI water fortified with sucralose to 100 ng/L. With every analysis batch, a negative blank (reagent and sampling) and a positive blank (fortified to 100 ng/L) were also used. Additionally, one duplicate sample and one laboratory fortified matrix (LFM) sample were analyzed every 10 field samples. The system was continuously tested for carryover by injecting a reagent blank after the highest calibration standard and after every calibration verification standard.

Compound identification was considered positive when the following conditions were met: signals (*S*/*N* ratios >3) and retention times ±0.01 min of that of $[D6-H]^-$ (*m*/*z* 401.0449) were present for the three main sucralose anions in the isotopic pattern seen in Fig. 1 ($[M-H]^-$, *m*/*z* 395.0072; $[M-H+2]^-$, *m*/*z* 397.0043; $[M-H+4]^-$, *m*/*z* 399.0014) using a mass tolerance window of 5 ppm. Additionally, the observed isotopic pattern for sucralose was monitored using the ratios of ($[M-H+2]^-$/$[M-H]^-$) and ($[M-H+4]^-$/$[M-H]^-$) which were required to fall within 10 % of their natural abundance ratios.

Results and discussion

Online SPE-LC procedure

Our previously reported online SPE-LC-MS/MS methodology for sucralose [14] was tested with drinking water and wastewater treatment plant effluents (reclaimed water). In order to accommodate the analysis of high-salinity samples, the SPE program from that methodology was modified to allow removal of salts, preventing their precipitation inside the ionization source. Our group previously released a seawater analysis procedure by online SPE-MS/MS [23] that included cleaning steps with large volumes of deionized water, which enabled long-term system stability and low matrix effects. The same approach was successfully applied for this work. The developed online SPE methodology presented an extraction recovery of 98 % (the procedure and results for extraction recovery measurement are shown in the ESM, fig. S3 and table S2). Additionally, since negative-mode HESI detection was intended, another modification was the introduction of an ammonium/ammonia buffer (pH=9.5) as a modifier to enhance analyte ionization. Figure S2 in the ESM presents the effect of adding buffer to the mobile phase on the quantitative signal ($[M-H]^-$ anion) from injecting artificial seawater fortified to 5 ng/L (similar to confirmation limits), demonstrating how buffer usage allows efficient ionization of all sucralose analytical signals and enables analyte confirmation at low levels. The introduction of the buffer increased the signal of sucralose by (64±4)% at 5 ng/L (*n*=3).

Table 2 Obtained method detection and confirmation limits in deionized water, seawater, and drinking waters (sample size was 10 mL)

Matrix	Fort. level (ng/L)	MDL $[M-H]^-$	MCL $[M-H+4]^-$	Rev. MDL[a] $[D6-H]^-$	Rev. MCL[a] $[D6-H+4]^-$
DIW	5.00	0.4	0.5	–	–
Seawater	10.0	1.4	5.7	–	–
Drinking water	25.0	–	–	11	18

[a] Reverse MDLs/MCLs (using sucralose-D6 as analyte)

Predominance of sucralose anion

In a recent communication, Wu et al. [18] performed LC-MS/MS analysis of sucralose with 0.1 % formic acid as modifier,

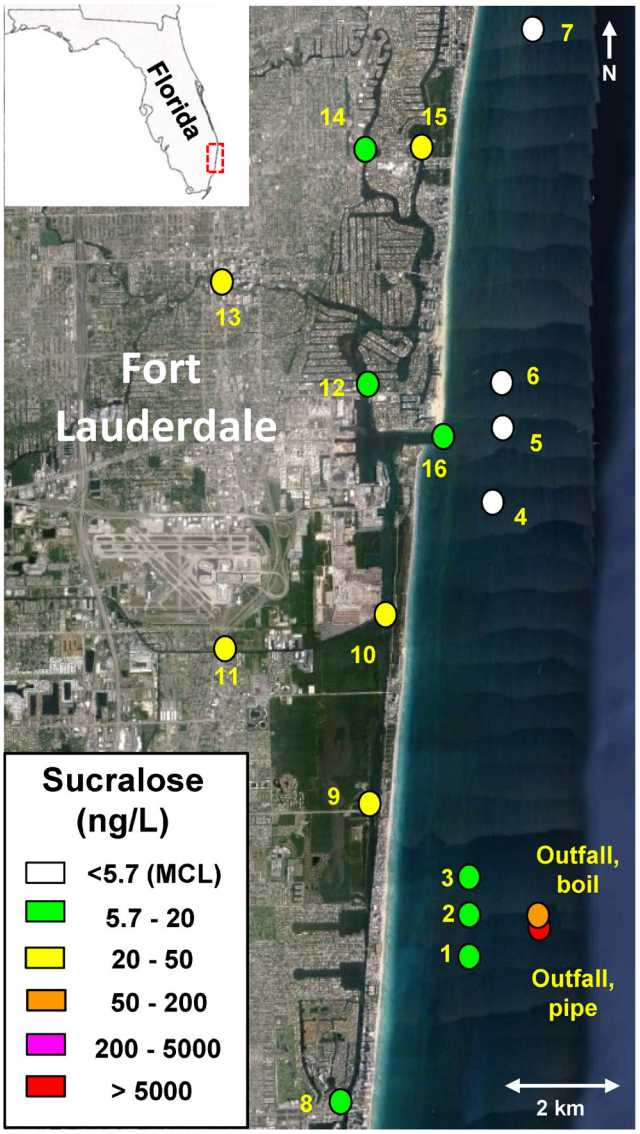

Fig. 3 Sample sites and measured concentrations in estuarine and nearshore oceanic sites from Broward County, FL, USA, showing the occurrence of sucralose in seawaters surrounding the oceanic outfall of the Southern Regional WWTP

observing that the main species formed under negative-mode ESI detection were the sucralose anion ($[M-H]^-$) and adducts with chloride ($[M+Cl]^-$) and formate ($[M+CHOO]^-$) as predominating species. In order to establish which anion was predominant under the basic mobile phase conditions described in this methodology, their contributions were compared by analyzing several replicates of a natural seawater sample fortified with 10 ng/L of sucralose. As can be seen in Fig. 2, abundance of the sucralose anion ($[M-H]^-$) was higher than that of the adducts with chloride o formate despite the presence of a high concentration of chloride in the matrix and formate in the mobile phase. These results suggest that the use of a basic mobile phase (instead of acidic conditions as reported by Wu et al.) enhances the deprotonation product minimizing the production of chloride and formate adducts that would decrease the yield of the analytical signal, enabling reliable detection at low levels in seawater. Therefore, the accurate mass of the sucralose anion was adopted for quantitation. No further gain in sensitivity was observed from increasing the mass tolerance window above 5 ppm at the data analysis software, and this value was selected for peak integration.

Method detection and confirmation limits

The use of method confirmation limits (MCLs, sometimes referred to as limits of qualification) has been gaining momentum in environmental applications of LC-MS [20, 24, 25], providing a statistical estimation of the ability of the secondary signals to confirm analyte identity, in a similar approach as the method detection limits (MDLs) provide an estimation of the lowest quantity that can be distinguished from a blank. However, MCLs are not provided in any previously reported sucralose methodology probably because of the low intensity of the secondary MS/MS transitions. Specifically for the anion, the weak secondary MS/MS transition is especially prone to interferences upon seawater analysis as it corresponds to a chloride ion (m/z 395→35) [16]. Therefore, the use of HRMS offers much higher sensitivity capabilities for analyte confirmation because the $[M-H+2]^-$ and $[M-H+4]^-$ signals have higher intensities (96 and 31 % relative to that of the $[M-H]^-$ anion) than secondary MS/MS products. Both MDLs and MCLs were determined according to USEPA guidelines [26], by measuring seven replicates of full-strength samples from each matrix (fortified to 10 ng/L)

Table 3 Measured sucralose concentrations, salinities, and quality controls for the sucralose snapshot of Broward County waters presented in Fig. 3

Site	Sal (PSU)	Lat. N	Long. W	Measured	DUP[a]	LFM[b] % Rec	[M+2]/M	Dev.[c]	[M+4]/[M]	Dev.[c]
1	39	26.0114	80.1000	18.9			97	1	30	−1
2	37	26.0185	80.1002	8.04			96	0	24	−7
3	38	26.0227	80.0998	14.8	15.6		93	−3	24	−7
4	40	26.0828	80.0955	–			–	–	–	–
5	38	26.0946	80.0922	–			–	–	–	–
6	38	26.1022	80.0936	–			–	–	–	–
7	40	26.1599	80.0880	–	–		–	–	–	–
8	21	25.9881	80.1217	13.5			97	1	27	−4
9	34	26.0359	80.1173	9.76			99	3	27	−4
10	32	26.0652	80.1139	26.9			99	3	28	−3
11	28	26.0595	80.1436	47.3			97	1	27	−4
12	28	26.1023	80.1187	8.90		100	96	0	25	−6
13	17	26.1179	80.1432	26.6			99	3	29	−2
14	13	26.1394	80.1180	13.4	13.0		94	−2	26	−5
15	11	26.1397	80.1083	44.8			94	−2	27	−4
16	37	26.0936	80.1050	18.8		99	99	3	29	−2
OF, boil	36	26.0086	80.0778	148			95	−1	28	−3
OF, pipe[d]	6	26.0086	80.0778	8418±3813			95	−1	28	−3

Concentration units are nanograms per liter

− Below method confirmation limit

[a] Duplicate analyses

[b] Laboratory fortified matrix experiment. Fortification level was 100 ng/L and results are expressed in terms of percent recoveries

[c] Deviation from natural abundance ratios ([M+2]=96 %; [M+4]=31 %)

[d] Collected by divers at the WWTP ocean outfall (OF) pipe end. Results shown are the averages of two deep-water collections

and multiplying the obtained standard deviation by the Student *t* value ($t_{(7-1,\ 99)}$=3.143). For the MCL determination, the isotopic signal with lowest intensity was used to calibrate and quantitate (response factor=$[M-H+4]^-/[D6-H]^-$). A summary of obtained MDLs and MCLs is shown in Table 2, and as can be observed, the obtained MDLs for seawater are lower than any of the reported MDLs/LODs in the previous methodologies (listed in Table 1), while the obtained MCLs are similar to the lowest MDL reported before. Therefore, data suggest that online SPE coupled to HRMS is able to quantify and confirm the occurrence of sucralose in environmental waters at lower concentrations than previous methods based on MS/MS.

As noted in our previous communication [14], sucralose is ubiquitous in the drinking water supply in the Miami Metropolitan Area; thus, a sucralose-free local drinking water sample was not readily available during the course of this research. The direct determination of MDLs in drinking water requires fortification at significantly higher levels than the occurring sucralose and subtraction of the non-fortified sample, possibly yielding artificially low MDLs as the SPE extraction and instrument response are occurring under a higher analyte load than in samples that are analyte free. Therefore, a reverse MDL strategy was implemented by reversing the roles of the compounds using sucralose-D6 as analyte and the occurring sucralose in a drinking water sample (ca. 150 ng/L) as internal standard (response factor=$[D6-H]^-/[M-H]^-$).

Example of environmental application: analysis of estuarine water and seawaters from Broward County, FL, USA

In order to demonstrate the applicability of the developed methodology, a set of seawater and estuarine samples was collected which included the oceanic outfall used by the Southern Regional Wastewater Treatment Plant (WWTP) that serves Broward County, FL. The outfall is located approximately 3 km east from the Florida coastline at a depth of 28 m and has a maximum daily discharge capacity of 1.9×10^8 L of WWTP effluents [27]. Samples were collected on August 8th, 2013, from the outfall pipe end, from the surface where the outfall boil was visible, and from other several oceanic and estuarine locations shown in Fig. 3 and described in Table 3. As expected, the water around the outfall pipe end contained very high concentrations of the artificial sweetener relative to the rest of the dataset (8418±3813 ng/L, n=2), and this observation is consistent with both our previously reported

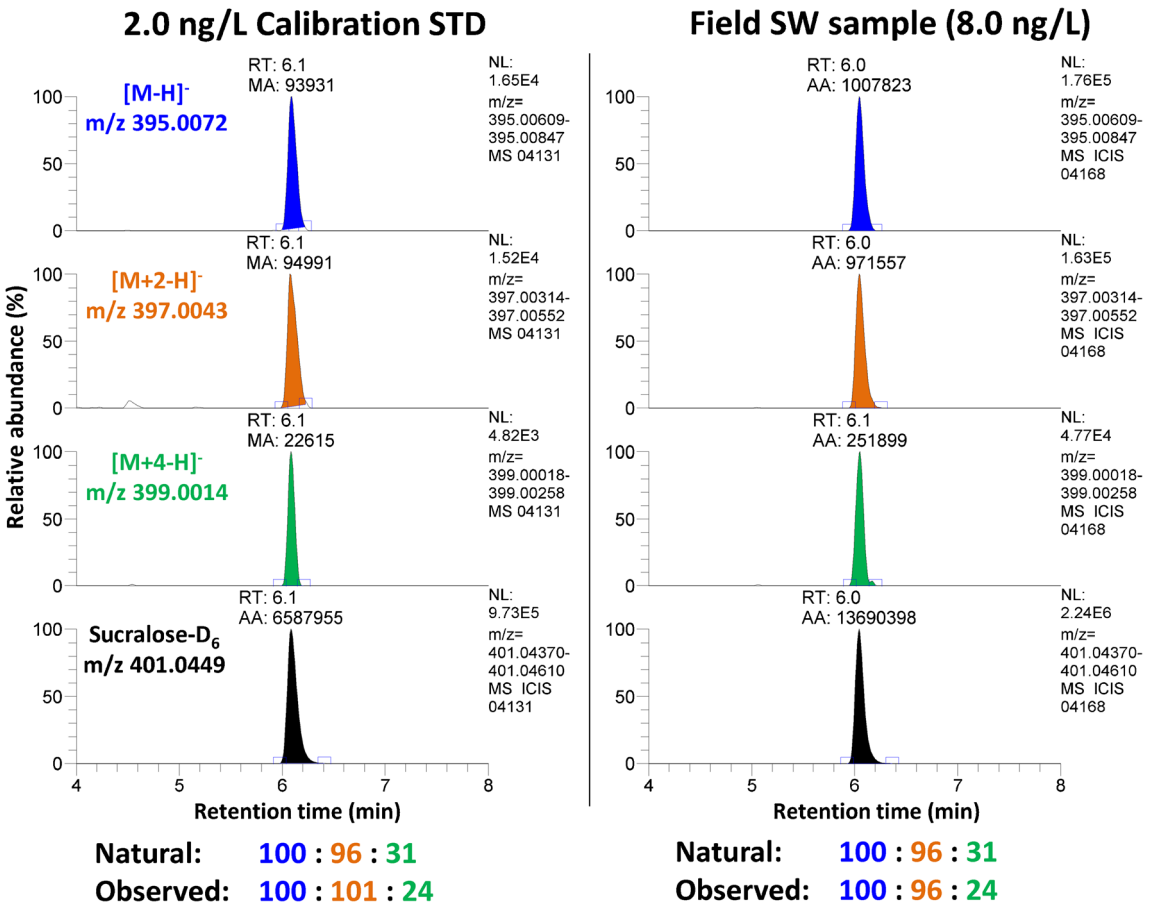

Fig. 4 Real seawater chromatograms from a nearshore Atlantic Ocean site and their comparison to a calibration standard. Clean backgrounds and isotopic ratios corresponding to natural abundances are observed in both cases, along with retention time match to sucralose-D6 internal standard

monthly average concentration of sucralose in effluents from the Miami-Dade North District WWTP (9100±2900 ng/L, n=56) [14] and the documented discharge of large amounts of sucralose by WWTPs in other regions [4]. Observed sucralose concentrations at the outfall boil were diluted ca. 60×, and sites 1, 2, and 3 (located equidistantly at 1.5 km W, NW, and SW from the OF site) contained sucralose with concentrations ca. 600× lower than those of the outfall pipe end.

The concentrations observed at the oceanic locations (8–18 ng/L) were lower than those observed by Mead et al. [8] in seawaters around the Florida Keys (150–394 ng/L, which authors attributed to leaking sewage lines and injection of WWTP effluents into the porous limestone) but in the same magnitude as those reported in the same work from open Atlantic Ocean waters in the Gulf Stream (1 to 68 ng/L). That work corresponds to the only seawater analysis of sucralose previously available in the literature in which the compound was extracted from 34 L of seawater using SPE, with GC-MS detection after derivatization. Therefore, our automated online SPE-LC-HRMS methodology was able to quantify and confirm the occurrence of the analyte in similar oceanic sites with comparable performance than that of the previous seawater work but using only 10 mL of sample. Additionally, the analysis of the whole sucralose snapshot from Broward County (including calibration, quality control runs, oceanic and estuarine samples) only took 13 h of unattended, automated analysis (56 injections, 14 min each), after approximately 45 min of sample preparation and instrument setup. Since the only materials required are a reusable LC vial and a disposable 10-mL pipette per sample, with fortification with labeled sucralose as the only preparation step, this methodology is very economical in terms of analyst time and materials for laboratories that have made the initial instrumental investment.

Regarding measurements in estuarine samples, the analyte was ubiquitous with similar concentrations in all sites (MCL to 50 ng/L). The Southern Regional WWTP (and other WWTPs in the South Florida area) provides a portion of effluents to be reused for irrigation in golf courses and public sites [27], and therefore, runoff from these activities could possibly explain the occurrence of the sweetener in the canals although direct inputs of raw wastewater from leaking pipes and septic tanks are also a possibility. The developed methodology was successfully applied to field samples of different salinity values (6 to 40 PSU) with demonstrated analyte confirmation and control of matrix effects (as suggested by excellent recoveries upon LFM experiments). Sample chromatograms presenting analytical signals for the quantification/confirmation of sucralose in a real field sample and their comparison to a calibration standard are presented in Fig. 4. The combined seawater/estuarine results demonstrate how the use of SPE-LC-HRMS had enough sensitivity, selectivity, and speed to quickly generate a snapshot of wastewater occurrence in this coastal region.

Conclusions

An online SPE-LC-HRMS method for the quantitation and unequivocal identification of sucralose in aqueous samples has been developed and field tested. Very high sensitivity and selectivity were obtained by adding a basic buffer to enhance negative-mode ionization of the complete sucralose isotopic signature and its detection using a benchtop orbitrap HRMS, eliminating the need to perform traditional MS/MS which is inadequate for the quantitation and confirmation of this particular analyte at ultra-trace levels. Method detection limits (MDL, 1.4 ng/L) are lower than any MDL reported before in the literature, and method confirmation limits (MCL, 5.7 ng/L) are reported for the first time in a sucralose application, allowing rapid, automated analysis of large numbers of seawater and estuarine samples for the first time. The methodology offers sensitivity, selectivity, and a very high sample throughput with minimal analyst time and consumable materials, and was applied to generate a wastewater occurrence snapshot within a coastal estuarine/oceanic environment under the influence of a large urban population.

Acknowledgments The authors want to gratefully acknowledge Dr. Ken Banks and Dr. Nancy Craig from Broward County Natural Resources Planning and Management Division, Environmental Protection and Growth Management Department (EPGMD-NRPMD), for providing the logistic support needed for sample collection. We also acknowledge the support from the Thermo Scientific Corporation in the development of this work. This is contribution number 715 from the Southeast Environmental Research Center at Florida International University.

References

1. Sharma VK, Oturan M, Kim H (2014) Oxidation of artificial sweetener sucralose by advanced oxidation processes: a review. Environ Sci Pollut Res Int 21:8525–8533
2. Tollefsen KE, Nizzetto L, Huggett DB (2012) Presence, fate and effects of the intense sweetener sucralose in the aquatic environment. Sci Total Environ 438:510–516
3. Soh L, Connors KA, Brooks BW, Zimmerman J (2011) Fate of sucralose through environmental and water treatment processes and impact on plant indicator species. Environ Sci Technol 45: 1363–1369
4. Torres CI, Ramakrishna S, Chiu C-A, Nelson KG, Westerhoff P, Krajmalnik-Brown R (2011) Fate of sucralose during wastewater treatment. Environ Eng Sci 28:325–331
5. Mawhinney DB, Young RB, Vanderford BJ, Borch T, Snyder SA (2011) Artificial sweetener sucralose in U.S. drinking water systems. Environ Sci Technol 45:8716–8722
6. Kokotou MG, Asimakopoulos AG, Thomaidis NS (2012) Artificial sweeteners as emerging pollutants in the environment: analytical methodologies and environmental impact. Anal Methods 4:3057
7. Oppenheimer J, Eaton A, Badruzzaman M, Haghani AW, Jacangelo JG (2011) Occurrence and suitability of sucralose as an indicator compound of wastewater loading to surface waters in urbanized regions. Water Res 45:4019–4027
8. Mead RN, Morgan JB, Avery GB, Kieber RJ, Kirk AM, Skrabal SA, Willey JD (2009) Occurrence of the artificial sweetener

sucralose in coastal and marine waters of the United States. Mar Chem 116:13–17
9. Loos R, Gawlik BM, Boettcher K, Locoro G, Contini S, Bidoglio G (2009) Sucralose screening in European surface waters using a solid-phase extraction-liquid chromatography-triple quadrupole mass spectrometry method. J Chromatogr A 1216:1126–1131
10. Ferrer I, Thurman EM (2010) Analysis of sucralose and other sweeteners in water and beverage samples by liquid chromatography/time-of-flight mass spectrometry. J Chromatogr A 1217:4127–4134
11. Minten J, Adolfsson-Erici M (2011) A method for the analysis of sucralose with electrospray LC/MS in recipient waters and in sewage effluent subjected to tertiary treatment technologies. Intern J Environ Anal Chem 91:357–366
12. Huntscha S, Singer HP, McArdell CS, Frank CE, Hollender J (2012) Multiresidue analysis of 88 polar organic micropollutants in ground, surface and wastewater using online mixed-bed multilayer solid-phase extraction coupled to high performance liquid chromatography-tandem mass spectrometry. J Chromatogr A 1268:74–83
13. Pasquini L, Munoz J-F, Rimlinger N, Dauchy X, France X, Pons M-N, Görner T (2013) Assessment of the fate of some household micropollutants in urban wastewater treatment plant. Chem Pap 67:601–612
14. Batchu SR, Quinete N, Panditi VR, Gardinali PR (2013) 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. Chem Cent J 7:141
15. Loos R, Carvalho R, António DC, Comero S, Locoro G, Tavazzi S, Paracchini B, Ghiani M, Lettieri T, Blaha L, Jarosova B, Voorspoels S, Servaes K, Haglund P, Fick J, Lindberg RH, Schwesig D, Gawlik BM (2013) EU-wide monitoring survey on emerging polar organic contaminants in wastewater treatment plant effluents. Water Res 47:6475–6487
16. Ferrer I, Zweigenbaum JA, Thurman EM (2013) Analytical methodologies for the detection of sucralose in water. Anal Chem 85:9581–9587
17. Perkola N, Sainio P (2014) Quantification of four artificial sweeteners in Finnish surface waters with isotope-dilution mass spectrometry. Environ Pollut 184:391–396
18. Wu M, Qian Y, Boyd JM, Hrudey SE, Le XC, Li X-F (2014) Direct large volume injection ultra-high performance liquid chromatography-tandem mass spectrometry determination of artificial sweeteners sucralose and acesulfame in well water. J Chromatogr A 1359:156–161
19. Zubarev RA, Makarov A (2013) Orbitrap mass spectrometry. Anal Chem 85:5288–5296
20. Fedorova G, Randak T, Lindberg RH, Grabic R (2013) Comparison of the quantitative performance of a Q-Exactive high-resolution mass spectrometer with that of a triple quadrupole tandem mass spectrometer for the analysis of illicit drugs in wastewater. Rapid Commun Mass Spectrom 27:1751–1762
21. Hernández F, Sancho JV, Ibáñez M, Abad E, Portolés T, Mattioli L (2012) Current use of high-resolution mass spectrometry in the environmental sciences. Anal Bioanal Chem 403:1251–1264
22. Krauss M, Singer H, Hollender J (2010) LC-high resolution MS in environmental analysis: from target screening to the identification of unknowns. Anal Bioanal Chem 397:943–951
23. Ramirez CE, Wang C, Gardinali PR (2014) Fully automated trace level determination of parent and alkylated PAHs in environmental waters by online SPE-LC-APPI-MS/MS. Anal Bioanal Chem 406: 329–344
24. Garcia-Ac A, Segura PA, Viglino L, Fürtös A, Gagnon C, Prévost M, Sauvé S (2009) On-line solid-phase extraction of large-volume injections coupled to liquid chromatography-tandem mass spectrometry for the quantitation and confirmation of 14 selected trace organic contaminants in drinking and surface water. J Chromatogr A 1216:8518–8527
25. Khan GA, Lindberg R, Grabic R, Fick J (2012) The development and application of a system for simultaneously determining antiinfectives and nasal decongestants using on-line solid-phase extraction and liquid chromatography-tandem mass spectrometry. J Pharm Biomed Anal 66:24–32
26. USEPA (2010) CFR 40 title 40 part 163 Appendix B: Definition and procedure for the determination of the method detection limit. 353–356
27. Koopman B, Heaney J, Rembold M, Indeglia P, Kini G (2006) Ocean outfall study. Final Report, Florida Department of Environmental Protection, Tallahassee, Florida