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Quantitative determination of triclocarban in wastewater effluent by stir bar sorptive extraction and liquid desorption–liquid chromatography–tandem mass spectrometry

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ABSTRACT

Triclocarban is an antimicrobial and antibacterial agent found in personal care products and subsequently is a prevalent wastewater contaminant. A quantitative method was developed for the analysis of triclocarban in wastewater effluents using stir bar sorptive extraction–liquid desorption (SBSE–LD) followed by liquid chromatography–tandem mass spectrometry (LC–MS/MS) by means of an electrospray interface. A stir bar coated with polydimethylsiloxane (PDMS) is placed within a vial containing wastewater effluent and is stirred for an hour at room temperature. The PDMS stir bar is then placed in a LC vial containing methanol and is desorbed in a sonicator bath. The methanol is evaporated to dryness and reconstituted in 75% methanol. Spike and recovery experiments in groundwater that did not contain native concentrations of triclocarban were performed at 0.5 μg/L and were 93 ± 8%. Recoveries in wastewater effluent that were corrected for the background levels of triclocarban were 92 ± 2% and 96 ± 5%, respectively, when spiked with 0.5 and 5 μg/L of triclocarban. The precision of the method as indicated by the relative standard error was 2%. The limit of quantitation was 10 ng/L. The SBSE–LD–LC/MS/MS method was applied to wastewater effluent samples collected from northeast Ohio. Triclocarban was quantitated in all five effluent samples, and its concentration ranged from 50 to 330 ng/L. The described method demonstrates a simple, green, low-sample volume, yet, sensitive method to measure triclocarban in aqueous matrices.

1. Introduction

Triclocarban (3,4,4′-trichlorocarbanilide) is a common antimicrobial and antibacterial agent found in many personal care products including antimicrobial soaps, antibacterial mouthwashes and toothpastes [1], and Americans release approximately 500,000–1,000,000 pounds of triclocarban into the environment per year [2]. Subsequently, triclocarban has been found to be a common wastewater contaminant due to its widespread use in personal care products that are often rinsed down the drain after use [3–11]. Environmental concentrations reported for triclocarban typically range from the parts-per-trillion concentrations for surface waters (receiving effluent discharge) to the parts-per-million level in biosolids; however concentrations have been reported as high as 5600 and 6750 ng/L in river water and wastewater, respectively [3]. Toxicological studies performed with triclocarban in fish indicate that acute and chronic toxicities are observed at concentrations of 49–180 and 5 μg/L, respectively, noting that the chronic effect threshold is within the environmental concentrations reported for surface waters [1]. Bioaccumulation studies have shown triclocarban to accumulate in algae [6] and in snails [10] downstream of a Texas wastewater treatment plant and in worms exposed to triclocarban-spiked sediment in a laboratory setting [12]. Interestingly, recent studies have classified triclocarban as a new type of endocrine disruptor that works synergistically to amplify the expression of testosterone, suggesting that triclocarban should be classified as a steroid hormone enhancer [13].

Despite widespread application for over 50 years little attention has been given until recently to triclocarban's possible presence in the environment, especially when compared to the attention its chemical cousin, triclosan, has received [4]. However in the last 5 years, analytical methods have emerged to measure its presence in the environment mainly relying on solid-phase extraction for sample preparation of aqueous samples and analysis by liquid chromatography/mass spectrometry with electrospray ionization [3,4,6,7]. Recently solvent-free extraction techniques, such as solid-phase microextraction (SPME) and stir bar sorptive extraction (SBSE) have become increasingly popular for sample extraction due to their ease of use, high selectivity and sensitivity, and are

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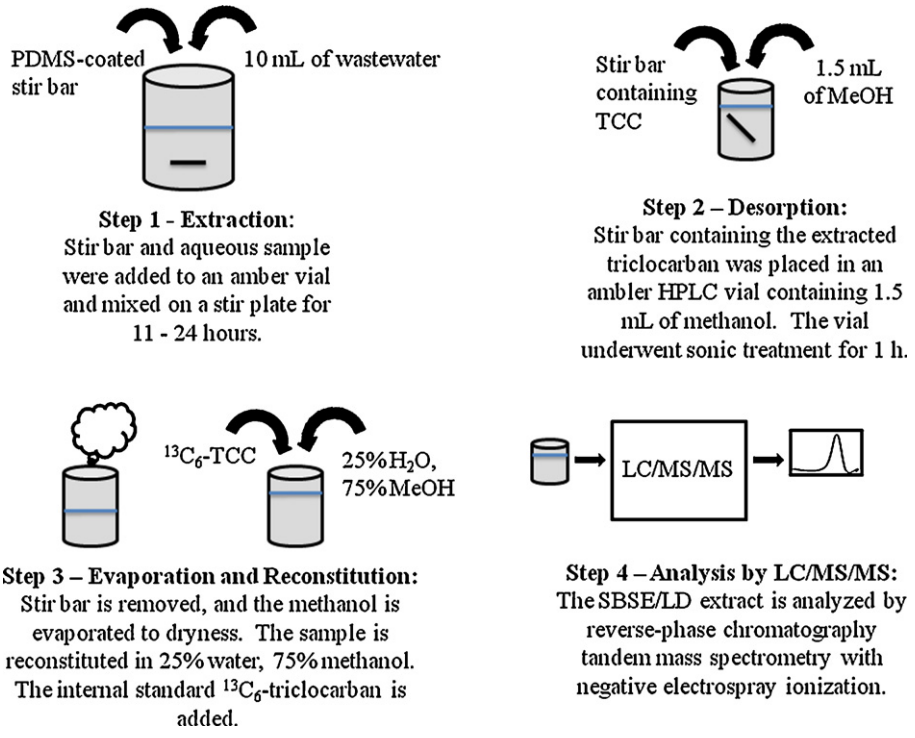

Fig. 1. Sample preparation and analysis procedure for the determination of triclocarban in wastewater samples using SBSE/LD–LC/MS/MS.

"greener" alternative to solvent intensive extractions [14–16]. The SBSE is an extraction technique in which analytes in an aqueous matrix are attracted to a polydimethylsiloxane coated stir bar. Recovery of the analytes is either by thermal desorption (TD), in which the stir bar is heated or by liquid desorption (LD), in which the stir bar is washed with a stronger solvent than the original matrix. The latter desorption technique is compatible with LC/MS analysis. To determine whether SBSE is an effective extraction technique for a particular analyte, the octanol–water partition coefficient ($K_{O/W}$) can be used as it has been shown to reliably predict the partitioning efficiency of analytes into the PDMS phase ($K_{PDMS/W} \approx K_{O/W}$) [17]. Just a small sampling reports SBSE has been used to extract other pharmaceuticals and personal care products including triclosan from biological and environmental matrices [18], triclosan from urine [19], bisphenol A in river water and body fluids [20], phthalates in drinking water [21], and non-steroidal anti-inflammatory drugs in environmental water matrices [22]. The predicted $\log K_{O/W}$ values reported for triclocarban is 4.9 [4] and the experimentally determined $\log K_{O/W}$ value is 3.5 ± 0.06 [23], suggesting that SBSE should be an effective extraction method for aqueous matrices.

The aim of this study was to develop a novel analytical approach to measure triclocarban in wastewater matrices utilizing a simple, green, and robust method. Once optimized, the validated SBSE–LD–LC/MS/MS methodology was applied to measure triclocarban in municipal wastewater effluents in northeast Ohio. To best of the authors' knowledge, this work is the first reported method utilizing SBSE–LD for the extraction of triclocarban from aqueous samples.

2. Experimental

2.1. Standards and reagents

Triclocarban (99%) was purchased from Sigma–Aldrich (St. Louis, MO). HPLC gradient grade methanol (MeOH; >99.8%) was purchased from Fluka (Sigma–Aldrich, United Kingdom). Acetonitrile (ACN; 99.9+%) was purchased from Burdick & Jackson (Honeywell International Inc.; Muskegon, MI). Acetone (99.9%) was purchased from BDH (VWR International; West Chester, PA). Ultra-pure water was obtained from Nanopure Diamond water purification systems (Barnstead International; Dubuque, IA). Isotope-labeled $^{13}C_6$-triclocarban (99%; 100 μg mL^{-1} in ACN) was purchased from Cambridge Isotope Laboratories (Andover, MA).

2.2. Experimental set-up

Prior to use, all stir bars (Twister, Gerstel; Müllheim, Germany) with a film thickness of 0.5 mm and a length of 10 mm were preconditioned by stirring in 5 mL of ACN for 30 min at 800 rpm and were air dried on Kimwipes. Carryover can occur on the stir bars after repeated use. If this is observed, increase the length of time of the preconditioning step with the ACN. All optimization studies were performed on Isotemp stir plates (Fischer-Scientific, Pittsburgh, PA). Stir bars were placed into clean 25-mL amber vials containing 10 mL of 15 μg L^{-1} triclocarban solution. Important parameters affecting SBSE were optimized for triclocarban including LD solvent (MeOH, ACN), time of extraction (0.25, 0.50, 1.0, 2.0, 4.0, 8.0, 11.0, 24.0 h), and desorption time (5, 10, 15, 30, 60, 240 min). All parameter optimizations were performed in triplicate with blanks also performed in triplicate. Stir bars were removed from the vials using plastic forceps and were placed into a 2-mL Agilent amber vial containing 1.5 mL of liquid desorption solvent and capped. Samples were put into a flotation device and underwent sonic treatment (Fischer-Scientific, Pittsburgh, PA) for desorption. Stir bars were removed from the vials and the solvent in the vials was blow to dryness under a gentle stream of nitrogen. Samples were reconstituted with 25% water and 75% MeOH and spiked to contain 12 μg/L of $^{13}C_6$-triclocarban, the internal standard. The 25% water present in the final sample extract was necessary for retention of triclocarban on the reverse-phase column. Triclocarban in 100% methanol was not retained on the reverse-phase column. The schematic further describing the extraction procedure is outlined in Fig. 1.

Table 1
Mass spectrometer parameters and ion transitions used for identification and quantitation for isotopically-labeled and native triclocarban.

	Precursor ion $[M-H]^-$ (m/z)	Fragmentor voltage (V)	Product ion (Quant) (m/z)	Structure of Quant ion	Collision energy Quant ion (eV)	Product ion (Qual) (m/z)	Structure of Qual ion	Collision energy Qual ion (eV)
Triclocarban	313	100	160	$[M-C_7H_5ONCl]^-$	25	126	$[M-C_7H_4ONCl_2]^-$	25
$^{13}C_6$-Triclocarban	319	100	160	$[M-C_7H_5ONCl]^-$	25	n/a	n/a	n/a

2.3. SBSE–LD spike and recovery

Spike and recovery experiments were performed to determine the accuracy and precision of the SBSE–LD extraction method in groundwater and wastewater effluent matrices.

2.3.1. Groundwater

Unfiltered groundwater that did not contain background levels of triclocarban was collected from Ashland, OH, and spiked to contain 0.5 μg/L of triclocarban. The stir bars were spun at 800 rpm for 22 h in the spiked groundwater solution and then placed in 1.5 mL of methanol in an amber vial. The vials underwent sonic desorption for 60 min before being evaporated to dryness using nitrogen. The samples were then reconstituted with 25% water and 75% MeOH and 12 μg/L of $^{13}C_6$-triclocarban. Three replicates were performed at each spiked concentration in addition to the three "controls" that were not spiked with triclocarban.

2.3.2. Wastewater effluent

The spike and recovery procedure for wastewater effluent was carried out using the same technique as the spiked groundwater samples with slight variations as noted. The unfiltered wastewater effluent was spiked to contain 0.5–5 μg/L concentrations of triclocarban. Three replicate extractions were carried out at each spiked level. The endogenous concentration of triclocarban in the effluent was determined from analyzing the unspiked replicates of wastewater and was subtracted from the measured concentration of each spiked sample before calculating recoveries.

2.4. Liquid chromatography–mass spectrometry

The SBSE–LD extracts were separated by an Agilent 1200 LC (Santa Clara, CA). A 3.5 μm, 3.0 mm × 150 mm Eclipse XDB-C18 column (Agilent) heated to 35 °C was used for all separations. The injection volume was 15 μL followed by a 5 s needle wash with methanol. Chromatographic parameters were controlled and data was obtained through the Agilent Masshunter Workstation-Data Acquisition program. The LC solvents were ultra-pure water and methanol. The gradient consisted of an initial 2 min hold at 30% methanol, then increasing from 30 to 100% methanol over 5 min followed by a 5-min hold at 100% methanol and 2-min of equilibration at 30% methanol. The LC was directly interfaced to the electrospray ionization (ESI) source coupled to an Agilent 6410 Triple Quadrupole. The ion source was operated in negative ESI mode and multiple-reaction-monitoring (MRM) transition mode was used for sample analysis. Two MRM transitions (Table 1), a quantitation ion and a confirmation ion, were acquired for triclocarban. The fragmentor voltage and collision energies were 100 V and 25 eV, respectively (Table 1).

2.5. Quantitation and confirmation

Quantitation was performed by internal standard calibration using standards prepared in 25% water/75% methanol. Weighted ($1/x$), linear regression was used to generate calibration curves from (at minimum) seven calibration standards, and the intercept was not forced through zero. Calibration standards ranged from 10 ng/L to 800 μg/L for each analyte and contained 12 μg/L of the internal standard, $^{13}C_6$-triclocarban. Points included in the calibration curves were required to be within 20% of the theoretical concentration. Calibration curves were analyzed at the beginning and end of each sample batch with methanol solvent blanks within the set after approximately every fifth sample. Confirmation was performed by quantitating on both monitored transitions for triclocarban (Table 1). The determined values for both transitions were in good agreement, typically <10% variation. Precision of the method was determined by calculating the relative standard deviation from five replicate analyses of the same wastewater sample. The limits of detection and limits of quantitation were defined as the concentrations that yielded signal-to-noise (S/N) ratio of 3:1 and 10:1, respectively, within the sample matrix. Samples and calibration standards were viewed qualitatively and quantitatively using Agilent Masshunter Workstation-Qualitative Analysis and Agilent Masshunter Workstation-Quantitative Analysis.

2.6. Wastewater sample collection

Grab samples of final effluents were collected from five municipal wastewater treatments in Northeast Ohio during the summer of 2009. Characteristic details of each wastewater treatment plant are located in Table 2. Samples were collected and brought back to the laboratory on ice. Samples were refrigerated at 4 °C until extraction by SBSE–LD which was performed within 48 h after arrival to the laboratory. Wastewater samples were analyzed in triplicate.

3. Results and discussion

3.1. Liquid chromatography/mass spectrometry

Initial experiments identified the most abundant precursor and product ions for triclocarban to be employed for quantita-

Table 2
Wastewater treatment plant characteristics and concentrations of triclocarban detected[a].

Plant ID	Population size	Average plant flow[b] (MGD)	Treatment process	Concentration[c] (ng/L)
Plant A	22,000	4.4	P + TF + UV	330 ± 30
Plant B	330,000	78.6	P + AS + Cl	244 ± 6
Plant C	26,000	5	P + AS + UV	120 ± 20
Plant D	50,000	12	P + AS + Cl	170 ± 30
Plant E	8400	1	P + TF + Cl	48 ± 2

[a] P: primary gravitational settling; TF: trickling filter; AS: activated sludge; Cl: chlorination/dechorination; UV: ultraviolet disinfection.
[b] Plant flow reported in million gallons per day (MGD).
[c] Average ± standard deviation.

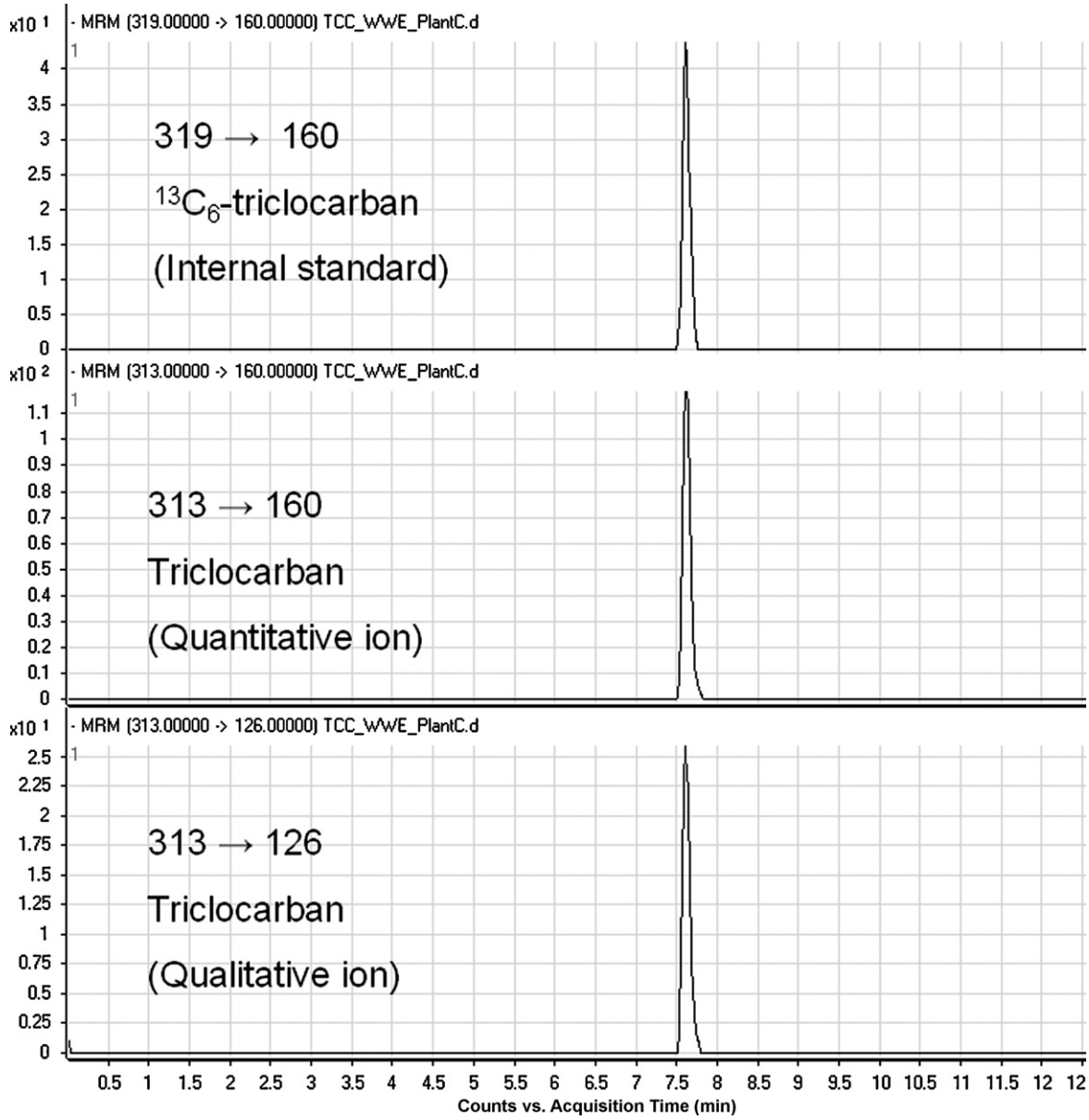

Fig. 2. Typical chromatogram of triclocarban in a wastewater effluent sample (Plant C) extracted and analyzed by SBSE–LD–LC/M/MS. Both the quantitative and qualitative ions are shown for triclocarban, as well as the trace for the internal standard, $^{13}C_6$-triclocarban.

tion (Table 1). The precursor ion (313 *m*/*z*) was determined to be a $[M-H]^-$. The primary product ion (160 *m*/*z*, quantitative ion) was the most abundant fragment ion produced from the precursor ion and its structure was $[M-C_7H_5ONCl]^-$, and likewise the secondary product ion (confirmation or qualitative ion) was the second most abundant fragment ion produced $[M-C_7H_4ONCl_2]^-$ (Table 1). Confirmation was performed by quantitating both product ion transitions at the identical retention time for each analyte. The resulting concentrations for each transition were compared for good agreement (within 10%), and the concentration associated with the quantitative product ion was reported.

Subsequently, the LC conditions using a water/methanol gradient were optimized for our system according to a previously published study for triclocarban analysis [5]. Good analytical performance was achieved for triclocarban using a convention reverse-phase column with a retention time of 7.6 min. The chromatographic separation of triclocarban and $^{13}C_6$-triclocarban determined in this study is shown in Fig. 2 for the final effluent collected from Plant C.

3.2. SBSE–LD optimization

Several important parameters were optimized to improve the efficiency of the SBSE–LD extraction of triclocarban including the LD solvent, desorption time, and analyte extraction time.

3.2.1. Effect of the LD conditions

The first SBSE parameter optimized was the LD solvent which back extracts the triclocarban from the stir bars. The other SBSE parameters were set as follows: an extraction time of 1 h, a stir rate of 750 rpm, and 15 min for desorption time under sonic treatment. The two solvents tested for their extraction efficiency were methanol and acetonitrile. The percent recovery of each of the solvents was calculated based on the starting concentration of triclocarban in each of the vials and the concentration that was ultimately detected in each of the vials after liquid desorption. The calculated recoveries for MeOH and ACN were $71 \pm 1\%$ and $70 \pm 6\%$, respectively. Although the recoveries were similar, methanol was chosen as the LD solvent due to its lower

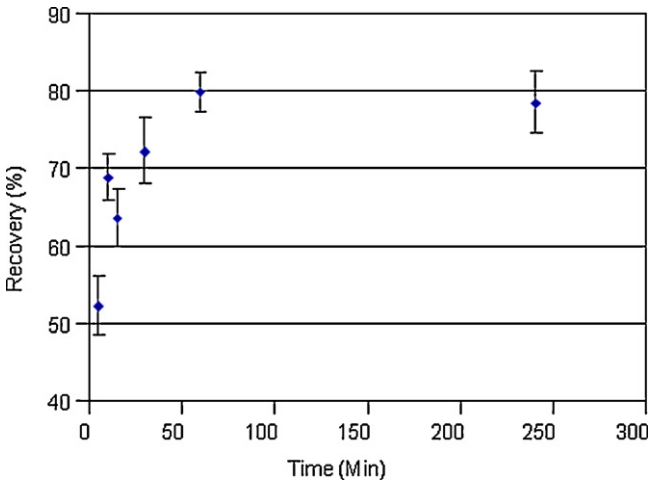

Fig. 3. Optimization of liquid desorption time.

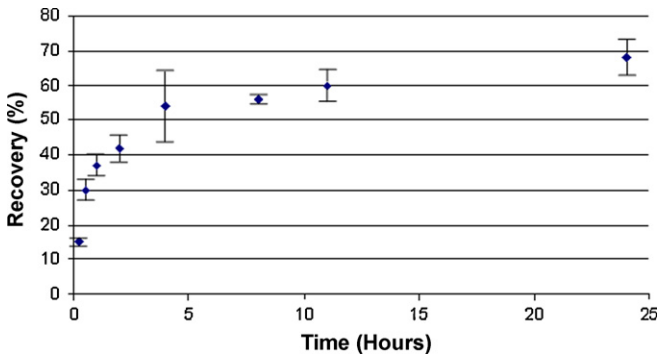

Fig. 4. Optimization of the of the extraction time for the stir bar sorptive extraction.

standard deviation and therefore higher degree of reproducibility.

The second LD parameter optimized was the desorption time using methanol as the LD solvent and 22 h for the extraction time. Following extraction, capped vials were placed in the sonic bath to desorb for varying amounts of time (5, 10, 15, 30, 60, 240 min). The optimal desorption time was determined to be 60 min with a recovery of 80 ± 3% as compared to the initial concentration (Fig. 3).

3.2.2. Effect of the SBSE parameters

The most important parameter affecting SBSE method is the extraction time. Other parameters that could affect SBSE are agitation speed and the ionic strength; however, previous work has shown that these two parameters have no effect on the SBSE efficiency of triclosan [18]; thus, these two parameters were not optimized for the presented triclocarban method. To determine the optimized extraction time, the other SBSE parameters were set as follows: a stir rate of 750 rpm, and 15 min for desorption time under sonic treatment in 1.5 mL of MeOH. Samples were extracted for 0.25, 0.50, 1, 2, 4, 8, 11, and 24 h. The extraction efficiency for the 11 and 24 h samples was 60 ± 3% and 68 ± 5%, respectively (Fig. 4). Since these values are statistically the same, it was determined that the optimal extraction time was somewhere between 11 and 24 h; 22 h was used as the optimal extraction time for wastewater samples.

3.3. Validation of the SBSE–LD extraction

The accuracy and precision of the optimized SBSE–LD method was determined from spike and recovery experiments performed with triclocarban in groundwater and wastewater. Groundwater was selected in addition to wastewater since it is an environmental aqueous matrix unlikely to contain endogenous concentrations of triclocarban. Groundwater was spiked at 0.5 μg/L, whereas the wastewater was spiked to contain 0.5 μg/L (low) and 5.0 μg/L (high) concentrations. The absolute recovery was 93 ± 8% in groundwater. The endogenous concentration of triclocarban present in the spiked wastewater effluent was 0.059 μg/L. The recoveries in wastewater were calculated after correcting for the endogenous concentration of triclocarban present. The absolute recoveries at the low and high concentrations by SBSE/LD were 92 ± 2% and 96 ± 5%, respectively, in wastewater. To date, most extraction methods for triclocarban in aqueous samples utilize solid-phase extraction [3,6,7]. The reported recoveries of triclocarban from aqueous samples using solid-phase extraction range from 80 to 95% (Table 3). The recoveries of triclocarban by SBSE/LD fall within this range, despite only requiring 10 mL of sample as compared to 200–1000 mL (Table 3) required for the solid-phase extraction methods. Additionally, SBSE/LD uses significantly less organic solvent than solid-phase extraction, and the stir bars can be reused for future extractions. Comparable recoveries, small sample volume, less organic solvent,

Table 3
A comparison of method reproducibility and sensitivity for triclocarban reported in aqueous samples[a].

Reference	Matrix	Extraction procedure	Analytical method	TCC reported recovery	Sample volume	Detection limit (ng/L)	Reported triclocarban concentrations (ng/L)
Halden and Paull [3,4]	Aqueous samples	SPE	LC–ESI-MS	95 ± 9%	1 L	3–50	33–5600 surface water [3], 6700 ± 100 influent [4], 110 ± 10 effluent [4]
Coogan et al. [6]	Surface water	SPE	LC–ESI-MS/MS	80%, 84% (n = 2)	1 L	15[b]	50–200
Sapkota et al. [7]	Surface water	SPE	LC–ESI-MS/MS	91 ± 8% low spike, 93 ± 17% high spike	200 mL	0.9	12 ± 15 upstream WWTP, 84 ± 110 downstream WWTP
This study	Wastewater	SBSE/LD	LC–ESI-MS/MS	93 ± 8% GW spike, 92 ± 2% WW low spike, 96 ± 5% WW high spike	10 mL	1	48–330

[a] Triclocarban: TCC; SPE: solid-phase extraction; LC–ESI-MS: liquid chromatography-electrospray ionization–mass spectrometry; WWTP: wastewater treatment plant; SBSE/LD: stir bar sorptive extraction/liquid desorption; GW: groundwater; WW: wastewater.
[b] Only the practical quantitation limit was reported which is 10× the instrument detection limit.

and future reuse make SBSE/LD a viable alternative to solid-phase extraction for extracting triclocarban from aqueous matrices.

The precision of the method as indicated by the relative standard error was 2% for triclocarban in the five replicate samples measured. The calculated LOD is 1 ng/L determined from the ratio of the compound's S/N signal being 3. The LOQ was defined as the analyte concentration required to produce a S/N ratio of 10:1 within the environmental matrix and was found to be 10 ng/L.

3.4. Application to environmental samples

The performance of the SBSE–LD–LC/MS/MS method was evaluated by analyzing wastewater effluent samples suspected to contain concentrations of triclocarban. Triclocarban was detected in all five samples of wastewater effluent collected from plants in Northeast Ohio and the concentrations ranged from 48 ± 2 to 330 ± 30 ng/L (Table 2). These observed concentrations are at the same order of magnitude as compared to previously reported levels for triclocarban in wastewater effluents in which 200 ng/L [6] and 110 ± 10 ng/L [4], respectively, were reported for samples collected in Denton, TX, and the Greater Baltimore Area, MD. Of the five plants sampled, two of the plants employ ultra-violet (UV) disinfection and the remaining three utilize chlorination/dechlorination as their final disinfection process. From the small data set it is inappropriate to draw a general conclusion; however, it appears from this study that UV disinfection does not remove or transform the triclocarban more effectively than the conventional chlorination/dechlorination disinfection process. The largest observed concentration of triclocarban was 330 ng/L collected from the discharge of a plant that uses UV disinfection and serves a small population of 22,000 people (Table 2).

4. Conclusions

The combination of the stir bar sorptive extraction and liquid desorption followed by liquid chromatography tandem mass spectrometry (SBSE–LD–LC/MS/MS) offers the opportunity of a new straightforward and reliable extraction and analysis for the determination of triclocarban in aqueous and serum samples. Key parameters of the SBSE–LD method were optimized including the extraction time, LD solvent, and desorption time. The optimized SBSE–LD–LC/MS/MS method shows satisfactory precision, recoveries, and limits of detection for environmental monitoring especially when taking into account the complexity of the matrices and small amounts of the samples (10 mL of wastewater). Performance of the method was demonstrated by its application to samples from regional WWTPs. Triclocarban was detected in all of the WWTP samples at the ng/L level further validating its status as a common wastewater contaminant. The SBSE–LD–LC/MS/MS methodology has proven to be an effective tool to monitor triclocarban that utilizes green chemistry, yet, provides sufficient sensitivity at trace levels to be reliably used in measuring environmental aqueous samples.

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