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Cyprosulfamide: Analysis of the Herbicide Safener and Two of Its Degradates in Surface Water and Groundwater from the Midwestern United States

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ABSTRACT: Herbicide safeners are commonly included in herbicide formulations to selectively protect crops from herbicide toxicity but are poorly understood in terms of their environmental occurrence and fate. This study established an analytical method for a newer safener, cyprosulfamide, and two of its degradates, cyprosulfamide desmethyl and *N*-cyclopropyl-4-sulfamoylbenzamide, in water via solid-phase extraction and liquid chromatography with tandem mass spectroscopy. To evaluate the potential for off-field transport and transformation of cyprosulfamide, the method was used to analyze groundwater and surface water samples collected near cornfields in the midwestern United States where cyprosulfamide had been applied. All three compounds were detected in surface water samples (N = 34); *N*-cyclopropyl-4-sulfamoylbenzamide was most frequently detected (56%), followed by cyprosulfamide (25%) and cyprosulfamide desmethyl (19%). Maximum concentrations ranged from 22.0 to 5185.9 ng/L, with the highest concentrations and detection rates during the growing season. None of our target analytes were detected in groundwater.

KEYWORDS: *safener, cyprosulfamide, solid-phase extraction, LC-MS/MS, surface water, groundwater*

INTRODUCTION

Herbicide safeners are a growing family of chemicals commonly included in commercial herbicide formulations to selectively protect crops from herbicide toxicity.[1−5] Safeners are used globally at levels that can surpass those of common herbicide active ingredients, and it is estimated that approximately 30% of global herbicide sales are associated with products containing a safener.[2] Despite widespread use, however, the environmental occurrence and fate of safeners are poorly understood.[1,2,6] Although they are classified and regulated as "inert" constituents under the U.S. Federal Insecticide, Fungicide, and Rodenticide Act and similar international legislation, herbicide safeners demonstrate broad toxicity toward nontarget organisms, and two safeners, AD-67 and furilazole, are classified by the U.S. Environmental Protection Agency (EPA) as "likely to be carcinogenic to humans".[7−10] Recent studies have also shown that some safeners can transform under environmentally relevant conditions into products with increased biological activity that may pose further human and environmental health risks.[11−13] Despite these concerns, safener applications are not closely monitored, and there are limited available environmental data regarding safener environmental occurrence, fate, and effects.[2,14]

Herbicide safeners are designed to have physicochemical properties similar to those of the herbicide co-formulants they support (solubility, log K_{ow}, and analogous structural moieties), thereby facilitating plant uptake and leading to high mobility in the environment.[3,15,16] Recent studies have demonstrated that dichloroacetamide safeners, like their herbicide co-formulants, undergo limited sorption to agricultural soils, leading to greater partitioning into aqueous environments.[17] The first study to investigate the occurrence of safeners in surface waters found that safener concentrations increased proportionally with their associated herbicides, suggesting that safeners likely co-occur with their active co-formulants, though at lower concentrations, and have the potential to impact drinking water supplies.[14] However, while several studies have detected herbicide degradates in surface water and groundwater, no studies to date have assessed safener transformation product occurrence in natural water systems.

The acylsulfonamide class of safeners (e.g., cyprosulfamide) is an example of a relatively new safener class that has received minimal scientific examination regarding its environmental fate and transport. Cyprosulfamide was first commercialized in 2008 for use on corn as the first of the acylsulfonamide safeners to be registered for use by the EPA.[6,18] Though residue tolerances have been established for cyprosulfamide and three of its degradates (sulfonamide-alanine, sulfonamide-lactate, and *N*-cyclopropyl-4-sulfamoylbenzamide), the biological transformation products cyprosulfamide desmethyl and *N*-cyclopropyl-4-sulfamoylbenzamide are recommended as "residues of concern" in drinking water by the EPA.[19,20] Cyprosulfamide is typically applied via spray formulations during the pre-emergence or early post-emergence stage of the planting season in the early spring, a time when heavy rains

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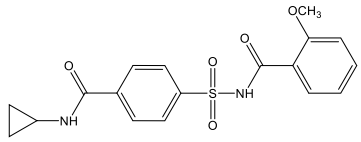
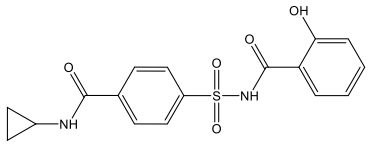
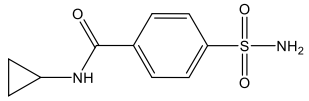
Table 1. Chemical Properties for Cyprosulfamide and Its Residues of Concern in Drinking Water

Compound (IUPAC Name) Chemical Abstracts Service (CAS) Number	Structure	Log K_{ow}	C_w^{sat} (mol/L)	K_{oc} (L/kg)
Cyprosulfamide ((N-{[4-(Cyclopropylcarbamoyl)phenyl]sulfonyl}-2-methoxybenzamide) CAS: 221667-31-8		-0.8[b] - 1.68	$6.53x10^{-4}$	134
Cyprosulfamide Desmethyl (N-{[4-(Cyclopropylcarbamoyl)phenyl]sulfonyl}-2-hydroxybenzamide) CAS: Unavailable		1.44[c]	Unknown	Unknown
N-cyclopropyl-4-sulfamoylbenzamide (N-cylopropyl-4-sulfamoylbenzamide) CAS: Unavailable		$-3.47x10^{-2}$	2.96	29.1

[a]Unless otherwise cited, octanol−water partition coefficient (K_{ow}), water solubility (C_w^{sat}, 25 °C), and soil adsorption coefficient (K_{oc}) data from ref 23. [b]From ref 29. [c]Estimated by ChemDraw.

and large amounts of runoff often occur in the midwest where corn is extensively grown.[18,21,22] The estimated log K_{ow} values for cyprosulfamide and its known transformation products range between −0.8 and 1.4 (Table 1), suggesting cyprosulfamide is likely to be at least as mobile as its active herbicide co-formulants, isoxaflutole, dicamba, thiencarbazone, tembotrione, and atrazine (log K_{ow} = 0.56−2.61).[23] Many of the herbicides commonly paired with cyprosulfamide have been widely detected in surface waters, suggesting that cyprosulfamide and its degradates are likely present in those environments also.[24−28]

At present, no published environmental data exist for cyprosulfamide or its degradates. Understanding the environmental presence, fate, and transport of cyprosulfamide in aqueous systems can help resource managers maintain ecosystem vitality and drinking water security and balance the needs of sustainable agricultural development. Here, we present an approach for simultaneously quantifying cyprosulfamide and two of its major degradates (cyprosulfamide desmethyl and *N*-cyclopropyl-4-sulfamoylbenzamide) in environmental water samples via solid-phase extraction. We later employed the method in evaluating 34 surface and groundwater samples near two cornfields in the midwestern United States where cyprosulfamide is applied.

MATERIALS AND METHODS

Chemicals. Cyprosulfamide, cyprosulfamide desmethyl, and *N*-cyclopropyl-4-sulfamoylbezamide were provided by Bayer Crop Science (Research Triangle Park, NC) at >98% purity. The internal standard (d_3-clothianidin) and surrogate (d_4-imidacloprid) were purchased from Cambridge Isotope Laboratories (Andover, MA), and standards were prepared in acetonitrile at concentrations of 5 and 1 ng/μL, respectively. To account for losses during sample treatment by solid-phase extraction (SPE), the surrogate was added to water samples prior to sample processing; the internal standard was spiked into LC vials immediately prior to liquid chromatography with tandem mass spectroscopy (LC-MS/MS) analysis to assess matrix effects and normalize sample recoveries. Both d_4-imidacloprid and d_3-clothianidin had been used in previously developed LC-MS/MS methods in our laboratory for a range of pesticides; given their retention times are similar to those of the compounds of interest and d_4-imidacloprid's method performance on HLB cartridges, we included them for this method. A spiking solution containing 2 ng/μL each of cyprosulfamide and the two degradates was prepared in acetonitrile for use in spiking water samples during method development. Standard calibration curves were prepared in acetonitrile using a seven-point calibration curve ranging from 0.01 to 1.0 ng/μL. All solvents and reagents were of optima grade (Fisher Scientific, Pittsburgh, PA).

Water Collection and Preparation. Filtered surface water from the American River (Sacramento, CA), a snowmelt-fed river with low concentrations of dissolved organic carbon (DOC) and circumneutral pH, was used for method development and verification.[30] Method performance at varying DOC concentrations was assessed with samples from the DOC-rich, agriculturally impacted Ulatis Creek (Elmira, CA) and Iowa River (Iowa City, IA). More information regarding sampling sites is provided in the Supporting Information.

All water samples were filtered through prebaked 0.7 μm GF/F filters (Whatman, Florham Park, NJ) and parceled into 1 L sample volumes. Each sample was spiked with 50 μL of a cyprosulfamide stock solution for a final vial concentration of 0.5 ng/μL and with 50 μL of surrogate (1 ng/μL d_4-imidacloprid). Water samples from each site were analyzed for background cyprosulfamide and degradate concentrations prior to spiking.

DOC Analysis. DOC concentrations for the American River, Ulatis Creek, and Iowa River samples were determined by the USGS Organic Matter Research Laboratory according to a modified version of EPA Method 415.3. Samples were vacuum-filtered through prebaked 0.3 μm GF/F filters (Advantec MFS, Dublin, CA) and analyzed by high-temperature catalytic combustion using a Shimadzu TOC-VCSH total organic carbon analyzer (Shimadzu Scientific Instruments, Columbia, MD).[31] DOC data are reported in Table S14.

SPE Method Optimization. Oasis HLB, MAX, and WAX extraction cartridges (6 cm^3, 500 mg; Waters Corp., Milford, MA) were assessed for optimal extraction of cyprosulfamide and its two degradates. Cartridges were preconditioned with 10 mL of each extraction solvent followed by 10 mL of organic-free water (Table S1). The stock solution containing cyprosulfamide, cyprosulfamide desmethyl, and *N*-cyclopropyl-4-sulfamoylbenzamide (50 μL for a

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Figure 1. Location map of field A (surface water) and field B (groundwater) sampling sites. Markers indicate locations at the field perimeter where well or tile drain samples were collected; arrows indicate the direction of water flow through tile drains (field A) or groundwater flow (field B).

total load of 100 ng of each analyte) was spiked directly onto each cartridge and eluted via gravity drip with one of the following solvent combinations, based on sorbent chemistry: methanol only, ethyl acetate followed by methanol, or a 1:1 mixture of acetone and dichloromethane. For the ethyl acetate and methanol elution, fractions were collected separately. Elutions were blown down under a gentle stream of nitrogen (N-evap; Organomation Associates, Berlin, MA), exchanged into acetonitrile, and brought to a volume of 0.2 mL. Samples were transferred into LC vials and spiked with 20 μL of the internal standard (5 ng/μL d_3-clothianidin, Cambridge Isotope) to account for potential matrix effects and instrument fluctuations. *t* tests showed no significant differences in the internal standard response between the calibration standards and the field samples (p = 0.81), indicating that d_3-clothianidin is an acceptable internal standard by which to normalize analyte concentrations.

Spike and recovery experiments were performed to determine an appropriate solvent for eluting cyprosulfamide and its degradation products from SPE cartridges and to determine the accuracy and precision of the SPE method for environmental matrices. Two sets of three replicate 1 L American River samples and one set of three replicate DI aliquots were each filtered and spiked with the cyprosulfamide stock solution (each analyte at 100 ng/L) and surrogate. Samples were pumped through preconditioned HLB cartridges at a rate of 10 mL/min, and cartridges were dried under nitrogen. Cartridges were eluted via gravity drip with either methanol or a 1:1 mixture of acetone and dichloromethane followed by a second elution with methanol, concentrated, and exchanged into acetonitrile. If precipitate formed following acetonitrile exchange, samples were filtered through 0.45 μm PTFE syringe filters (Restek Corp., Bellefonte, PA). The endogenous concentrations in the river water, if any, were subtracted from the measured concentration of each spiked sample before recoveries were calculated (Table S6).

Triplicate samples (1 L) collected from Ulatis Creek and the American and Iowa Rivers were processed as previously described to determine the effect of dissolved organic carbon on cyprosulfamide and degradate recoveries. Samples were extracted using HLB cartridges eluted with a 1:1 mixture of acetone and dichloromethane followed by a second elution with methanol.

Instrumental Analysis. Sample extracts were analyzed on an Agilent (Palo Alto, CA) model 1260 bioinert liquid chromatograph (LC) coupled to an Agilent 6430 triple quadrupole tandem mass spectrometer (MS/MS). The analytical method used in this study was previously optimized for multiple classes of pesticides.[32] Briefly, a Zorbax Eclipse XDB-C18 column (2.1 mm × 150 mm × 3.5 μm, Agilent) with a Zorbax Eclipse XDB-C8 guard cartridge (2.1 mm × 12.5 mm, 5 μm) was used for all separations with organic-free DI water with 0.1% formic acid and HPLC grade acetonitrile at a flow rate of 0.6 mL/min. Mass spectrometer analysis was conducted in positive ESI mode with multiple-reaction monitoring (MRM). Mass spectrometer settings and MRM transitions are provided in the Supporting Information.

A seven-point calibration curve (0.01−1.0 ng/L), with internal standard calibration, was analyzed at the beginning and end of each sample batch, with blanks and calibration verification standards analyzed within the batch after approximately every tenth sample. Confirmation of compound identification was performed by quantifying MRM transitions for each analyte. Calibrations were calculated using a linear regression (R^2 > 0.995). Instrument limits of detection (iLODs) were determined using an EPA-recommended method of 3 times the standard deviation of seven replicate injections of a standard. Method limits of detection (mLODs) were determined from 3 times the standard deviation of seven replicate injections of the lowest standard, handled as environmental samples (see the Supporting Information for details).[33] Sample concentrations that were higher than the calibration curve were diluted with acetonitrile containing the internal standard and rerun.

Field Sample Collection. The optimized SPE method was used to assess cyprosulfamide and degradate concentrations in surface and groundwater samples that were collected near agricultural fields in the midwestern United States where cyprosulfamide had been applied to corn. Samples were collected from April 2019 to October 2019, which encompassed one growing season with one cyprosulfamide application. Groundwater and surface water samples were collected at the perimeters of two different fields (Figure 1).

Surface Water Sampling. Surface water samples were collected on an event-driven basis from five sites at the perimeter of field A (1.6 km^2). Cyprosulfamide was applied to the field on the day of planting as an ingredient in the BalanceFlexx herbicide formulation with an application rate of 10.54 kg of cyprosulfamide/km^2, and the field was not irrigated. A tile drain flows along the western edge of the property from south to north and along the north edge of the property from east to west. Samples were collected from water flowing within the drain at sites 1−3 using the equal-width-increment (EWI) method. Sites 1 and 2 are located upgradient from the subject field, and site 3 is located downgradient from the field. Site 4 (tile) samples were collected from the tile outlet using a composite sampler. Sample collection began upon detection of flow and continued and as the flow increased, at intervals of 20−30 min; sample collection was stopped as

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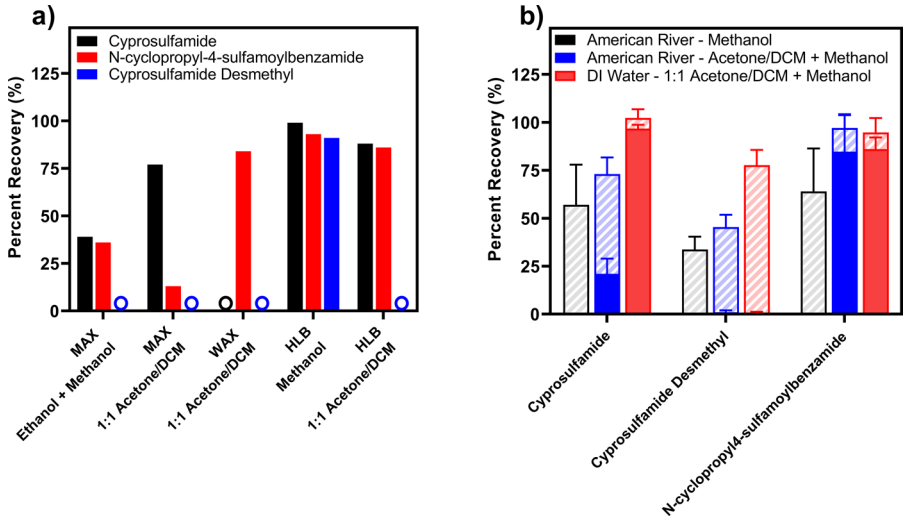

Figure 2. (a) Cyprosulfamide and product recoveries with various SPE cartridge−eluent combinations after directly spiking cartridges with a stock solution. A circle indicates no measurable recovery. (b) Spiked water recoveries for cyprosulfamide and degradates using HLB cartridges. Solid bars represent the percent eluted in the acetone/DCM fraction; shaded bars represent the percent eluted in the methanol fraction. Error bars indicate the standard deviation (n = 3).

the flow rate decreased, and all samples were stored in a chilled 10 L glass jar until sample retrieval. Site 5 (runoff) samples were collected from the north edge of the field where it was apparent that water occasionally flowed off of the field. A small weir was set up in that area to assist sample collection, and a composite sampler collected samples as previously described. Two quality assurance/quality control (QA/QC) samples were collected over the course of sampling (one blank and one field replicate), and results are reported in the Supporting Information.

Groundwater Sampling. Groundwater samples were collected from five wells at the perimeter of field B (0.97 km^2). One surface water sample was collected from a pond at the edge of the field. Field B was treated 4 days post-planting with the cyprosulfamide-containing herbicide formulation Corvus at a rate of 3.59 kg of cyprosulfamide/km^2. Field B was irrigated occasionally as needed. Well sites were chosen in relation to the direction of water flow. Groundwater at the site flows generally east to southeast toward wells 3−5 and the pond; wells 1 and 2 were selected as background indicator wells. Well 3 is approximately 9−14 feet deeper than the other wells to be within the surficial aquifer, providing an indication of whether cyprosulfamide and its degradates are detected on a deeper flow path. Pond samples were collected as grab samples from two to three locations. Four QA/QC samples were collected (two blanks and two field replicates), and the results are reported in Table S18.

All field samples were collected in 1 L volumes in amber bottles and shipped to the laboratory on ice. Upon receipt, each sample was immediately filtered through a prebaked 0.7 μm GF/F filter (Whatman, Florham Park, NJ) and spiked with 50 μL of surrogate (1 ng/μL d_4-imidacloprid).

RESULTS AND DISCUSSION

Development and Optimization of the Solid-Phase Extraction (SPE) Method. HLB cartridges yielded higher recoveries for cyprosulfamide and its transformation products cyprosulfamide desmethyl and *N*-cyclopropyl-4-sulfamoylbenzamide than MAX or WAX cartridges (Figure 2a). The greatest recoveries (91−100%) for cyprosulfamide and both products were achieved via methanol elution. HLB cartridges that were eluted with a 1:1 mixture of acetone and dichloromethane yielded acceptable recoveries for cyprosulfamide and *N*-cyclopropyl-4-sulfamoylbenzamide (88% and 86%, respectively) but not for cyprosulfamide desmethyl. Neither the MAX nor WAX mixed-mode reversed-phase/anionic exchange cartridges achieved acceptable recoveries of 70−130% for more than one compound (Table S5).

Recoveries for cyprosulfamide and its degradates were lower (34 ± 7% to 64 ± 22%) in spiked American River water using HLB cartridges and methanol as the eluent compared to HLB cartridges that were directly spiked with the stock solution. Eluting first with a 1:1 acetone/dichloromethane mixture followed by methanol elution resulted in higher total recoveries (45 ± 6% to 97 ± 13%) than eluting with methanol alone (Figure 2b). The degradate cyprosulfamide desmethyl is eluted by only the methanol fraction, suggesting this compound is more polar than the others; this is supported by higher estimated K_{ow} values for cyprosulfamide desmethyl in chemical databases. Additionally, a greater percentage of cyprosulfamide desmethyl was recovered from the methanol elution fraction when the cartridges were first eluted with a 1:1 acetone/dichloromethane mixture. Higher recoveries of cyprosulfamide and cyprosulfamide desmethyl were achieved (78 ± 8% and 102 ± 4%, respectively) in deionized water compared to American River water, suggesting that environmental matrix effects may impede recovery of the target compounds. To mitigate matrix effects, we assessed additional sample processing steps, including pre-elution cartridge washes with 0−5% methanol and post-elution sample cleanup using carbon/alumina SPE columns. Neither washing nor cleanup was effective in increasing compound recoveries. Additional experiments were conducted substituting the d_3-clothianidin internal standard with various labeled internal standard compounds (d_4-tebuconazole, d_4-myclobutanil, and $^{13}C_6$-sulfamethoxazole) that are more structurally similar to the compounds of interest. Recoveries obtained using alternate internal standards were not significantly higher than recoveries obtained using a d_3-clothianidin internal standard (see the Supporting Information for more details). In addition, we assessed the possibility of matrix suppression on analyte detection by performing SPE on unspiked samples of DI and American River water and then spiking the samples immediately prior to analysis; we calculated the percent signal suppression/enhancement (SSE%) and the recovery of extraction (R_E%) (see the Supporting Information).[34] SSE

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calculations (95−102% for the DI extract and 89−116% for the American River extract) indicated that signal suppression/enhancement only slightly influenced analyte recoveries, and all were within the acceptable range (Table S9). The recovery of extraction calculations indicated that extraction recoveries were significantly lower in American River water than in DI water for cyprosulfamide (p = 0.003) and cyprosulfamide desmethyl (p = 0.009), but not for *N*-cyclopropyl-4-sulfamoylbenzamide (p = 0.67). These results suggest that matrix effects may reduce extraction efficiencies for cyprosulfamide and cyprosulfamide desmethyl (Table S10).

SPE performed on spiked American River, Ulatis Creek, and Iowa River samples using HLB cartridges and a two-step elution (with a 1:1 acetone/dichloromethane mixture and methanol) at circumneutral pH (7.2−8.2) indicate analyte recovery was not significantly influenced by DOC concentration [p = 0.14−0.59 (see the Supporting Information for details)].

Application to Environmental Samples. The optimized SPE method was applied to surface water and groundwater samples collected near two fields in the midwestern United States where cyprosulfamide is applied to evaluate the potential for off-field transport and transformation of cyprosulfamide. Cyprosulfamide and its degradates cyprosulfamide desmethyl and *N*-cyclopropyl-4-sulfamoylbenzamide were detected in field A surface water with 63% of samples containing at least one analyte of interest (the recovery of the surrogate d_4-imidacloprid was 105.3 ± 11.4% across all surface water samples) (Figure 3). Among the 10 (of 16 total) samples that had detectable concentrations of cyprosulfamide or its degradates, 50% had at least two compounds present and 10% had all three compounds present. Cyprosulfamide had an overall detection frequency of 25%, with concentrations ranging from 9.6 to 5185.9 ng/L. The degradate cyprosulfamide desmethyl had a 19% detection frequency (3.7−22.0 ng/L), and *N*-cyclopropyl-4-sulfamoylbenzamide had the highest detection frequency of 56%. The optimized method for measuring cyprosulfamide and its degradates is highly variable for cyprosulfamide desmethyl and was unable to achieve higher recoveries for that degradate; recoveries of extraction tests further suggest that matrix effects may reduce extraction efficiencies for cyprosulfamide and cyprosulfamide desmethyl. As a result, the method is likely underreporting the presence of cyprosulfamide desmethyl and concentrations in the field. In seven of the nine samples in which *N*-cyclopropyl-4-sulfamoylbenzamide was detected, *N*-cyclopropyl-4-sulfamoylbenzamide had the highest concentration among the three compounds; its concentrations ranged from 1.9 to 616.9 ng/L.

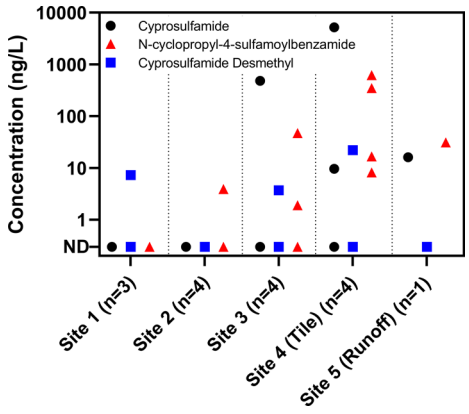

Figure 3. Cyprosulfamide and product concentrations for samples collected from the five surface water sites. ND, not detected. Maximum concentrations were higher for cyprosulfamide (5185.9 ng/L) and *N*-cyclopropyl-4-sulfamoylbenzamide (616.9 ng/L) than for cyprosulfamide desmethyl (22 ng/L). *N*-Cyclopropyl-4-sulfamoylbenzamide had the highest detection frequency (56%) among the three compounds.

Surface water samples collected before (April) and during (June, September, and October) the growing season showed seasonal trends. Among the four samples collected in April prior to herbicide application, there was one detection of (*N*-cyclopropyl-4-sulfamoylbenzamide), with a concentration of 16.6 ng/L. Following pesticide and safener applications in the late spring, the detection frequency increased to 67% in June (n = 3) samples, with concentrations averaging 1270.4 ± 2204.4 ng/L. Samples collected near the end of the growing season had the highest detection frequencies of 67% (September; n = 3) and 83% (October; n = 6) with average concentrations of 2.9 ± 1.4 and 58.9 ± 117.9 ng/L, respectively, suggesting continued field runoff associated with seasonal rain and, potentially, soil disturbance due to crop harvesting.

Neither cyprosulfamide nor its degradates were detected in groundwater samples from field B. Cyprosulfamide and *N*-cyclopropyl-4-sulfamoylbenzamide were detected in the pond at field B, with detections occurring in two of three samples. These results indicate that while cyprosulfamide and its degradates were present, transported, and transformed at field B, the compounds did not reach the subsurface during the course of this study. Site history indicates that cyprosulfamide was not applied to the field during the year prior to this study (2018) but had been used at this site in the past (2015 and 2017). On the basis of nationwide groundwater studies and statistical comparison procedures, the California Department of Pesticide Regulation has established a K_{oc} of 1900 L/kg as the high-end cutoff value for designating pesticides as potential groundwater contaminants that are likely to be mobile enough in soils to leach into groundwater.[35] Estimated K_{oc} values for cyprosulfamide and *N*-cyclopropyl-4-sulfamoylbenzamide are 134 and 29.1 L/kg, respectively, indicating that they are not likely to leach into the subsurface.

Overall, surface water samples indicate that cyprosulfamide is readily transported off site and transforms in the environment. In 8 of the 10 surface water samples in which analytes were detected, degradate concentrations exceeded those of the parent compound, which is of concern because both cyprosulfamide desmethyl and *N*-cyclopropyl-4-sulfamoylbenzamide have been recommended by the EPA as "residues of concern in drinking water".[19] The detection frequencies for cyprosulfamide and its degradates are generally consistent with estimated log K_{ow} values, which suggest that *N*-cyclopropyl-4-sulfamoylbenzamide partitions more readily into the aqueous phase than cyprosulfamide and cyprosulfamide desmethyl do.

Environmental Implications. This study is the first to establish a method for the recovery and analysis of the safener cyprosulfamide and two of its degradates, cyprosulfamide desmethyl and *N*-cyclopropyl-4-sulfamoylbenzamide, in ideal laboratory systems and in aqueous environmental solutions. This is also the first study to measure cyprosulfamide and two of its degradates in environmental samples from agricultural fields where cyprosulfamide was applied. Accurate and precise recoveries were achieved for cyprosulfamide and its trans-

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formation product *N*-cyclopropyl-4-sulfamoylbenzamide (average of 90 ± 17% to 96 ± 6% across all samples in DI, Ulatis Creek, American River, and Iowa River water that used the final method); cyprosulfamide desmethyl recovery was variable and outside the acceptable range, 54 ± 15%.

With the development of an SPE method, we were able not only to detect the presence of cyprosulfamide but also to observe its transformation products cyprosulfamide desmethyl and *N*-cyclopropyl-4-sulfamoylbenzamide in agricultural drainage from fields where cyprosulfamide was applied. These findings indicate there is potential for off-field transport into waterways and transformation into degradates that have been identified as residues of concern. Detected concentrations were several orders of magnitude below toxicological end points for human consumption, including the established chronic dietary "no observed adverse effect level" (NOAEL) of 39 mg kg^{-1} day^{-1}; however, there have been no acute toxicity levels established for aquatic organisms.[20] Moreover, long-term and mixture effects on nontarget aquatic and microbial organisms are unknown, and transformation products could be more susceptible to biological breakdown or bioaccumulation compared to the parent compound. Overall, this study demonstrated that cyprosulfamide is transported off-field via surface water and transforms over relatively short time scales into products that have been designated as "residues of concern" in drinking water at levels that are currently understood to pose a minimal risk to humans but whose full environmental and mixture effects require further study.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsagscitech.1c00050.

Sampling site information, cartridge conditioning protocol, analytical methods, LOD calculation, and results (PDF)

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Notes

The authors declare no competing financial interest.

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