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# Rapid determination of sixteen sulfonylurea herbicides in surface water by solid phase extraction cleanup and ultra-high-pressure liquid chromatography coupled with tandem mass spectrometry

Cuimin Yan [a], Beibei Zhang [b], Wenyuan Liu [a,c,*], Feng Feng [d,**], Yonggang Zhao [b], Hui Du [a]

[a] Department of Pharmaceutical Analysis, China Pharmaceutical University, 24 Tongjiaxiang, Nanjing 210009, China
[b] Jiangsu Province Environmental Monitoring Centre, Nanjing 210036, China
[c] Key Laboratory of Drug Quality Control and Pharmacovigilance (China Pharmaceutical University), Ministry of Education, China Pharmaceutical University, 24 Tongjiaxiang, Nanjing 210009, China
[d] Department of Phytochemistry, China Pharmaceutical University, 24 Tongjiaxiang, Nanjing 210009, China

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ABSTRACT

A sensitive and very fast analytical method has been developed for the simultaneous quantification of sixteen sulfonylurea herbicides in surface water. An ultra-high-pressure liquid chromatography coupled with tandem mass spectrometry method with solid phase extraction for sample cleanup has been developed for screening sixteen sulfonylurea herbicides (oxasulfuron, thifensulfuron-methyl, cinosulfuron, metsulfuron methyl, sulfometuron methyl, triasulfuron, rimsulfuron, ethametsulfuron methyl, sulfosulfuron, tribenuron methyl, bensulfuron methyl, iodosulfuron methyl, pyrazosulfuron ethyl, prosulfuron, chlorimuron ethyl, ethoxysulfuron) in water samples simultaneously within 12 min. Water samples were acidified, and the target herbicides were extracted by passing through ProElut C18 extraction cartridges. After drying by nitrogen flow, the cartridges were eluted with elution solvents, and the eluate was then evaporated to dryness, redissolved and analyzed. The mobile phase composed of 0.02% formic acid and acetonitrile using gradient elution. A triple quadrupole mass spectrometer equipped with an electrospray ionization source operated in the positive ion with selective reaction monitoring mode. Each of the analytes in all the samples was monitored using protonated molecule and its two characteristic fragment ions for confirmation. The limits of detection for all analytes were below 1.0 ng/mL, except for sulfosulfuron and prosulfuron, and limits of quantitation were between 1 and 8 ng/mL for this method. Three water types were used for the validation of the method.



## 1. Introduction

Sulfonylurea herbicides (Sus) are a group of about twenty-five compounds, which are the most common inhibitors of plant growth. Sus are extremely active against a wide spectrum of weeds by relatively low application rates, typically less than 100 g of active ingredient per hectare, which consequently, makes their detection and analysis difficult compared to that of traditional herbicides.

With their increasing use in agricultural applications, concern has been raised by the public regarding their residue problems. And increasingly strict maximum residue limits (MRLs) of Sus in the environment or agricultural products have been set by many countries. In USA, the MRLs of Sus are 0.05 mg/kg in rice. In Japan, the MRLs of imazosulfuron, bensulfuron methyl and azimsulfuron are set at 0.1 mg/kg, chlorimuron ethyl and metsulfuron methyl at 0.05 mg/kg in rice. MRLs of foramsulfuron and flazasulfuron are 0.01 mg/kg for litchi fruit in European Union. Therefore, a more sensitive and faster analytical method is required for residue analysis of Sus in the environmental matrices.

Due to the low level present and complexity in sample constituents, clean-up and enrichment before analysis is necessary and become a crucial step for the determination of Sus in environmental samples. Many clean-up methods have been developed (Table 1), including liquid–liquid extraction (LLE) [1,4,19], solid phase extraction (SPE) [2,3,7,9–18,22,24–26], immunoaffinity (IA) [6,29], molecularly imprinted polymers (MIP) [8,20], continuous flow liquid membrane extraction (CFLME) [21,27] and microwave assisted solvent extraction (MASE) [28]. However, due to the simplicity, high speed and less consumption of organic solvents, SPE is the most widely used one.

Analytical methods employed for analysis of Sus are summarized in Table 1. Basically, all conventional separation methods are

* Corresponding authors at: Department of Pharmaceutical Analysis, China Pharmaceutical University, 24 Tongjiaxiang, Nanjing 210009, China.
Tel.: +86 25 83271038.
** Co-corresponding author.
*E-mail address:* liuwenyuan8506@163.com (W. Liu).

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**Table 1**
Summary of the analytical methods about sulfonylurea herbicides.

| Reference | Matrix | Analysis method | Cleanup | Sulfonylurea herbicides | LOD | Recovery (%) |
|---|---|---|---|---|---|---|
| [1] | Bean | GC–MS | LLE | Chlorimuron ethyl | 0.035 mg/L | 79.5–85.3 |
| [2] | Soil | CE-UV | SPE | Sulfometuron, Triasulfuron, Tribenuron, Thifensulfuron, Chlorsulfuron | 0.05–0.1 mg/L | 65–103 |
| [3] | Soil | CE-UV | SPE | Chlorsulfuron, Metsulfuron methyl, Chlorimuron ethyl | 10–50 ng/kg | 94.4 |
| [4] | Water | CE-DAD | LLE | Metsulfuron methyl, Bensulfuron methyl, Sulfometuron methyl, Ethametsulfuron, Tribenuron methyl | 0.5–1.2 ng/g | 89–97 |
| [5] | Water | ELISA | Filter | Bensulfuron methyl | 8–26 ng/L | 81–125 |
| [6] | Soil | ELISA | IAC | Triasulfuron | 0.002–0.03 μg/L | 90.6–98 |
| [7] | Water | HPLC-DAD | SPE | Chlorsulfuron, Triasulfuron | <50 ng/L | 70–95 |
| [8] | Water | HPLC-UV | MIP | Triasulfuron, Metsulfuron methyl, Chlorsulfuron, Bensulfuron methyl, Triflusulfuron methyl, Chlorimuron ethyl | | 75 |
| [9] | Soil | HPLC-MS | SPE | Nicosulfuron, Thifensulfuron methyl, Metsulfuron methyl, Sulfometuronmethyl, Chlorsulfuron, Ethametsulfuron methyl, Tribenuron, Bensulfuron methyl, Pyrazosulfuron ethyl, Chlorimuron ethyl | 0.6–3.5 μg/kg | 80.2–104.5 |
| [10] | Water | HPLC-MS | SPE | Bensulfuron methyl, Imazosulfuron, Pyrazosulfuron ethyl, Flazasulfuron, Halosulfuron methyl | 0.005 mg/L | 70–120 |
| [11] | Soil Rice | HPLC-DAD | SPE | Imazosulfuron | 10–50 ng/kg | 90–96<br>70–90 |
| [12] | Water | HPLC-UV | SPE | Chlorsulfuron, Metsulfuron methyl, Tribenuron, Ethametsulfuron methyl, Thifensulfuron | 0.02–0.22 μg/mL | 72.8–103.0 |
| [13] | Water | HPLC-UV | SPE | Metsulfuron methyl, Chlorsulfuron, Bensulfuron methyl, Tribenuron, Pyrazosulfuron ethyl | 0.30–0.7 μg/L | 73.0–99.4 |
| [14] | Water | HPLC-UV | SPE | Bensulfuron methyl | 0.01 mg/L | 75.0–88.1 |
| [15] | Water | HPLC | SPE | Nicosulfuron, Thifensulfuron, Metsulfuron methyl, Tribenuron, Chlorsulfuron, Chlorimuron ethyl, Cyclosulfamuron | 0.32–0.62 μg/L | 87.9–102 |
| [16] | Bean | HPLC-UV | SPE | Metsulfuron methyl, Chlorsulfuron, Bensulfuron methyl, Pyrazosulfuron ethyl | 0.003 mg/kg | 97.04–113.6 |
| [17] | Bean | HPLC-MS | SPE | Oxasulfuron, Thifensulfuron methyl, Metsulfuron methyl, Triasulfuron, Chlorsulfuron, Chlorimuron ethyl | <10 μg/kg | 72–99 |
| [18] | Rice | HPLC-UV | SPE | Nicosulfuron, Metsulfuron methyl, Chlorsulfuron, Ethametsulfuron methyl, Triasulfuron, Bensulfuron methyl, Pyrazosulfuron ethyl, Tribenuron, Chlorimuron ethyl, Cyclosulfamuron, Primisulfuron, Flazasulfuron | 0.01–0.02 μg/g | 72.2–106.5 |
| [19] | Bean | HPLC-DAD-MS | LLE | Thifensulfuron methyl, Oxasulfuron, Triasulfuron, Metsulfuron methyl, Chlorsulfuron, Bensulfuron methyl, Prosulfuron, Pyrazosulfuron ethyl, Chlorimuron ethyl, Primisulfuron | 0.01–0.02 μg/g | 69.8–100.7<br>72.1–98.8 |
| [20] | Bean | HPLC-UV | MIP | Bensulfuron methyl, Tribenuron methyl, Metsulfuron methyl, Nicosulfuron | | 70.3–97.5 |
| [21] | Water | HPLC-UV | CFLME | Metsulfuron methyl, Bensulfuron methyl, Tribenuron methyl, Sulfometuron methyl, Ethametsulfuron | | 83–111 |
| [22] | Water | HPLC-MS/MS | SPE | Metsulfuron methyl, Thifensulfuron, Chlorsulfuron | 10–50 ng/L | 91–98 |
| [23] | Maize | HPLC-MS/MS | MISPE | Chlorsulfuron, Monosulfuron, Thifensulfuron methyl | | 75–110 |
| [24] | Soil | HPLC-UV | SPE | Chlorsulfuron, Metsulfuron methyl, Thifensulfuron methyl, Tribenuron methyl | 0.02–1.45 μg/kg | 78–92 |
| [25] | Soil | HPLC-DAD | SPE | Metsulfuron methyl, Chlorsulfuron, Bensulfuron methyl, Chlorimuron ethyl | 10–50 μg/kg | 76.3–92.5 |
| [26] | Water Soil | HPLC-UV | SPE | Thifensulfuron methyl, Metsulfuron methyl, Chlorsulfuron, Sulfometuron methyl, Rimsulfuron, Ethametsulfuron, Tribenuronmethyl, Bensulfuron methyl, Prosulfuron, Pyrazosulfuron, Chlorimuron ethyl, Primisulfuron | 0.4 ng/mL | 53.8–1128.2<br>60.9–121.3 |
| [27] | Water | HPLC-DAD | CFLME | Metsulfuron methyl, Ethametsulfuron methyl | 0.012–0.142 μg/L<br>0.08–1.00 μg/kg | 83–95<br>88–100 |
| [28] | Soil | HPLC-UV | MASE | Cinosulfuron, Thifensulfuron methyl, Metsulfuron methyl, Sulfometuronmethyl, Chlorsulfuron | 0.05–100 μg/L<br>0.1–96 μg/L | 70–100 |
| [29] | WaterFood | HPLC-DAD-MS | IAS | Thirteen sulfonylurea herbicides Chlorimuron ethyl, Imazosulfuron, Chlorsulfuron, Cyclosulfamuron, Pyrazosulfuron ethyl, Sulfosulfuron, Triasulfuron, MSM, Iodosulfuron methyl, Prosulfuron, Thifensulfuron methyl, Cinosulfuron, Sulfometuron methyl, Triflusulfuron methyl, Ethoxysulfuron, Nicosulfuron | 20–100 ng/L<br>1.1–6.9 μg/kg | 53.5–118.4 |

used, such as gas chromatography (GC) [1], capillary electrophoresis (CE) [2–4], enzyme linked immunoassay (ELISA) [5,6] and high performance liquid chromatography (HPLC) [7–29]. Sus are polar compounds with low vapor pressures requiring derivatization technology prior to GC analysis. CE using micellar electrokinetic chromatography has been used to detect these herbicides in soil samples. HPLC is the preferred approach for these polar and thermally labile herbicides. Conventional ultraviolet (UV) or diode array detection (DAD) has been extensively used. HPLC coupled with mass spectrometry (MS) or tandem mass spectrometry (MS/MS) methods, which have the advantages of high sensitivity and high degree of selectivity, have been proven to be a powerful tool for residue determination of Sus in environmental samples.

However, with the everincreasing numbers and diversity of compounds entering screen, analysis time (sample throughput) is one of the challenges analysts face when analyzing environmental samples. Due to the complexity in sample constituents and necessity to eliminate matrix effect and ion suppressions, in general, using the HPLC method to determine Sus in environmental samples normally takes 20–60 min for an analysis. Ultra-high-pressure liquid chromatography (UHPLC) using 1.7 μm particles and a holistically designed system provide significantly more resolution (information) while reducing run times, and improve sensitivity for the analyses of many compound types.

In this paper, we describe a UHPLC–MS/MS method for the identification and quantification of 16 sulfonylurea herbicides (Table 1) in surface water. To our knowledge, this is a sensitive and the fastest method developed to quantitate and confirm this number of Sus in water. The major advantage of this method over other methods developed for an individual compound or type of compounds is that simultaneous information is provided about a much greater number of compounds; other advantages are time and money savings for the laboratory performing the analysis.

## 2. Experimental

### 2.1. Chemicals

Standards of 16 Sus (oxasulfuron, thifensulfuron methyl, cinosulfuron, metsulfuron methyl, sulfometuron methyl, triasulfuron, rimsulfuron, ethametsulfuron methyl, sulfosulfuron, tribenuron methyl, bensulfuron methyl, iodosulfuron methyl, pyrazosulfuron ethyl, prosulfuron, chlorimuron ethyl, ethoxysulfuron) were kindly provided by Environment Monitoring Centre of Jiangsu Province (Nanjing), with their purity all over 96.7% except iodosulfuronmethyl (purity 89.0%). Methanol (MeOH) and acetonitrile (ACN) of chromatography grade were obtained from Merck (China) Limited. Pure water was purified by using a Millipore Milli Q-Plus system (Millipore Corp., MA, USA). All solutions were filtered through 0.2 μm GH Polypro filters before use. All sample solutions were filtered through 0.22 μm PVDF filters before use (Millipore, Bedford, MA, USA).

### 2.2. Instrumentation

Autotrace SPE System (Zymark, USA) was employed for sample preparation. The target compounds were extracted from water samples using ProElut C18 (1 g, 6 mL) (DIKMA) SPE cartridges. The analysis was performed with the equipments consisted of a Waters Acquity UPLC autosampler, column manager and thermostat, binary solvent manager. Separations were carried out on a Waters Acquity UPLC Inertsil ODS-3 column (150 mm × 2.1 mm, 1.7 μm). The column and autosampler were maintained at a temperature of 30 and 4 °C, respectively. The mobile phase was composed of 0.02% formic acid (solvent A) and ACN (solvent B) with flow rate at 0.45 mL/min. The following gradient profile was used: 0–1 min: linear from 75% to 70% A; 1–8 min: linear from 70% to 67% A; 8–12 min: linear from 67% to 58% A and then re-equilibrium of the column. 10 μL was injected using full loop injection.

The UHPLC system was coupled to a TQD triple quadrupole mass spectrometer (Waters, Milford, MA) equipped with an electrospray ionization (ESI) source operated in the positive ion mode with selective reaction monitoring (SRM). The experimental conditions for the operation of the instrument were optimized by direct infusion of the standard solution of each Sus compound. The optimal conditions were as follows: capillary voltage 4000 V, extractor voltage 4 V, cone voltage 30 V, source temperature 150 °C, desolvation temperature 350 °C, RF lens 0.1 V, desolvation gas flow 700 L/h, cone gas flow 50 L/h. The quantification of all compounds was performed using the SRM mode to increase selectivity. All data were recorded and processed using Masslynx software, version 4.1 (Waters). To generate fragment ions in addition to the molecular ion $[M+H]^+$ from each compound, collision-induced dissociation (CID) was optimized. For each compound, a protonated molecule $[M+H]^+$ and two characteristic fragment ions were monitored for confirmation. To increase sensitivity, only molecular ion $[M+H]^+$ and its most intense fragment ion were selected for quantification (Table 2).

### 2.3. Source of samples

Water from three sources was used for this method validation. River water was obtained from the Changjiang River, Nanjing; lake water was obtained from Xuanwu lake, Nanjing and tap water was from our lab. The water samples were stored in a refrigerator if the samples were not going to be analyzed the day they were collected. Each water sample of 500 mL was weighted and acidified with glacial acetic acid to pH 3.0 immediately prior to the extraction procedure, then fortified according to the sample fortification procedure described below and filtered.

### 2.4. Preparation of standard and fortified samples

Individual stock solutions (100 μg/mL) of each Sus standard were prepared in acetonitrile. Then, 1.0 mL of each individual stock solution was pipetted into a 100-mL volumetric flask and diluted with acetonitrile to obtain a (1 μg/mL) combined standard stock solution. To validate the method, a set of validation samples for each matrix were prepared: two control samples in triplicate (10 and 50 ng/mL), five level standards for calibration curves in the range of 1–300 ng/mL by spiking the extracts with appropriate volume of combined working standard solutions. For recovery studies, a water sample was spiked before the SPE extraction procedure with the mixture of the studied Sus at two concentration levels: 10 and 50 ng/mL.

### 2.5. Sample treatment

The target compounds were extracted using solid-phase extraction with DIKMA C18 SPE cartridges. The cartridges were first conditioned with MeOH (10 mL), followed by water (10 mL) at a flow rate of 5 mL/min. After the conditioning step, aliquots of 500 mL of sample, which were filtered and adjusted to pH 3 with glacial acetic acid, were slowly passed through the column at a flow rate of 30 mL/min. After drying nitrogen flow, the cartridges are eluted with 6 mL elution solvents of MeOH:ACN (1:1, v/v) at 1 mL/min. This eluate was then evaporated until near dryness by a gentle nitrogen stream and taken up with 10 milli Q water:ACN (75:25, v/v). Then this extract was filtered through a 0.22 μm PVDF filters.

**Table 2**
Precursor and fragment ions monitored for identification and quantification of the sulfonylurea herbicides in UHPLC–ESI-MS/MS.

| Analyte | Precursor ion ($m/z$) | Fragment ion 1[a] ($m/z$) | Fragment ion 2 ($m/z$) | Collision energy (eV) |
|---|---|---|---|---|
| Metsulfuron ethyl | 382.1 | 167.1 | 141.1 | 15 |
| Sulfosulfuron | 471.1 | 211.1 | 261.0 | 15 |
| Sulfometuron methyl | 365.1 | 150.0 | 199.1 | 20 |
| Tribenuron methyl | 396.1 | 155.2 | 199.1 | 15 |
| Oxasulfuron | 407.1 | 150.0 | 124.1 | 20 |
| Ethametsulfuron methyl | 411.2 | 196.1 | 170.1 | 15 |
| Triasulfuron | 402.0 | 167.1 | 141.0 | 20 |
| Rimsulfuron | 432.1 | 182.0 | 325.1 | 20 |
| Iodosulfuron methyl | 508.0 | 167.0 | 140.8 | 20 |
| Pyrazosulfuron ethyl | 415.2 | 182.1 | 369.0 | 20 |
| Chlorimuron ethyl | 415.1 | 186.0 | 213.1 | 20 |
| Bensulfuron methyl | 411.2 | 149.1 | 181.9 | 20 |
| Thifensulfuron methyl | 388.1 | 167.1 | 141.1 | 15 |
| Cinosulfuron | 414.1 | 183.0 | 157.1 | 15 |
| Ethoxysulfuron | 399.1 | 261.1 | 218.0 | 15 |
| Prosulfuron | 420.1 | 167.1 | 141.1 | 20 |

[a] Fragment ion selected for quantification.

## 3. Results and discussion

### 3.1. Optimal SPE conditions for sample pretreatment

The optimization of an appropriate SPE cartridge with different sorbent materials plays a key role for method development. The most commonly used sorbents are porous silica particles, surface-bonded with C18. In this study, different C18 cartridges, e.g. Sep-Pak C18 (Waters), Bond Elut C18 (VARIAN), ProElut C18 (DIKMA), Oasis HLB (Waters) and Oasis MCX (Waters) were tested and compared for the evaluation of extraction efficiency of 16 Sus. As a result, cartridge of ProElut C18 (1 g, 6 mL) gave the best recoveries for all target compounds (all over 75%, except tribenuron methyl 72%) with satisfactory reproducibility (relative standard deviation ≤13%).

In this study, different pH values of water sample were tested based on the recoveries of target compounds. We found that the recoveries of all analytes increased when the pH value was changed from 2.0 to 3.0, but slightly decreased when the pH value was further increased up to 3.0, which was due to their acidic properties. The pH 3.0 was consequently selected as the sample pH condition.

Sample amount (volume) is also a critical component of the analytical procedure of the compounds in water sample. In this study, we investigated the recoveries of the analytes from the SPE cartridges using four different volumes of water sample (0.5, 1, 1.5 and 2 L). As the sample volume was over 1.5 L, the recoveries were decreased. It is concluded that ProElut C18 could be used for analysis of 0.5–1.5 L of water sample and the volume of 0.5 L was chosen for further tests. Five loading rates (10, 20, 30, 40 and 50 mL/min) were also compared and minor influence was found based on their recoveries of target compounds. Flow rate of 30 mL/min was employed.

In the view of polarity of the analytes, MeOH, ACN and mixture of ACN and MeOH in different ratios (8:2, 5:5, 2:8, v/v) were tested as eluents for their recoveries from SPE cartridges. The results suggested that MeOH:ACN (1:1, v/v) gave satisfactory recoveries for all the analytes. Also, we investigated the SPE recoveries using five different volumes of elution solvent (2, 3, 4, 5 and 6 mL). The results showed that recoveries for all target compounds were 30–40% by 2 mL, 50–70% by 3 mL and 90–100% by 4–6 mL of elution solvent, and therefore 6 mL of MeOH:ACN (1:1, v/v) was chosen as SPE eluting solvent.

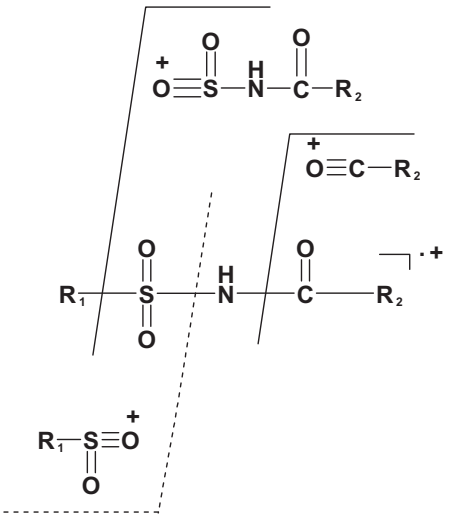

**Fig. 1.** The fragmentation pathways of the 16 sulfonylurea herbicides in UHPLC–ESI-MS/MS.

### 3.2. Optimization of UHPLC–MS/MS conditions

Parameters affecting UHPLC–MS/MS performance were systemically optimized in this study. Both ESI (−) and ESI (+) modes were tested for the ionization efficiency, and signal intensity obtained under ESI (+) was found to be about higher than that under ESI (−) over tenfold.

Sus tend to form hydrogen adduct in the mobile phase. The precursor ion of $[M+H]^+$ was set for each analyte to provide the best detection sensitivity. The precursor ion and its most intense fragment ion for each analyte were selected as the quantification ions with the SRM mode (Table 2). The second most intense fragment ion was also monitored for each analyte to increase the specificity of detection. The dissociation pathways of the analytes are shown in Fig. 1. It is noted that Sus usually exhibited three types of fragment ions, which are $[M+H-R_1]^+$, $[M+H-NHCOR_2]^+$ and $[M+H-NHSO_2R_1]^+$. These fragmentation pathways could be used to characterize Sus in environmental samples. Collision energy was shown to have profound effect on the signal intensity. Optimum value selected for each analyte is also shown in Table 2.

The UHPLC mobile phase was optimized to provide the best selectivity and the highest signal intensity in this study. All the Sus are acid compounds with their $pK_a$ value being 3.3–5.2 because of the sulfonic group in their structure. Due to the acidic properties of the analytes, the acidic mobile phase gave better retention

**Table 3**
Analytical parameters for determination of 16 sulfonylurea herbicides by UHPLC–MS/MS method.

| Compound | Regression equation | Linearity ($r^2$) | Conc. range test (ng/mL) | Matrix effect[a] (%) | LOD (ng/mL) | LOQ (ng/mL) | RSD (%)[b] ($n$ = 6) |
|---|---|---|---|---|---|---|---|
| Oxasulfuron | $Y = 5.14 \times 10^2 C - 1.38 \times 10^3$ | 0.9991 | 1–300 | 0.84 | 0.3 | 1.0 | 3.7 |
| Thifensulfuron methyl | $Y = 2.25 \times 10^2 C - 1.61 \times 10^3$ | 0.9966 | 1–300 | 0.76 | 0.3 | 1.0 | 6.9 |
| Cinosulfuron | $Y = 3.31 \times 10^2 C - 2.20 \times 10^3$ | 0.9992 | 1–300 | 0.91 | 0.2 | 1.0 | 5.2 |
| Metsulfuron methyl | $Y = 2.54 \times 10^2 C + 1.20 \times 10^2$ | 0.9987 | 1–300 | 0.77 | 0.2 | 1.0 | 3.4 |
| Sulfometuron methyl | $Y = 7.30 \times 10^2 C - 1.20 \times 10^3$ | 0.9997 | 1–300 | 1.01 | 0.2 | 1.0 | 8.9 |
| Triasulfuron | $Y = 1.35 \times 10^2 C - 1.12 \times 10^3$ | 0.9995 | 1–300 | 1.11 | 0.2 | 1.0 | 7.2 |
| Rimsulfuron | $Y = 1.719 \times 10^2 C - 2.01 \times 10^3$ | 0.9986 | 1–300 | 0.83 | 0.2 | 1.0 | 5.1 |
| Ethametsulfuron methyl | $Y = 2.80 \times 10^2 C - 1.82 \times 10^3$ | 0.9996 | 1–300 | 0.79 | 0.2 | 1.0 | 4.4 |
| Sulfosulfuron | $Y = 8.15 \times 10^1 C - 1.67 \times 10^3$ | 0.9994 | 10–300 | 0.78 | 0.8 | 5.0 | 6.1 |
| Tribenuron methyl | $Y = 1.93 \times 10^2 C - 2.02 \times 10^3$ | 0.9992 | 1–300 | 1.05 | 0.5 | 1.0 | 4.7 |
| Bensulfuron methyl | $Y = 3.06 \times 10^2 C - 3.23 \times 10^3$ | 0.9998 | 1–300 | 0.72 | 0.6 | 2.0 | 8.3 |
| Iodosulfuron methyl | $Y = 2.20 \times 10^2 C - 1.41 \times 10^3$ | 0.9998 | 1–300 | 0.85 | 0.3 | 1.0 | 7.2 |
| Pyrazosulfuron ethyl | $Y = 2.55 \times 10^2 C - 1.14 \times 10^3$ | 0.9998 | 1–300 | 0.82 | 0.3 | 1.0 | 8.1 |
| Prosulfuron | $Y = 9.36 \times 10^1 C - 1.20 \times 10^3$ | 0.9997 | 10–300 | 1.05 | 0.8 | 5.0 | 3.3 |
| Chlorimuron ethyl | $Y = 1.442 \times 10^2 C - 8.81 \times 10^2$ | 0.9997 | 1–300 | 0.86 | 0.5 | 2.0 | 6.1 |
| Ethoxysulfuron | $Y = 2.13 \times 10^2 C - 1.93 \times 10^3$ | 0.9990 | 1–300 | 1.04 | 0.3 | 1.0 | 3.6 |

[a] Ratio: matrix-matched calibration slope/solvent calibration slope.
[b] Concentration level: 50 ng/mL.

and chromatographic separation in the reversed phase column. The addition of buffer also assisted the ESI analysis.

In this study, mobile phase with the use of different concentrations of formic acid was compared to see their effects on MS peak intensity. It was found that the MS response increased when the concentration of formic acid was changed from 0.01% to 0.02%, but showed no difference when the concentration value was further increased up to 0.05%. Therefore, 0.02% formic acid was selected as the buffer system. The influence of organic solvent on the peak intensity was also investigated. Peak efficiencies were improved when ACN instead of MeOH was used as the organic solvent in the mobile phase. Moreover, signal intensities obtained under the ACN system were higher than those under the MeOH system. ACN was, therefore, chosen as the organic solvent in the mobile phase. The total ion current of the 16 Sus obtained under the optimum conditions is shown in Fig. 2.

### 3.3. Matrix effects and recovery studies

Matrix effects, which originated in the interface when the matrix constituents influence the ionization of a coeluted analyte, cause ion suppression/enhancement. To evaluate the impact of the matrix effects, the slopes obtained in the calibration with matrix-matched standards were compared with those obtained with solvent-based standards, calculating slope ratios matrix/solvent for each of the 16 studied analytes. The results are summarized in Table 3. For all 16 compounds, signal suppression was equal or lower than 20%. These values are low enough to provide accurate quantitative data if matrix-matched standard calibration curves were used throughout the study to minimize errors due to matrix effects.

Different recovery studies were carried out using tap water sample, in which the presence of Sus was examined to make sure that the matrix does not contain the studied analytes. The obtaining recoveries in two concentration levels were between 72 and 120% for the 16 studied Sus with *RSD* (%) below 13% in most cases, as can be seen in Table 4. These results show the feasibility of the studied extraction method for multi-residue Sus analysis in surface water samples.

### 3.4. Analytical performance

The results of calibration curves obtained are shown in Table 3, where the calibration curves are summarized together with the limits of quantitation, matrix effects and *RSD* (%). The linearity of the analytical response across the studied range is excellent with correlation coefficients higher than 0.998. The relative standard

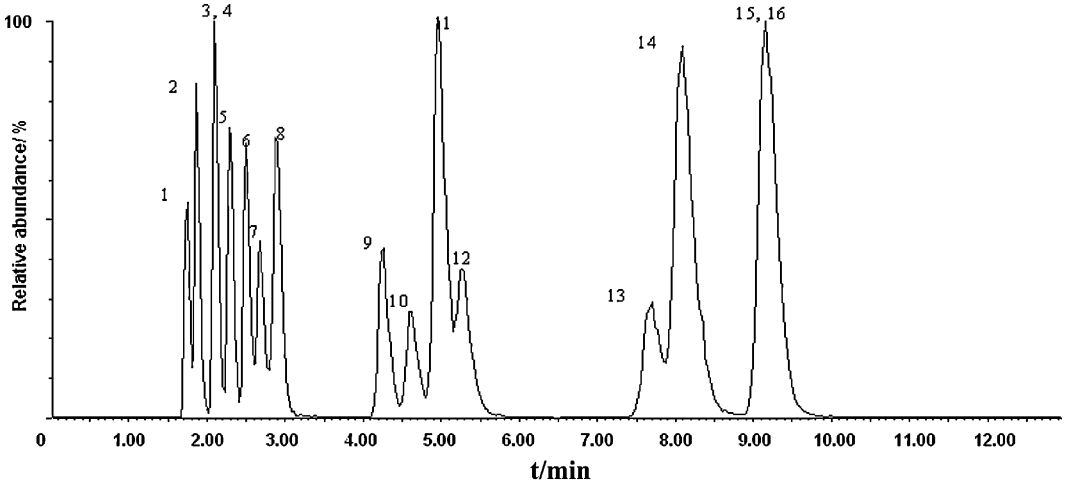


**Fig. 2.** The typical total ion chromatogram of the 16 sulfonylurea herbicides obtained in developed UHPLC–MS/MS system. (1: Oxasulfuron, 2: Thifensulfuron methyl, 3: Cinosulfuron, 4: Metsulfuron methyl, 5: Sulfometuron methyl, 6: Triasulfuron, 7: Rimsulfuron, 8: Ethametsulfuron methyl, 9: Sulfosulfuron, 10: Tribenuron methyl, 11: Bensulfuron methyl, 12: Iodosulfuron methyl, 13: Pyrazosulfuron ethyl, 14: Prosulfuron, 15: Chlorimuron ethyl, 16: Ethoxysulfuron.)

**Table 4**
Recovery studies on tap water fortified with the sulfonylurea herbicides mixture at two concentration levels.

| Sulfonylurea herbicide | Spiking level (ng/mL) | Recovery (%) | RSD (%) ($n$ = 6) |
|---|---|---|---|
| Oxasulfuron | 10 | 82.0 | 7.4 |
| | 50 | 104.0 | 3.5 |
| Thifensulfuron methyl | 10 | 82.7 | 8.5. |
| | 50 | 117.6 | 6.2 |
| Cinosulfuron | 10 | 81.0 | 7.1 |
| | 50 | 113.0 | 5.6 |
| Metsulfuron methyl | 10 | 88.0 | 6.2 |
| | 50 | 94.0 | 5.1 |
| Sulfometuron methyl | 10 | 92.0 | 10.3 |
| | 50 | 100.0 | 5.5 |
| Triasulfuron | 10 | 87.2 | 11.2 |
| | 50 | 114.7 | 6.5 |
| Rimsulfuron | 10 | 91.2 | 9.4 |
| | 50 | 113.9 | 7.6 |
| Ethametsulfuron methyl | 10 | 88.0 | 8.2 |
| | 50 | 94.0 | 8.4 |
| Sulfosulfuron | 10 | 90.3 | 10.2 |
| | 50 | 98.9 | 5.6 |
| Tribenuron methyl | 10 | 72.1 | 7.7 |
| | 50 | 84.3 | 8.2 |
| Bensulfuron methyl | 10 | 77.2 | 11.3 |
| | 50 | 90.2 | 7.5 |
| Iodosulfuron methyl | 10 | 85.6 | 8.6 |
| | 50 | 96.1 | 9.4 |
| Pyrazosulfuron ethyl | 10 | 82.9 | 12.4 |
| | 50 | 87.4 | 8.8 |
| Prosulfuron | 10 | 82.0 | 6.9 |
| | 50 | 118.3 | 5.6 |
| Chlorimuron ethyl | 10 | 79.0 | 10.5 |
| | 50 | 86.3 | 9.2 |
| Ethoxysulfuron | 10 | 90.6 | 8.5 |
| | 50 | 104.7 | 5.8 |

deviation (*RSD*) ($n$ = 6) values for run-to-run study were in the range 4.4–5.9%. Inter-day RSD ($n$ = 5) weekly values are typically in the range 5.6–14.2%. These results demonstrate the precision of the developed method and the potential of the proposed approach for quantitative purposes.

The limit of quantitation (LOQ) is defined as the lowest fortification level evaluated at which acceptable average recoveries and precision (70–120% and *RSD* < 20%, respectively) are demonstrated. This was experimentally calculated from the injection of matrix-matched standard solutions at low concentration levels. The results obtained for each herbicide are also shown in Table 3. The LOQs obtained in real samples are as low as 1 ng/mL for most of the studied herbicides and 5 ng/mL for prosulfuron and sulfosulfuron. The limit of detection (LOD) was determined as the sample concentration that produces a peak with a height three times of the level of baseline noise. The instrument LODs for all the analytes were between 0.2 and 0.8 ng/mL.

### 3.5. Standard and sample analysis

Standards and samples were analyzed in order of increasing concentration. The standards were analyzed at the beginning and end of an automated sequence to confirm their stability as well as that of the instrument. The standards showed less than a 20% change in peak area response over the course of the analysis of the sample set.

## 4. Conclusions

A sensitive and fast analytical method has been developed for the simultaneous quantification of 16 sulfonylurea herbicides in surface water. SPE cartridges of ProElut C18 were employed for sample cleanup. An UHPLC coupled with tandem mass spectrometry method was used for identification and quantification of the target analytes. The developed method was sensitivity, high specificity, accuracy and rapid. This method is intended for use on agricultural runoff waters or waters from other rural areas.

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