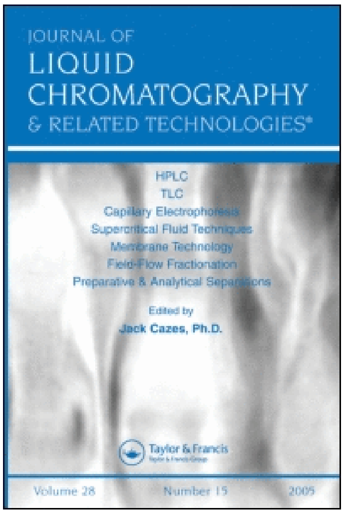

Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

Rapid and Accurate Determination of Dichlorvos in Water by Liquid Chromatography-Electrospray Ionization-Tandem Mass Spectrometry

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To cite this Article Yang, Lan , Liu, Yan Hong , An, Li Zhe and Li, You-bin(2006) 'Rapid and Accurate Determination of Dichlorvos in Water by Liquid Chromatography-Electrospray Ionization-Tandem Mass Spectrometry', Journal of Liquid Chromatography & Related Technologies, 29: 20, 2943 — 2955

To link to this Article: DOI: 10.1080/10826070600981025

URL: http://dx.doi.org/10.1080/10826070600981025

Journal of Liquid Chromatography & Related Technologies®, 29: 2943–2955, 2006

ISSN 1082-6076 print/1520-572X online
DOI: 10.1080/10826070600981025

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Abstract: An LC-MS/MS method has been developed and validated for the determination of dichlorvos in ground and surface waters. The aqueous samples (20.0 mL) are led through a silica-based C_8 + WAX mixed-mode SPE cartridges. Such a step successfully eliminates humic substances and other interferences that induce a matrix effect. Since the recovery of dichlorvos is 100% and the matrix effect is eliminated, the calibration standards prepared in DI water can be used for accurate and rapid determination of dichlorvos in various aqueous samples. The quantification limit is 0.01 μg/L.

Keywords: Dichlorvos, LC-MS/MS, Matrix effect, C8 + WAX mixed-mode

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INTRODUCTION

The increasingly intensive and widespread use of organophosphorus pesticides has resulted in significant contamination of surface and ground water. These pesticides are usually non-biodegradable and quite persistent in the environment. They are toxic to all animals and humans by binding to the enzyme acetylcholinesterase, disrupting nerve function, resulting in paralysis and death.[1] Thus, in order to evaluate ground and surface water resources for preparation of drinking water, it is essential to accurately determine the concentrations of these pesticide residues in the ground and surface. Similar to the European Union,[2] a maximum allowable concentration of 0.1 μg/mL for each individual organophosporus pesticide in drinking water is in force in China.

In the last few years, tandem mass spectrometry detection (MS-MS) coupled to LC has become a very valuable technique for the determination of pesticide residues in water samples.[3,4] Ingelse et al.[5] directly injected 1.0 mL of aqueous samples into an aqueous C_{18} HPLC column for the determination of polar organophosphorus pesticides using MS/MS MRM detection. Nakazawa et al.[6] used flow injection ion spay ionization tandem mass spectrometry for rapid and simultaneous analysis of dichlorvos, malathion, carbaryl, and 2,4-dichlorophenoxy acetic acid. Huang et al.[7] used a direct aqueous injection LC-ESI-MS/MS technology for determination of arazine, simazine, and their chlorotriazine metabolites. Several groups developed and validated on-line SPE-LC/MS-MS methods for multiclass determination of pesticides and transformation products in water.[8–10] Nevertheless, the presence of matrix co-eluting organic compounds can interfere with the ionization of the target analyte and, thus, severely affect the qualification.[11] The matrix effect has not been well solved in nearly all the previous studies. In order to minimize the matrix effect, Ingelse et al. used atmospheric pressure chemical ionization (APCI) instead of more sensitive electrospray ionization.[5] Even with the less sensitive APCI mode, a slight matrix enhancement effect was generally observed, and therefore, the authors recommended the matrix matched calibration for an accurate quantification.[5] The matrix matched calibration is not always permitted by regulatory agencies. Furthermore, the variability of the matrix between series of samples misadvises the matrix matched calibration. Flow injection without HPLC separation even showed a worse solution, although, the authors used the stable labeled isotope internal standards for the compensation.[6] Huang et al. diluted the water samples 1:4.[7] Although, the method reduced the matrix effect, the dilution could not eliminate it. In addition, it also increased the detection limit. The on-line SPE-LC/MS-MS methods applied reversed-phase SPE materials with low selectivity to concentrate analyte targets.[8–10] Obviously, co-eluting matrix interferences were also concentrated. Therefore, one of the further efforts should focus on how to eliminate the matrix effect.

This present study describes a rapid and reliable LC-MS/MS method for the qualification of dichlorvos in aquatic samples. Water samples are led through silica-based $C_8 + WAX$ mixed mode cartridges to eliminate humic substances and other interferences, which may induce the matrix effect. Since the recovery of dichlorvos is 100% and the matrix effect becomes zero, one set of solution calibration made by DI water can be used for accurate quantification of surface and ground waters in the real environment, as well as in drinking water. The quantification limit for dichlorvos is 0.01 μg/L.

EXPERIMENTAL

Reagents and Chemicals

Dichlorvos (99.4%) was purchased from Sigma-Aldrich (Shanghai Office, China) and its stable labeled isotope standard, dichlorvos-d_6 (99.6% purity), was purchased from Hayashi Pure Chemical Industry, Ltd. (Osaka, Japan). A $C_8 + WAX$ mixed mode SPE product (1 g/10 mL) and an Innovation® stable amide 3 um 5 cm × 2.1 mm column were purchased from Chrom-Matrix Inc. (Richland, WA, USA). Both suwannee river humic acid standard II and fulvic acid standard II were purchased from International Humic Substances Society. Other chemicals are at least analytical grades, and water was purified and deionized by the Milli-Q-UF system (Millipore, Milford, MA, USA).

Preparation of Stock Solutions, Calibration, and Quality Control Standards

Stock Solutions

Stock standard solutions were prepared dissolving 10 mg dichlorvos, accurately weighted and corrected for the purity, into 1.0 L water:acetontrile (50:50). The stock solutions of dichlorvos were made in duplicate. Six replicated samples were made by the 1000-fold dilution of each stock solution and then their LC/MS/MS responses were determined. The peak areas of the six replicated samples for each stock were integrated and averaged. The purpose was to ensure that the difference of both stocks was less than 5%. Then, one of the stocks was used to make calibration standard spiking solutions, and the other for quality control standard spiking solutions.

For making the spiking solutions, the stock solutions were serially diluted.

A stock solution (10 mg/L) and the spiking solution (10 μg/L) of the labeled internal standard, dichlorvos-d_6, were made by a similar way.

Preparation of Calibration and Quality Control Standards

Eight calibration standards were freshly made daily. A dichlorvos spiking solution, 0.500 mL, and 0.500 mL of the internal standard spiking solution were added into 49.0 mL of DI water or aquatic sample to make a calibration standard. The concentrations of the spiking solutions and the calibration standards were listed in Table 1.

Four levels of quality control standards (LLOQ, LOW, MID, and HIGH) were prepared at a volume of 1 liter. In more detail, 10.0 mL of a dichlorvos spiking solution and 10.0 mL of the dichlorvos-d_6 spiking solution were added into 980 mL of DI water. The QC standards were stored in amber glass bottles, in the dark, at refrigerator temperature (4°C) until analyzed.

Sample Pretreatment Protocol

A typical sample pretreatment protocol was described as follows. A 1 g/10 mL $C_8 + WAX$ mixed-mode SPE cartridge from Chrom-Matrix Inc. (Richland, WA, USA) was conditioned by 2 mL acetontrile and 2 mL DI

Table 1. Protocol for making dichlorvos calibration and QC standards

Standard	Dichlorvos spiking conc. (ug/L)	Dichlorvos-d6 spiking conc. (ug/L)	Final volume (mL)	Final dichlorvos conc. (ug/L)	Final dichlorvos-d6 conc. (ug/L)
Calibration Std-1	1.00	10.0	50.0	0.0100	0.0100
Calibration Std-2	2.00	10.0	50.0	0.0200	0.0100
Calibration Std-3	4.00	10.0	50.0	0.0400	0.0100
Calibration Std-4	7.00	10.0	50.0	0.0700	0.0100
Calibration Std-5	14.0	10.0	50.0	0.140	0.0100
Calibration Std-6	26.0	10.0	50.0	0.260	0.0100
Calibration Std-7	50.0	10.0	50.0	0.500	0.0100
Calibration Std-8	100	10.0	50.0	1.00	0.0100
LLOQ-QC	1.00	10.0	1000	0.010	0.0100
LOW-QC	3.00	10.0	1000	0.030	0.0100
MID-QC	10.0	10.0	1000	0.100	0.0100
HIGH-QC	80.0	10.0	1000	0.800	0.0100

water. Then, 20 mL of a calibration standard, QC standard, or a real sample spiked with the internal standard spiking solution was rapidly led through the SPE cartridge via a vacuum manifold (Supelco, Bellefonte, PA, USA). The cartridge was washed with 10 mL DI water. Finally dichlorvos and its internal standard, dichlorvos-d_6, were recovered by 2 mL acetontrile. The eluate was concentrated less than 0.5 mL, and then a 1.0% formic acid aquatic solution was added to make the final volume to 1.00 mL.

LC-MS/MS Analysis

The instruments used were a Perkin-Elmer Series LC-200 HPLC system, a Perkin-Elmer Series autosampler, and a Sciex API 4000 triple quadrupole mass spectrometer with a turbo ion spray interface and the positive mode. The Analyst software (version 1.4.1) was used to operate the integrated system.

A HPLC linear gradient run was completed within 4 min. HPLC column: Chrom-Matrix stable amide (3 um 5 cm × 2.1 mm); flow rate: 0.4 mL/min; injection volume: 100 μL; mobile phase A: DI water containing 0.1% formic acid; mobile phase B: acetontrile. Between injections, the needle was rinsed by acetontrile:water (50:50, v/v). An isocratic run was done with 75% mobile phase A within the first 0.2 min; than from 0.2 min to 3.8 min. A linear gradient was done from 75% mobile phase A to 10% mobile phase A; at the final step, a linear gradient run back to 75% mobile phase A.

Dichlorvos and dichlorvos-d_6 were determined by electrospray MRM scan mode with positive ion. According to the 2002/657/EC European commission Decision (Commission Decision 2002/657/CE of 12 August 2002), two MS/MS transitions were necessary in order to have a confident positive. Thus, for dichlorvos, two nominal transitions, m/z 220.95 → 108.90 and m/z 220.95 → 126.90, were recorded. The first transition was more sensitive and, thus, was used for the quantification purpose. On the other hand, the ratio between the integration area of the first transition and that from the second transition was 1.84 ± 0.11. It was found, that the ratio was constant over a range of concentration during the present study. For the internal standard, two corresponding MS/MS transitions, m/z 226.88 → 114.81 and m/z 226.66 → 132.75, were also monitored. The MRM parameters were: DP = 64; EP = 10; CE = 25; CXP = 9; collision gas; 4 ψ curtain gas: 50 ψ ion source gas 1:70 ψ ion source gas 2: 50 ψ ion spray voltage: 5500 v; temperature: 400°C.

Method Validation

Three day by day validation batches were first run to test the precision and the accuracy.

The fourth batch was used to evaluate the recovery and matrix effect in both LOW-QC and HIGH-QC levels. Surface, ground or drinking water

(20 mL) without dichlorvos was treated by the same SPE protocol. Then, the acetontrile eluate containing matrix blank samples was dried and reconstituted by 1.0 mL of water:acetontrile:formic acid (50:49.5:0.5) containing 0.03 μg/L (LOW-QC) or 0.8 μg/L (HIGH-QC) dichlorvos. On the other hand, 20 mL of DI water purified by the Millipore system was treated by the same way, and finally reconstituted by 1.0 mL of water:acetontrile:formic acid (50:49.5:0.5) containing 0.03 μg/L (LOW-QC) or 0.8 μg/L (HIGH-QC) dichlorvos.

The fifth batch was used to evaluate the relative matrix effect from six unique matrix lots, at the LOW-QC level.

Carryover assessment was also done. The integration area of the carryover from the highest calibration standard should be less than 20% of LLOQ.

Chromatograms were automatically integrated using Analyst to compute the 1/X weighted least squares linear regression.

Sample Analysis

Ground and surface waters were collected for the determination of dichlorvos concentration. Dichlorvos-d_6 spiking solution (20 μL) was added into 20 mL of the tested sample prior to the SPE process.

A typical LC-MS/MS running sequence was as follows: the first set of matrix blank, solution calibration standards, control blank, three LOW-QC, 1/3 of the real samples, three MID-QC, 1/3 of the real samples, three HIGH-QC, the last part of real samples, the second set of matrix blank, solution calibration standards, and control blank.

RESULTS AND DISCUSSION

Dichlorvos (2,2-dichlorovinyl-*o,o*-dimethyl phosphate) has been extensively used for more than 40 years for insect control in food storage areas, greenhouses, and barns. It is also used for controlling parasites and insects in houses, aircraft and outdoor areas (as aerosols, liquid sprays). The chemical structures of dichlorvos and its stable isotopically labeled internal standard, dichlorvos-d_6, are shown in Figure 1.

U.S. EPA has classified dichlorvos as a Group B2, probably human carcinogen (U.S. Environmental Protection Agency, Integrated Risk Information

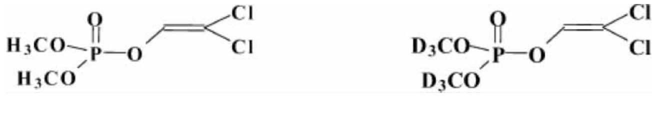

Figure 1. Chemical structures of dichlorvos and its internal standard, dichlorvos-d_6.

System on Dichlorvos, Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH, USA, 1994). The determination of dichlorvos is an important indication for the evaluation of water quality.

Figures 2–4 are the MRM chromatograms of dichlorvos at 200 μg/L, its carryover, and 2.00 μg/L. All the samples were preconcentrated 20-fold by the SPE protocol described in the Experimental section. The injection concentration of 2.00 μg/L corresponds to the value of the lowest calibration standard (0.01 μg/L) when the injection concentration of 200 μg/L corresponds to the value of the highest calibration standard (10.0 μg/L).

When the LC-MS/MS technique is used for the determination of pesticide residues, the first test should focus on the carryover assessment. The carryover effect frequently happens in LC-MS/MS analysis and results in false positive findings. Two potential sources contribute to the carryover effect. One is from the HPLC column, and the second is from the other parts of the LC-MS/MS system. The latter one can be judged when the

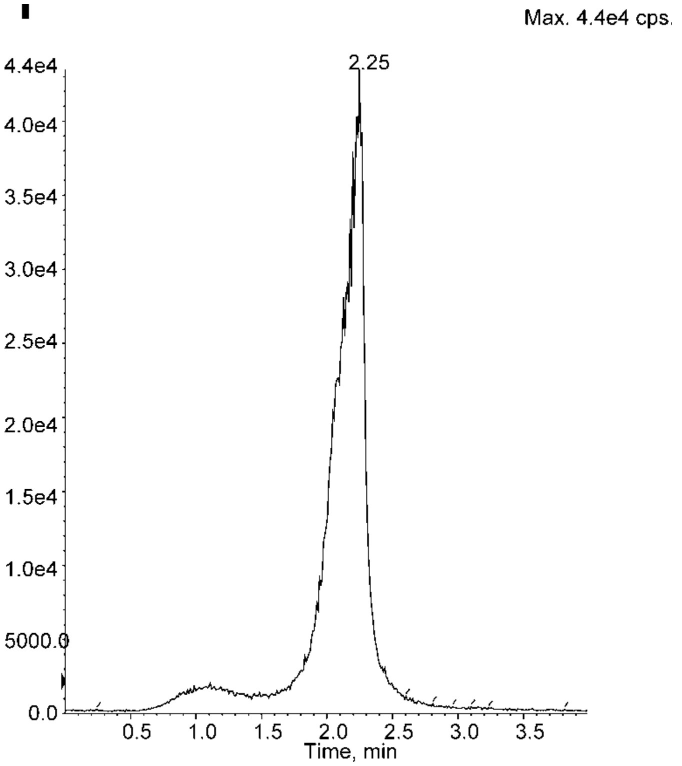

Figure 2. MRM chromatogram of dichlorvos at a concentration of 20.0 μg/L (MS/MS transition: m/z 220.95 → 108.90).

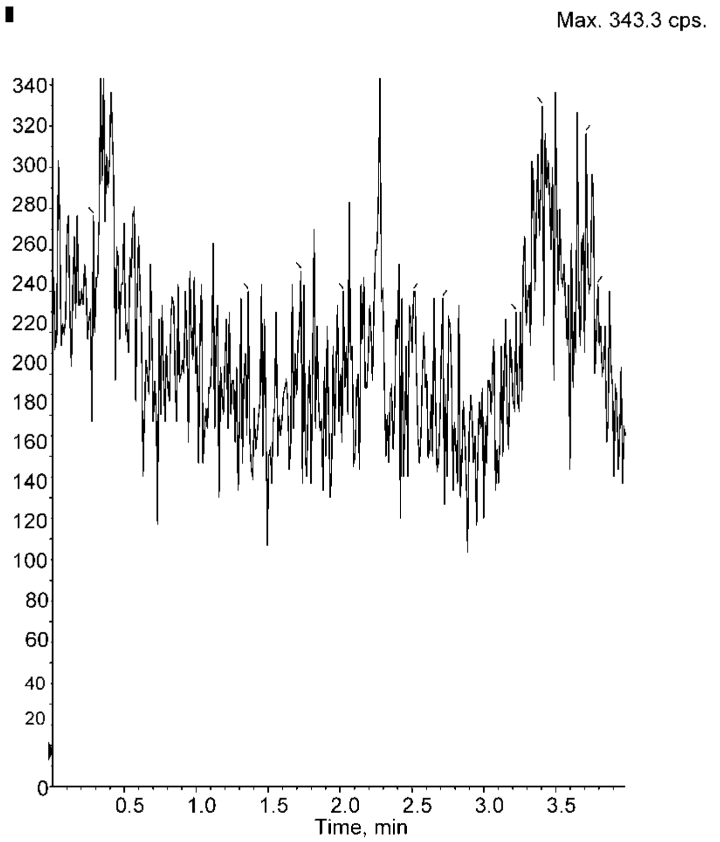

Figure 3. Carryover from Figure 1.

highest standard is injected into the system without a HPLC column. After the injection, a blank is injected again. If the MRM signal is observed again, a carryover effect from the system itself is confirmed. In most cases, the carryover effect from the latter source can be eliminated by the optimization of needle rinse solutions. After that, a HPLC column is connected to evaluate the carryover effect from the column itself. The carryover effect frequently happens when the conventional reversed phase HPLC columns such as C_{18} and C_8 are used. In the present study, a polar embedded reversed phase was chosen to get a zero carryover (Figure 3). Therefore, the limit of detection can be decreased as much as that reached by the detection limit of the instrument. In the present study, the lowest detection limit of dichlorvos is fixed at 2.00 μg/L per 100 μL of the injection volume (Figure 4).

The second evaluation is to focus on the sample pretreatment strategy. In the majority of current publications,[3,4,8–10] solid-phase extraction processes and, in some cases, liquid–liquid extraction processes have been used to

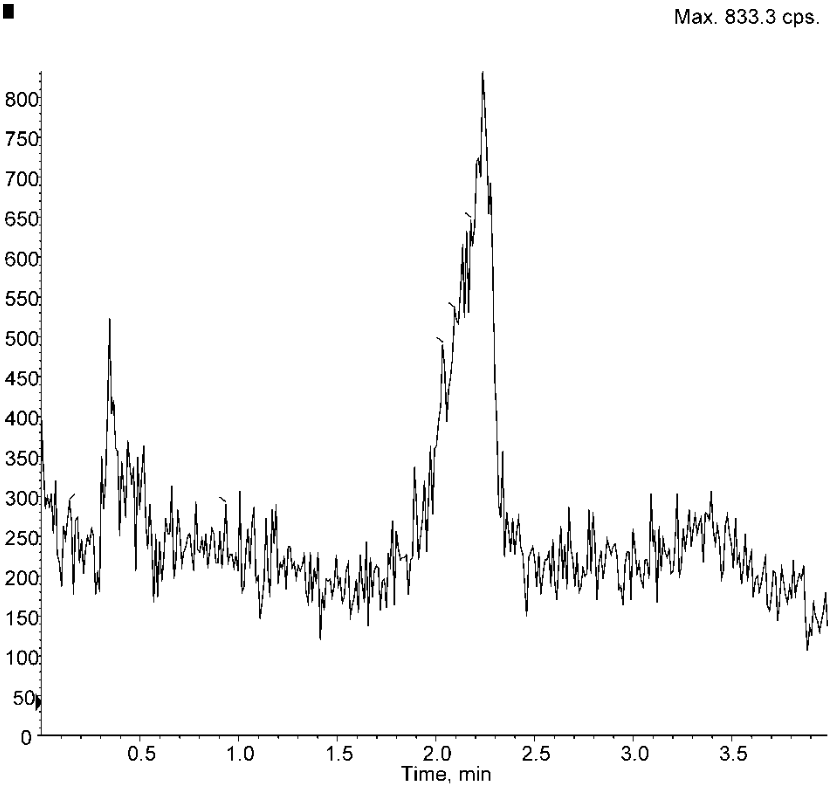

Figure 4. MRM chromatogram of dichlorvos at a concentration of 0.200 μg/L (MS/MS transition: m/z 220.95 → 108.90).

concentrate pesticides at trace concentrations. However, almost all the extraction processes, due to their inherent low selectivity, concentrate both the analyte targets and the coeluting matrix interferences. In the present study, an alternative sample cleanup strategy was developed. A $C_8 + WAX$ mixed mode SPE cartridge was chosen for the concentration of dichlorvos and removal of interferences. When aquatic samples were led through the SPE cartridges, dichlorvos was retained on the cartridge via reversed-phase interaction with C_8 when inorganic components passed through the cartridge. On the other hand, humic substances and other negative interferences that might induce the matrix effect should be retained on the cartridges by ionic exchange interaction. Finally, dichlorvos and other components that only had reversed-phase adsorption were selectively recovered from the cartridges by acetontrile. Probably inorganic salts and humic substances were major resources that induce the matrix effect.[12] Humic substances and other negative interferences were rapidly and irreversibly adsorbed on aminopropyl silica.[13] It was found, that the step was very successful to eliminate the matrix effect.

The quantitative assessment of the matrix effect by fulvic and humic acids were done according to Matuszewski et al. method.[11] The integration areas for standards post spiked into the water extract were divided by the corresponding integration areas of the same concentration of standards in neat solution. When the value was higher than 100%, it implied the matrix enhancement effect. When the value was less than 100%, there was an ion suppression effect. Water (20 mL) containing 1.0 mg/L fulvic acid or 1.0 mg/L humic acid was led through a 1 g/10 mL $C_8 + $WAX SPE cartridge, and the acetontrile eluate was dried. Dichlorvos (1.0 mL 0.6 μg/L) was added. In another experiment, dichlorvos was spiked into the 1.0 mg/L fulvic acid or humic acid aquatic solution and the spiked concentration was 0.6 μg/L. The four samples, as well as the pure dichlorvos aquatic solution (0.6 μg/L), were injected for the LC-MS/MS analysis. The matrix effect was calculated by comparing the integration areas of the samples with that of the pure solution. The data were listed in Table 2.

Fulvic acid and humic acid did make the ion suppression effect (Table 2). However, the SPE cleanup successfully removed humic substances and, thus, the matrix effect was eliminated.

Steen et al.[14] reported a use of a tandem aminopropyl/LiChrolut EN SPE set up. Although, a substantial amount of humic material was removed, the tandem SPE procedure did not effect an improvement with respect to signal suppression. Another two groups observed remarkable improvement.[15,16] Geerdink et al.[15] used a tandem SPE to first retain humic acids at pH 1-2, and quantitatively recovered and isolated triazines by a C_{18} SPE at pH 7. Li and Lee[16] used dynamic ion exchange mechanism to obviate the adsorption of humic substances on C_{18}-SPE. Our experience revealed that the quality of SPE material may have an influence. Ion exchange SPE materials from some vendors actually had quite significant bleeding. Obviously, some humic and fulvic acids adsorbed on these SPE materials should elute into the final fraction to induce the matrix effect. In addition, it seemed that silica based weak anion exchange material offered better cleanup than polymer based SPE and/or strong anion exchange materials. The SPE model used by Li and Lee[16] was also a mixed mode SPE. Nevertheless, the ion exchange component was a strong anion exchange surfactant.

Table 2. Evaluation of matrix effect of dichlorvos (average value from six replicates)

Aquatic sample	Suppression/ enhancement (%)	CV (%)
Fulvic acid	86.5	9.8
Humic acid	76.4	8.7
Removal of fulvic acid by SPE	101	5.4
Removal of humic acid by SPE	99.2	4.9

In addition, the WAX component of the used $C_8 + WAX$ mixed mode SPE cartridges was a kind of primary and secondary amine. It was expected that the WAX component had a strong capacity to capture humic substances.

Since the matrix effect was absent, dichlorvos and its internal standard, dichlorvos-d_6, are spiked into DI water and tap water to make the calibration standards, in order to determine the concentration of dichlorvos from surface water and ground water. All the calibration standards, quality control standards, and real samples were submitted for the SPE pretreatment.

Over the range of 0.0100–1.00 μg/L, the calibration curves were well fitted with linear models using 1/X weighting factors. The least square linear regression constants (r^2) were always ≥ 0.996. Concentrations of quality control standards were calculated from each curve. The accuracy was obtained by comparing the averaged calculated concentrations to their nominal values (%), and the precision by the percent of coefficient of variation (CV%). The data regarding the intra- and inter-assay precision and accuracy for the dichlorvos quality control standards were listed in Table 3.

The relative matrix effect from six different lots of stream water was listed in Table 4. Since the absolute matrix effect was absent, it was no surprise that there was no difference from lot to lot.

More than fifty samples of ground and surface water, at specific sites in Gansu Province, P.R. China, and the quality of several commercial drinking waters had been determined by the validation method. When dichlorvos was not detected in the drinking water products, as well as the tap water samples purified by a water plant, dichlorvos was detected in a few surface and ground sources. About half of the areas monitored presented surface

Table 3. Intra- and inter-assays accuracy and precision of dichlorvos QC samples in surface and ground waters

QC standard	Theoretical nominal concentration (ug/L)	Mean concentration found (ug/L)	Intra-assay precision (n = 6) CV (%)	Inter-assay precision (n = 18) CV (%)	Accuracy derivation (%)
Surface water					
LLOQ	0.0100	0.0112	17.7	14.6	12
LOW-QC	0.0300	0.0310	11.5	12.3	3.3
MID-QC	0.100	0.0956	8.8	8.2	−4.4
HIGH-QC	0.800	0.788	7.9	4.5	−1.5
Ground water					
LLOQ	0.0100	0.0105	14.4	12.2	5.0
LOW-QC	0.0300	0.0307	13.2	10.4	2.3
MID-QC	0.100	0.104	6.7	7.0	4.0
HIGH-QC	0.800	0.796	7.4	7.1	−0.5

Table 4. Relative matrix effect from six unique LOW-QC standards on quantitative assessment

Dichlorvos spiked in stream waters	Lot 1	Lot 2	Lot 3	Lot 4	Lot 5	Lot 6
Mean concentration found (ug/L)	0.0322	0.0314	0.0292	0.0294	0.0315	0.0327
% CV	9.6	11.2	6.3	5.5	13.2	9.6
Accuracy derivation (%)	7.3	4.7	−2.7	−2.0	5.0	9.0
n	6	6	6	6	6	6

water contamination by dichlorvos, as well as a few ground water sites, although, the determined concentration was generally less than 0.1 μg/L.

CONCLUSIONS

A simple and straightforward LC-MS/MS analytical method has been developed and validated to determine dichlorvos in various aquatic resources. The method includes the use of a $C_8 + WAX$ mixed-mode SPE for elimination of the matrix effect, as well as concentration of dichlorvos, the use of a polar embedded HPLC column for minimization of carryover effect, and the use of two MRM transitions for confirmation of the findings. The method should be applicable, with some modification, to determine other neutral and basic pesticides from various aquatic sources.

ACKNOWLEDGMENT

This study was funded in part by the National Science Foundation of China (30470277), Gansu National Science Foundation (3ZS061-A25-070) and Gansu Key Technologies R&D Program (ZGS052-A41-0006-03). The content of the work reflects the personal view of the author and not necessarily the view of the organization.

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Received July 25, 2006
Accepted August 31, 2006
Manuscript 6913