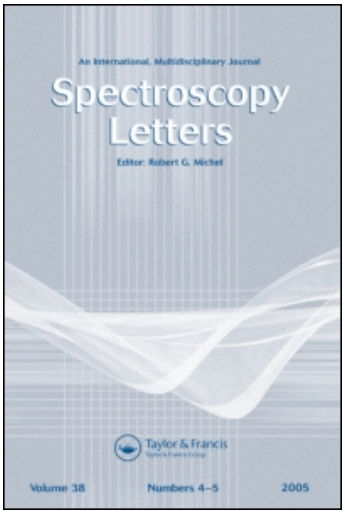

Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Solid-Phase Microextraction Coupled to Gas Chromatography-Mass Spectrometry for the Analysis of Famoxadone in Wines, Fruits, and Vegetables

N. Aguinaga[a]; N. Campillo[a]; P. Viñas[a]; M. Hernández-Córdoba[a]
[a] Department of Analytical Chemistry, Faculty of Chemistry, University of Murcia, Murcia, Spain

Online publication date: 01 December 2009

To cite this Article Aguinaga, N. , Campillo, N. , Viñas, P. and Hernández-Córdoba, M.(2009) 'Solid-Phase Microextraction Coupled to Gas Chromatography-Mass Spectrometry for the Analysis of Famoxadone in Wines, Fruits, and Vegetables', Spectroscopy Letters, 42: 6, 320 — 326
To link to this Article: DOI: 10.1080/00387010903178723
URL: http://dx.doi.org/10.1080/00387010903178723

Spectroscopy Letters, 42:320–326, 2009

ISSN: 0038-7010 print/1532-2289 online
DOI: 10.1080/00387010903178723

Taylor & Francis
Taylor & Francis Group

Solid-Phase Microextraction Coupled to Gas Chromatography-Mass Spectrometry for the Analysis of Famoxadone in Wines, Fruits, and Vegetables

N. Aguinaga,
N. Campillo,
P. Viñas,
and M. Hernández-Córdoba

Department of Analytical Chemistry, Faculty of Chemistry, University of Murcia, Murcia, Spain

ABSTRACT A sensitive, selective, and solvent-free method based on direct immersion solid-phase microextraction (DI-SPME) followed by gas chromatography with mass spectrometry (GC-MS) is proposed for the determination of trace amounts of famoxadone in wines, fruits, and vegetables. Parameters affecting the sample enrichment step, such as sample mass, ionic strength, adsorption and desorption times, and temperatures were carefully optimized. A polar 85 μm polyacrylate fiber was found to be suitable for extraction at 60°C in 20 min under continuous stirring. Desorption was carried out at 270°C for 5 min. Undiluted wine samples and diluted extracts obtained from the solid samples submitted to an ultrasound treatment in the presence of ethanol were quantified against external aqueous standards prepared in 12% ethanol (v/v). Under the optimized conditions, detection limits of 5 ng L^{-1} and 10 pg g^{-1} were obtained for liquid and solid samples, respectively. SPME-GC-MS analysis yielded good repeatability (RSD under 10% in all cases). The method provided recoveries of 91.6–110.9% from spiked samples. The method was applied to different samples, and none of them was found to contain famoxadone at concentrations above the corresponding detection limits.

KEYWORDS direct immersion-solid phase microextraction (DI-SPME), famoxadone, fruits, gas chromatography-mass spectrometry (GC-MS), vegetables, wine

An invited paper submitted to a special issue on Green Spectroscopy and Analytical Techniques, organized by Professor Miguel de la Guardia, of the Department of Chemistry, University of Valencia, Spain, and Professor Arabinda Kumar Das, of the Department of Chemistry, University of Burdwan, West Bengal, India.

Received 11 July 2008; accepted 5 September 2008.

Address correspondence to Prof. M. Hernández-Córdoba, Department of Analytical Chemistry, Faculty of Chemistry, University of Murcia, E-30071 Murcia, Spain. E-mail: hcordoba@um.es

INTRODUCTION

Famoxadone is a synthetic fungicide included in the oxazolidinedione family, which was first sold in 1997. This chemical is cataloged as a Quinone outside Inhibitor (QoI) fungicide, and is therefore effective when applied early in the disease cycle. Famoxadone has been widely applied because of its effectiveness against a broad spectrum of fungi that infect grapes, cereals, tomatoes, and many other crops.[1] In order to minimize possible risks to human health, the agricultural products obtained from these crops

must be subject to famoxadone residues control. Maximum residue limits (MRLs) for famoxadone of 2 μg g^{-1} in table and wine grapes, 0.02 μg g^{-1} in citrus and pome fruits, 1 μg g^{-1} in fruiting vegetables such as tomatoes and 0.02 μg g^{-1} in leaf vegetables, have been stablished by European Union.[2] No MRL has been established in wines, but the Organisation Internationale de la Vigne et du Vin (OIV) suggests as MRL for fungicides in wines should be about 1/10 of the corresponding MRL set for grapes,[3] meaning that an MRL of 0.2 μg mL^{-1} for famoxadone in wines could be established.

The literature contains few analytical studies for the determination of famoxadone in fruits, vegetables and derived products,[4–14] half of them multiresidue methods. Residues of this fungicide have been analyzed by gas chromatography (GC) separation with selective and sensitive detectors such as mass spectrometry (MS),[5,6,8,12,14] electron capture detector (ECD),[8,10] and nitrogen-phosphorus detector (NPD).[10] Liquid chromatography (LC) with diode array detector (DAD) or MS has also been used.[4,7,9,11–13]

The complex matrix of food samples makes it necessary to include steps for isolating the analyte from the sample matrix and sometimes even clean-up stages. In this sense, the most widely used methods are based on extraction organic solvents (LLE),[4–13] some of them including solid-phase extraction (SPE) for extract cleaning purposes.[5,12] There is no doubt in the success of these sample treatments, but their inherent disadvantages of being rather labor-intensive, time-consuming and requiring large volumes of solvents (which may be toxic), and frequently requiring an additional cleaning step prior to chromatographic separation, are clear. Green analytical chemistry is concerned with the design, development, and implementation of products and chemical processes that reduce or eliminate the use or generation of substances harmful to human health and the environment.[15–17] The subject has aroused considerable interest last years and its main strategies and benefits have been recently discussed in depth.[18]

Sample preparation techniques have been developed, which are clean, selective, rapid, and efficient; ideally, they can be automated and are economical, simple, and solvent-free. One of such techniques is solid-phase microextraction (SPME), developed by Pawliszyn and co-workers.[19–22] SPME has gained widespread acceptance because it allows the concentration of both volatile and non-volatile compounds at low analyte concentrations from a large variety of matrices. The preconcentration of pesticides by SPME is a well-established procedure; nevertheless, as far we know, only one method based on this technique has been developed for the analytical determination of famoxadone.[14] This article can be treated as an extension of that analytical procedure. Here, sensitivity is enhanced and the optimized procedure applied for other samples that can be quantified by external calibration. This article reports a method for the determination of famoxadone in wine, fruits, and vegetables using the SPME in the direct immersion mode followed by GC-MS. Compared to other sample preparation methods involving the use of LLE and SPE followed by GC-MS,[5,6,8,12] the present procedure has the two main advantages of being time-saving and showing increased sensitivity.

MATERIALS AND METHODS

Reagents and Apparatus

Famoxadone ((RS)-3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione) standard solution with a purity higher than 99% was supplied by Riedel-de-Haën (Steinheim, Germany) as a 100 μg mL^{-1} solution in acetonitrile. A more diluted solution of 10 μg mL^{-1} was prepared monthly in acetonitrile and stored in the dark at 4°C. A working standard solution was prepared daily.

Analytical-reagent grade acetonitrile, methanol, and ethanol were purchased from Lab-Scan (Dublin, Ireland). Sodium chloride, sodium hydroxide, sodium acetate, and di-sodium hydrogen phosphate were obtained from Panreac (Barcelona, Spain). Acetic acid (99.8% (v/v), Fluka, Buchs, Switzerland) and phosphoric acid (85% (v/v), Panreac) were used to prepare buffer solutions. Deionized water was obtained from a Milli-Q water purification system (Millipore, Bedford, MA, USA).

The commercial SPME holders for manual use and fibers coated with 100 μm polydimethylsiloxane (PDMS, apolar), 65 μm polydimethylsiloxane-divinylbenzene (PDMS/DVB, bipolar), 85 μm polyacrylate (PA, polar), 75 μm Carboxen-polydimethylsiloxane

(CAR/PDMS, medium polar), 70 μm Carbowax-divinylbenzene (CW/DVB, polar), and 50/30 μm divinylbenzene-Carboxen-polydimethylsiloxane (DVB/CAR/PDMS, medium polar) were purchased from Supelco (Bellefonte, PA, USA). The fibers were conditioned by heating in the injection port of the GC according to the manufacturer. All analyses were performed in 15 mL clear glass vials and the solutions were stirred with a magnetic stirrer (IKA RH KT/C, Supelco) at 1700 rpm using PTFE-coated magnetic stir bars (10 mm × 6 mm-o.d.). To prevent analyte evaporation, vials sealed with hole-caps and PTFE/silicone septa were used. A laboratory-made heating system, built in the Central Laboratory Service of the University of Murcia and consisting of a drilled block provided with an electronic temperature control system was used for heating sample solutions during the SPME adsorption step.

GC analyses were performed on an Agilent 6890 N (Agilent, Waldbronn, Germany) gas chromatograph, equipped with a split/splitless injector, coupled to an Agilent 5973 quadrupole mass selective spectrometer equipped with an inert ion source. The mass spectrometer was operated using electron-impact (EI) mode (70 eV). An SPME liner (Supelco) of 0.75 mm-i.d. was used. The compound was quantified in the selected ion monitoring (SIM) mode in order to improve the detection limit using one target and two qualifier ions. The experimental conditions for the SPME-GC-MS system are summarized in Table 1.

An IKA A11 grinder (IKA, Staufen, Germany) and a Hettich centrifuge (Tuttlingen, Germany) were used for treating the solid samples. An ultrasonic probe processor UP 200 H with an effective output of 200 W in liquid media (Dr. Hielscher, Teltow, Germany) equipped with a titanium (13 mm i.d.) sonotrode was used for leaching the analyte from solid samples. The ultrasonic probe was used in continuous mode at 100% power, corresponding to an operating frequency of 24 kHz.

Samples and Analytical Procedure

A series of white, rosé, and red wines and different fruit and vegetable samples (white grape, peeled canned grape, orange, lemon, pear, tomato, and lettuce) were purchased in a local supermarket. Wine samples were stored in sterile glass jars at 4°C until analysis. Solid samples were ground and placed in a 50 mL polyethylene closed flask before storing at 4°C until analysis. Lemon and orange samples were peeled before being ground, and analysis was carried out in the pulp.

For the liquid sample extractions, 15 mL of wine were placed in a 15 mL SPME-vial, which was immediately sealed with the cap after introducing the magnetic stir bar. The vial was then placed in the home-made heating module previously programmed at 60°C and was maintained under magnetic stirring (1700 rpm) for 1 min. After this homogenization step, the fiber was totally immersed in the solution for 20 min at 60°C and desorbed in the injection port of the GC in the splitless mode at 270°C for 5 min.

For fruits and vegetables, 8 g sample mass were weighed into a capped 50 mL polycarbonate centrifuge tube and 2 mL of ethanol were added for extraction. The mixture was sonicated at ambient temperature for 1 min by means of a probe (50% amplitude) directly immersed in the solution, and then centrifuged for 5 min at 3000 rpm. The resulting supernatant fluid was made up to 15 mL volume with water and submitted to the optimized SPME procedure. Each sampling was performed in duplicate.

TABLE 1 Experimental Conditions of the SPME-GC-MS System

SPME conditions	Adsorption step	20 min at 60°C (immersion mode)
	Desorption step	5 min at 270°C (splitless mode)
	Fiber material	PA, 85 μm
GC conditions	Capillary column	HP-5MS (5% diphenyl-95% dimethylpolysiloxane) (30 m x 0.25 mm-i.d., 0.25 μm film thickness)
	Carrier gas	Helium, 2 mL min^{-1} (constant flow)
	Oven program	100–300°C at 30°C min^{-1} (4 min)
MS conditions	Ion source temperature	230°C
	Transfer line temperature	325°C
	Solvent vent off	0–5 min

Recovery Assays

Since no reference materials are currently available for the validation of the method, recovery studies were carried out by spiking three wines (white, rosé, and red wine) and four solid samples (grape, orange, tomato, and pear) at two concentration levels. The samples were spiked adding 25 μL of an acetonitrile standard solution to 15 mL of liquid sample or 8 g of solid sample. The fortified samples were set aside for at least 2 hr at room temperature to let the organic solvent evaporate before being analyzed, as described earlier. Three replicates corresponding to three aliquots of each sample independently fortified and analyzed, were analyzed in each case.

RESULTS AND DISCUSSION

Chromatographic Conditions

Famoxadone was eluted with a mean retention time ± standard deviation of 9.55 ± 0.02 min (N = 20) using the chromatographic conditions summarized in Table 1. A shorter retention time was not suitable because of the noise produced by the sample matrix in the first 8 min of the chromatogram.

The target or quantitation ion was 330 and the qualifier ions were 196 and 224. The identification of famoxadone was confirmed by the retention time of the target ion and the qualifier-to-target ion ratios, 55.5 and 40.2% for 196 and 224, respectively.

SPME Conditions

Selection of the Extraction Mode and the Type of Fiber

A comparison of six different fiber coatings for SPME was made using both the headspace (HS) and the direct immersion mode (DI). These experiments were carried out by exposing the fibers to 5 mL of a 25 ng mL^{-1} standard aqueous solution for 20 min at 40 and 80°C for DI and HS mode, respectively. As expected, best results were obtained in DI mode for all fibers, due to the high molecular weight of the analyte, and so this extraction mode was selected. The highest extraction efficiencies in DI mode were attained using the CAR/PDMS and CW/DVB fibers. Nevertheless, none was selected; indeed, CW/DVB has been commercially withdrawn because of its very short lifetime owing to the hydrosoluble character of the Carbowax material; in the present case, the need to apply the direct immersion mode has reduced even further the useful lifetime of this material coating. On the other hand, CAR/PDMS provided very poor repeatability when famoxadone was extracted from aqueous solutions in the presence of ethanol. The medium polar PDMS/DVB fiber provided the worst result. Of the other three fibers, PA, PDMS, and DVB/CAR/PDMS, PDMS showed the lowest sensitivity, and PA was selected because it provided similar sensitivity to DVB/CAR/PDMS but the repeatability was higher.

Influence of the Composition of the Extraction Medium

It is known that the addition of hydrophilic solvents may modify the extraction efficiency of some analytes. Taking into account that the purpose was to use the optimized procedure for wine analysis, the presence of 12% (v/v) of ethanol in the extraction medium was evaluated. This ethanol concentration roughly corresponds to the alcohol level of a wide variety of wines. In fact, when comparing the analytical signals obtained for 1 ng mL^{-1} of famoxadone prepared in water, a 12% (v/v) ethanolic solution, and a red wine fortified at this concentration level, no significant differences were observed between the wine and the ethanolic solution, the signal obtained being approximately 10% higher than when famoxadone was extracted in the absence of alcohol. Further experiments were carried out using standard solutions prepared in the presence of 12% (v/v) of ethanol.

No salting out effect was observed when the extraction medium contained sodium chloride concentrations ranging between 0 and 35% (w/v). The influence of the pH of the extraction medium was studied by adding 0.5 mL of acetate buffer solution (1 M) (for pH values up to 5) and 0.5 mL of phosphate buffer solution (1 M) (for pH values ranging between 6 and 10). No effect was observed when varying the pH of the extraction medium. Consequently, no salting out agent or buffer solution was added to the extraction vial.

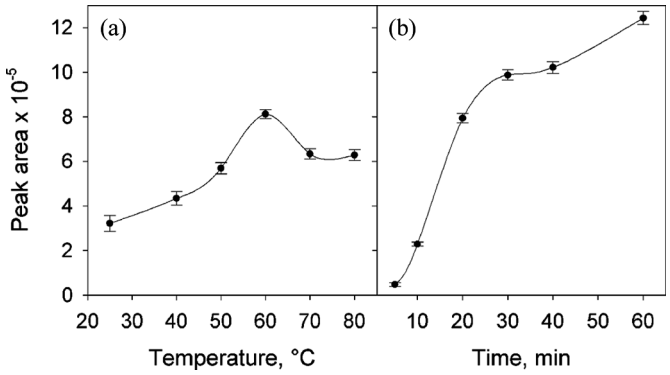

FIGURE 1 **Influence of: (a) extraction temperature and (b) extraction time on the SPME process for a spiked wine sample at a concentration level of 1 ng mL^{-1}. Vertical bars indicate standard deviation for N = 3.**

Extraction Temperature and Time. Stirring Speed

The temperature and adsorption time strongly influence the extraction efficiencies, and so both parameters were investigated. These experiments were carried out using 5 mL of a red wine sample spiked with famoxadone at a concentration level of 1 ng mL^{-1}. The influence of sample temperature was examined from 25 to 80°C with a time exposure of 20 min. Fig. 1a shows that the extraction efficiency was significantly enhanced as the temperature increased up to 60°C, after which it decreased. Therefore, 60°C was selected. Fig. 1b shows the influence of the adsorption time on the extraction efficiency between 5 and 60 min. Sensitivity increased in the entire range studied, the maximum rise in peak area being attained from 10 to 20 min. Twenty minutes was the value finally adopted, in order to not prolong the whole procedure.

The stirring speed was varied between 0 to 2000 rpm, the highest signal being obtained at 1700 rpm, which was the value selected.

Desorption Parameters

The desorption temperature was studied in the operating temperature range recommended by the manufacturer for PA fiber coatings (from 220°C to 310°C). The signal increased up to 270°C and then decreased, and so 270°C was selected. As regards desorption time, 5 min was sufficient to achieve the total desorption of the analyte with no memory effects.

Extraction Solution Volume

The sample volume submitted to the SPME procedure was selected using a red wine fortified at a famoxadone concentration level of 1 ng mL^{-1}. Sample volumes of 5, 10, and 15 mL were assayed using 15 mL SPME-vials. To study higher volumes (20, 30, and 40 mL), 40 mL SPME-vials were used. A sample volume of 15 mL was finally selected, which provided similar signals to those obtained with higher sample volumes.

Optimization of the Solid Sample Extraction Procedure

The sample treatment for fruits and vegetables was optimized by using spiked samples at the 0.5 ng g^{-1} analyte concentration level. Direct extraction by exposing the fiber to a suspension containing the solid sample was not possible because suspended particles might damage the fiber. Therefore, a previous extraction step was required and the liquid extract was submitted to the SPME procedure.

Preliminary experiments were carried out in order to select the extraction solvent by magnetically stirring 4 g of the ground sample with 5 mL of solvent for 10 min. The supernatant obtained after centrifugation was diluted to 15 mL with water and submitted to the SPME stage. The extraction solvents studied were water, methanol, acetonitrile, and ethanol, with recoveries of 16, 65, 90, and 100%, respectively. Consequently, ethanol was selected.

A decrease in the sample treatment time was achieved by sonicating the sample in the presence of ethanol by means of a probe directly immersed in the sample mixture, instead of conventional extraction. In this way, it was possible to attain in 60 s similar extraction efficiencies to those obtained when the sample mixture was magnetically agitated for 10 min.

To check the performance of the procedure, sample masses of 4–8 g were submitted to the optimized extraction procedure. Higher masses than 8 g were not assayed because of poor homogenization. No significant decrease in the recovery values were observed when the sample mass was increased. Therefore, a sample mass of 8 g was selected.

Taking into account the time of 20 min adopted for the SPME adsorption step and the retention time of the analyte, a sensitive analysis of each sample

TABLE 2 Calibration Parameters for Different Samples Under the Optimized Conditions

Sample	Slope[a] (L ng^{-1})	Intercept[a]	Correlation coefficient
12% (v/v) ethanol	303 ± 5.1	4975 ± 560	0.9999
White wine	310 ± 5.2	3045 ± 636	0.9998
Rosé wine	298 ± 6.0	4041 ± 1020	0.9998
Red wine	305 ± 3.2	2916 ± 868	0.9997
Grape	309 ± 5.0	5315 ± 985	0.9996
Orange	295 ± 7.1	6068 ± 1004	0.9997
Tomato	300 ± 6.0	4297 ± 662	0.9995
Pear	302 ± 5.0	4125 ± 751	0.9994

[a]Mean value ± standard deviation (N = 5).

TABLE 3 Analytical Data for Famoxadone

Parameter	Value
Slope[a] (L ng^{-1})	303 ± 5
Correlation coefficient	0.9999
Linearity (ng L^{-1})	15–1500
Detection limit (ng L^{-1})	5
Quantitation limit (ng L^{-1})	17
Detection limit (pg g^{-1})[b]	10
Quantitation limit (pg g^{-1})[b]	35

[a]Mean ± standard deviation (N = 5).
[b]Solid samples.

took no more than 30 min for both liquid and solid samples.

Analytical Characteristics of the Method

The standard additions calibration method was applied to three different types of wine and four different solid samples, the data obtained by plotting concentration (at five different levels) against peak area and following linear regression analysis being compared with those provided by 12% (v/v) ethanolic standard solutions. In all cases, two replicates for each concentration level were made. No significant differences were observed when comparing the slopes obtained, as shown in Table 2; in fact, when the paired *t*-test was applied to compare the slopes of the aqueous calibration and those obtained with the standard additions method for the different samples, p-values ranged between 0.058 and 0.76. Consequently, sample quantitation was carried out directly against aqueous-ethanolic standards.

Table 3 shows the analytical characteristics of the calibration graph used for quantitation purposes. The high correlation coefficient obtained demonstrated a high degree of correlation between peak area and concentration. The detection and quantitation limits were calculated using the signal-to-noise ratios of 3 and 10, respectively, and considering the slope of the calibration graph. The obtained values are shown in Table 3 for wines and solid samples. The repeatability of the proposed methods was demonstrated by repeated analyses, calculating the average relative standard deviation (RSD) for 10 successive aliquots of a fortified red wine and grape sample at a concentration level of five-fold the corresponding quantitation limit, being 9.6 and 7.4% (RSD) for liquid and solid sample, respectively.

Recovery and Real Samples

As no reference materials were available, recovery studies were carried out to check the accuracy of the proposed method by fortifying three different wines and four different solid samples at two concentration levels, as described earlier. The recoveries of famoxadone from spiked samples varied from 91.6 to 110.9%, as can be seen from Table 4.

Famoxadone in the different spiked samples was identified by comparing the retention time, identifying the target (T) and qualifier ions (Q), and comparing the qualifier-to-target ratios (Q/T%) of the peaks in both the sample and the standard solution. The T and Q abundances were determined by injecting the famoxadone standard under the same chromatograpic conditions, except in full scan

TABLE 4 Recovery of Famoxadone in Spiked Samples for the Optimized Procedure

Spike level (ng L^{-1})	Found level (ng L^{-1})[a]			Spike level (pg g^{-1})	Found level (pg g^{-1})[a]			
	White wine	Rosé wine	Red wine		Grape	Orange	Tomato	Pear
160	164 ± 1	158 ± 1	177 ± 1	300	277 ± 1	275 ± 2	275 ± 3	292 ± 3
330	349 ± 2	344 ± 2	361 ± 2	620	585 ± 3	572 ± 3	593 ± 4	614 ± 5

[a]Mean value ± standard deviation (N = 3).

mode. The Q/T percentage was determined by dividing the abundance of the selected qualifier ion by the target ion.

After identification of the peaks, the different samples were submitted to analysis and no famoxadone was detected above the detection limit.

CONCLUSIONS

The high concentration effect achieved by solid-phase microextraction allows a rapid and sensitive procedure for the determination of famoxadone in wine samples, including extraction, cleanup, and preconcentration in a single, straightforward step without the use of toxic organic solvents, minimizing as well waste generation. These aspects represent important advantages over other published analytical methods based on classical extraction methodologies. In addition, the use of a simple ultrasound probe, for leaching the fungicide from fruit and vegetable matrices, simplifies considerably sample manipulation, which is another relevant aspect of green analytical procedures. The analytical characteristics and the excellent recovery data prove the reliability of the procedure for wine, fruits, and vegetable samples.

ACKNOWLEDGMENTS

The authors are grateful to Comunidad Autónoma de la Región de Murcia (CARM, Fundación Séneca, Project 02993/PI/05) and to the Spanish Ministerio de Educación y Ciencia, MEC (Project CTQ2006-08037/BQU) for financial support. N. Aguinaga also acknowledges a fellowhip from CajaMurcia, Spain.

REFERENCES

1. Tomlin, C. D. S. *The Pesticide Manual;* 12th ed., British Crop Protection Council: Suffolk, U.K., 2000.
2. Commission Directive 2004/95/EC of 24 September 2004 amending Council Directive 90/642/EEC as regards the maximum residues levels of bifenthrin and famoxadone fixed therein. Off. J. Eur. Union, No. L301/42 September 2004.
3. OIV, Résidus de Pesticides, Limites Autorisées: Classement par Pays et par Pesticide, Office Internacional de la Vigne et du Vin, Paris, 1995.
4. Sannino, A.; Bandini, M. Determination of fludioxonil and famoxadone in processed fruits and vegetables by liquid chromatography/electrospray tandem mass spectrometry. *J. AOAC. Int.* **2005**, *88*, 1822–1826.
5. Lehotay, S. J.; de Kok, A.; Hiemstra, M.; van Bodegraven, P. Validation of a fast and easy method for the determination of residues from 229 pesticides in fruits and vegetables using gas and liquid chromatography and mass spectrometric detection. *J. AOAC. Int.* **2005**, *88*, 595–614.
6. de Melo Abreu, S.; Caboni, P.; Pirisi, F. M.; Cabras, P.; Alves, A.; Garau, V. L. Residues of the fungicide famoxadone in grapes and its fate during wine production. *Food Addit. Contam.* **2006**, *23*, 289–294.
7. de Melo Abreu, S.; Caboni, P.; Cabras, P.; Garau, V. L.; Alves, A. Validation and global uncertainty of a liquid chromatographic with diode array detection method for the screening of azoxystrobin, kresoxim-methyl, trifloxystrobin, famoxadone, pyraclostrobin and fenamidone in grapes and wine. *Anal. Chim. Acta* **2006**, *573–574*, 291–297.
8. de Melo Abreu, S.; Caboni, P.; Cabras, P.; Alves, A.; Garau, V. L. A comparison of a gas chromatographic with electron-capture detection and a gas chromatographic with mass spectrometric detection screening methods for the analysis of famoxadone in grapes and wines. *J. Chromatogr. A* **2006**, *1103*, 362–367.
9. Pizzutti, I. R.; de Kok, A.; Zanella, R.; Adaime, M. B.; Hiemstra, M.; Wickert, C.; Prestes, O. D. Method validation for the analysis of 169 pesticides in soya grain, without clean up, by liquid chromatography-tandem mass spectrometry using positive and negative electrospray ionization. *J. Chromatogr. A* **2007**, *1142*, 123–136.
10. Likas, D. T.; Tsiropoulos, N. G.; Miliadis, G. E. Rapid gas chromatographic method for the determination of famoxadone, trifloxystrobin and fenhexamid residues in tomato, grape and wine samples. *J. Chromatogr. A* **2007**, *1150*, 208–214.
11. Hiemstra, M.; de Kok, A. Comprehensive multi-residue method for the target analysis of pesticides in crops using liquid chromatography-tandem mass spectrometry, *J. Chromatogr. A* **2007**, *1154*, 3–25.
12. Mol, H. G. J.; Rooseboom, A.; van Dam, R.; Roding, M.; Arondeus, K.; Sunarto, S. Modification and re-validation of the ethyl acetate-based multi-residue method for pesticides in produce. *Anal. Bioanal. Chem.* **2007**, *389*, 1715–1754.
13. Pihlström, T.; Blomkvist, G.; Friman, P.; Pagard, U.; Österdahl, B. Analysis of pesticide residues in fruit and vegetables with ethyl acetate extraction using gas and liquid chromatography with tandem mass spectrometric detection. *Anal. Bioanal. Chem.* **2007**, *389*, 1773–1789.
14. Viñas, P.; Campillo, N.; Aguinaga, N.; Martínez-Castillo, N.; Hernández-Córdoba, M. Solid-phase microextraction for the gas chromatography mass spectrometric determination of oxazole fungicides in malt beverages. *Anal. Bioanal. Chem.* **2008**, *391*, 1425–1431.
15. Anastas, P. T. Green chemistry and the role of analytical methodology development. *Crit. Rev. Anal. Chem.* **1999**, *29*, 167–175.
16. Namiesnik, J. Green analytical chemistry—Some remarks. *J. Sep. Sci.* **2001**, *24*, 151–153.
17. He, Y. H.; Tang, L.; Wu, X.; Hou, X. D.; Lee, Y. I. Spectroscopy: The best way toward green analytical chemistry?. *Appl. Spectrosc. Rev.* **2007**, *42*, 119–138.
18. Armenta, S.; Garrigues, S.; de la Guardia, M. Green analytical chemistry. *Trends in Anal. Chem.* **2008**, *27*, 497–511.
19. Arthur, C. L.; Pawliszyn, J. Solid-phase microextraction with thermal desorption using fused silica optical fibers. *Anal. Chem.* **1990**, *62*, 2145–2148.
20. Chen, J.; Pawliszyn, J. *Solid Phase Microextraction, Theory and Practice*; Wiley-VCH: New York, 1997.
21. Pawliszyn, J. (Ed.), *Applications of Solid Phase Microextraction*; Royal Institute of Chemistry: Cambridge, 1999.
22. *Solid Phase Microextraction: Theory and Optimization of Conditions*: Bulletin 923A, Supelco, Bellefonte, PA, 1998.