A multi-component method to determine pesticides in surface water by liquid-chromatography tandem quadrupole mass spectrometry

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Abstract

Pesticide pollution of surface water is a major concern in many agricultural catchments The development of rapid and accurate methods for determining pesticide concentrations in water samples is, therefore, important. Here we describe a method for the simultaneous analysis of six pesticides (metaldehyde, quinmerac, carbetamide, metazachlor, propyzamide and pendimethalin) in natural waters by direct aqueous injection with liquid chromatography-tandem mass spectrometry. The method validation showed good linearity from 0.2 to 50.0 µg L^{-1} with correlation coefficients between 0.995 to 0.999. Method accuracy ranged from 84 to 100% and precision (RSD) from 4 to 15%. The limits of detection for the targeted pesticides ranged from 0.03 to 0.36 µg L^{-1}. No significant matrix effects on quantification were observed (*t* test). The method was tested on water samples from a small arable catchment in eastern England. Peak concentrations for the determinands ranged from 1 to 10 µg L^{-1}.

Key Words

Pesticide pollution, surface water, direct injection, LC-MS/MS

1. Introduction

Agriculture is generally considered to be the greatest contributor to pesticide pollution in many ground and surface waters, although in some catchments runoff from hard surfaces may be locally important [1]. Pesticide monitoring is a challenging task because a high number of active ingredients is typically used in agricultural catchments with mixed land use (presenting a wide range of physico-chemical properties) which are applied at different times of year and at different rates. This means that several different analytical methods may need to be employed on a single sample in order to detect the compounds of interest. The challenges of detecting target compounds can also be exacerbated by the episodic nature of pesticide transport from land to water (which tend to occur predominantly during storm events) [2]. Hence, high sampling frequencies may be required to capture representative temporal patterns, which results in significant analytical costs.

Most methods for pesticide analysis at the low concentrations generally encountered in natural water bodies require a sample pre-concentration step such as solid phase extraction (SPE), solid phase micro-extraction, or liquid-liquid extraction. Of these techniques, SPE is most commonly employed because it often provides good sample extraction, concentration and clean up[3][4]. However, there are several disadvantages with this technique including potential for low recoveries, long processing times per sample, the high cost of SPE cartridges and differing extraction procedures for different classes of pesticide owing to their polarities.

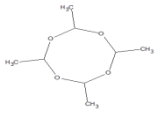
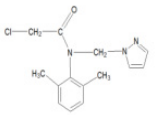
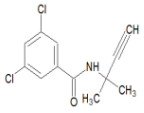
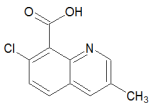
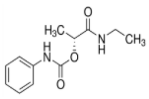
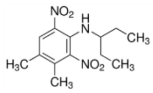
As an alternative, direct aqueous injection (DAI) methods have been developed for the analysis of a wide range of pesticides in various sample matrices. Applications include analysis of polar organophosphorus pesticides in fruit and vegetables [5][7] and analysis of pesticides in potable water[8][9]. The main advantages of DAI are easy sample preparation/ manipulation, low consumable costs and reduced analysis time allowing high sample throughput as well as low limits of detection.

In this paper, we describe a DAI multi-component method for the determination of six pesticides by LC-MS/MS in environmental waters. The specific requirements of the method were to be accurate and rapid so as to allow the efficient processing of a large number of samples. The pesticides analysed were metaldehyde, quinmerac, metazachlor, carbetamide, propyzamide and pendimethalin. Molecular structures and relevant physico-chemical properties are listed in Table 1. With the exception of pendimethalin, all the compounds examined have organic carbon-water partition coefficient (K_{oc}) values less than 217 L kg^{-1},

85 which suggests that they will be moderately mobile in soil and, hence, prone to leaching
86 losses. All six pesticides are widely used in arable agriculture in Europe and have been
87 previously detected at concentrations of concern in UK water bodies [2][10]. Metaldehdye is
88 a particular problem for the UK water industry and has been responsible for the highest
89 number of compliance failures in recent years [10][11]. It is a selective molluscicide which is
90 widely used to control slugs and snails in several crops. It is only moderately mobile (K_{oc} =
91 240 L kg^{-1}) and has been observed to degrade in water-sediment interface with a median
92 dissipation time (DT_{50}) of 12.2 days (Table 1) which should, in principle reduce the risk of
93 leaching loss from soil.
94 Quinmerac is used to control *Galium aparine*, *Veronica* spp and other broad leaved weeds in
95 cereals, oil seed rape and sugar beet. Carbetamide and propyzamide are herbicides used to
96 control black grass infestations predominantly in oil seed rape [12]. Metazacahlor and
97 pendimethalin are also herbicides used to control grass and broad-leaved weeds in a range of
98 crops including oil seed rape and Brussel sprouts [12]. Pendimethalin is not expected to be
99 particulary mobile and was included to provide a contrast to the other more mobile
100 compounds.
101 There are few published papers that report on the analysis of more than one of our target
102 pesticides. In general, these protocols only included 2 or 3 pesticides at the most with fruits
103 and vegetables being the studied matrices. Analysis in food stuffs requires an extraction step
104 before any determination can take place. A popular method is QuEChERS which includes
105 SPE followed by LC-MS/MS. Pesticides detected by this method include metazachlor,
106 pendimethalin and quinmerac [13][14][15]. Others used homogenisation followed by
107 evaporation or supercritical fluid extraction as the extraction step followed by GC-MS or GC-
108 NPD (Nitrogen, Phosphorus Detection). Pesticides detected following these methods included
109 carbetamide, propyzamide and pendimethalin [1][15. Other protocols dealt with several of
110 our target pesticides in water samples, namely carbetamide, metazachlor, propyzamide [14]
111 metazachlor and pendimethalin [15]. These protocols involved SPE followed by LC-MS and
112 GC-MS retraspectively, although the method by Irace-Guigand (2004) required additional
113 UV-DAD detection.
114 Of the six target pestices, metaldehyde appears to be one of the more difficult compounds to
115 detect in complex samples containing several analytes. To the best of our knowledge, no
116 method has been previously reported for the combined rapid determination of these particular
117 six pesticides with minimal sample preparation approach in environmental water samples.

The method improves upon existing knowledge in order to produce a robust value analytical tool in which minimal sample preparation is needed to monitor pesticide concentrations from agricultural runoff.

Table 1. Physico-chemical properties for the pesticides considered in this method.

Pesticide	Type	Molecular mass (gmol^{-1})	Chemical structure	Chemical formula	DT_{50} (days)[1]			*Koc* (L kg^{-1})[2]	Log K_{ow}[3]	Solubility (mgL^{-1})[4]	pKa
					Soil	Water-sediment	Water				
Metaldehyde	Molluscicide	176.21		$C_8H_{16}O_4$	5.1	12.2	11.5	240	0.12	188	n/a
Metazachlor		277.75		$C_{14}H_{16}ClN_3O$	8.6	20.6	216	54	0.03	450	n/a
Propyzamide		256.13		$C_{12}H_8Cl_2NO$	47	94	21	840	0.002	9	n/a
Quinmerac	Herbicide	221.6		$C_{11}H_8ClNO_2$	30	179.4	88.7	86	0.039	10700	4.31
Carbetamide		236.27		$C_{12}H_{16}N_2O_3$	12.4	55.5	9.1	89	1.78	3270	11.3
Pendimethalin		281.21		$C_{13}H_{19}N_3O_4$	90	16	4	17581	5.2	0.33	2.8

[1]DT_{50} – Median dissipation time in different test systems; [2]K_{oc} – organic carbon-water partition coefficient (L kg^{-1}); [3]Log K_{ow} – octanol-water partition coefficient; [4]Solubility in water (mg L^{-1}) [16]

2. Experimental

2.1. Chemicals and reagents

Pesticide standards were purchased from QMX laboratories (UK), methanol (HPLC grade) and acetic acid (HPLC grade) were obtained from Sigma-Aldrich (UK). Ultra pure water was produced by PURELAB® ultra, Elga.

2.2. Standards and stock solutions

Pesticide stock solutions (100 µg L^{-1}) were prepared by dissolving the neat pesticides in methanol. Working standards were prepared by diluting with ultra pure water with concentrations of 0.2, 0.5, 1.0, 2.0, 5.0, 8.0 and 10.0 µg L^{-1} for each pesticide. All standards were stored at 4 °C for a maximum of one month.

2.3. Instrumentation

All analyses were performed with a Waters Alliance 2695 liquid-chromatography system coupled to a Quattro premier XE tandem quadrupole. A Kinetex C18 column (5µm 150 × 2.1 mm, Phenomenex, UK) thermostated at 60 °C was used for chromatographic separation. The flow rate was 0.3 mL min^{-1} and the injection volume was 50 µL. The mobile phase consisted of ultra-pure water with 0.1% acetic acid (A) and methanol with 0.1% acetic acid (B). The elution started at 10% B and was linearly increased to 98% over 12 min, then maintained for 3 min before returning to the intital composition. The total time of analysis per sample was 18 min.

Operating conditions of the mass spectrometer were optimized by infusion of each individual pesticide at a concentration of 1 mg L^{-1} in a solution of 70% A and 30% B. Electrospray ionization (ESI) was performed in positive mode. The mass spectrometer was operated under multiple reaction monitoring (MRM) with two reactions monitored for each analyte (Table 2), with the exception of metaldehyde, which forms a Na^+ adduct and its fragmentation $[M+Na]^+$ showed a reaction whose precursor and fragment ions were *m/z* 198.9 and *m/z* 66.9, respectively. The UK Environment Agency recommends this reaction for quantitative purposes [12].

153

154 **Table 2.** SRM transitions used for target compounds.

Analytes	1st transition – quantification				2nd transition – confirmation				Retention Time (min)
	Percursor ion *(m/z)*	Product ion *(m/z)*	cone	collision	Percursor ion *(m/z)*	Product ion *(m/z)*	cone	collision	
Metaldehyde	198.9	66.9	25	12	-	-	-	-	5.69
Quinmerac	222.3	204.3	30	25	222.3	176.3	30	25	6.57
Carbetamide	237.1	191.9	15	10	237.1	117.9	15	8	7.85
Metazachlor	278.1	133.8	15	15	278.1	209.9	15	15	9.43
Propyzamide	256.0	189.9	15	15	256.0	172.8	15	15	10.37
Pendimethalin	282.1	212.0	25	10	282.1	193.9	25	25	12.59

155

156 ## 2.4. Sample collection and Analysis

157 The method was tested on samples collected from a monitoring study in a small headwater
158 stream at Hope farm in Knapwell, Cambridgeshire, UK (Figure 1). The stream drains a low
159 relief catchment (elevation range 41-78 m above mean sea level) of approximately 3.9 km^2,
160 which is dominated by arable land.

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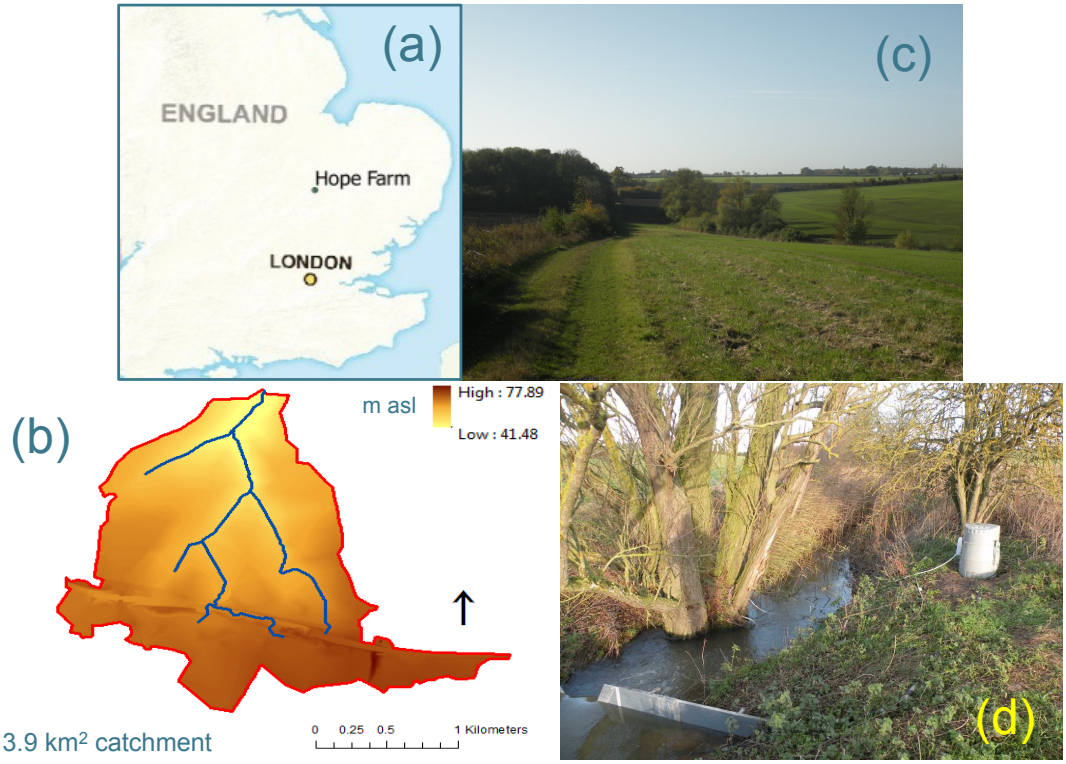

Figure 1. (a) Location of study catchment ; (b) Catchment boundary, stream network and digital elevation model; (c) Catchement relief looking upstream ; (d) Automatic water sampler and v-notch weir installed at the catchment outlet.

The predominant crop rotation is wheat-oil seed rape and most of the soils belong to the Hanslope Soil Association, which is a typically under-drained. Stream discharge is low (but usually perennial) in summer, which suggests minimal baseflow contributions and is flashy in winter with flows often exceeding 150 L s^{-1} during storm events. The stream was monitored for five months between August and December 2014. Discharge was measured with a 90° v-notch weir, equipped with an ISCO AV2150 water level and a velocity sensor. Samples were collected with an ISCO 6712 automatic water sampler at constant sampling intervals of 8 h, with a sample volume of 250 mL. Sample bottles were changed approximately every 7 days and replaced with fresh bottles which had been thoroughly pre-cleaned before each change-over using water and methanol. Pesticide concentrations in field bottle blanks, prepared with ultra pure water, were always less than the limits of detection (LOD) and often not detectable.

180 Samples were refrigerated immediately upon arrival to the laboratory (typically less than 2 h
181 after sample collection) and filtered through 0.2 µm syringe-mounted disc filters (Milipore
182 Millex^{TM}, Fisher Scientific, UK) within 24 h of collection.
183
184 **2.5. Sample injection and data processing**
185 Sample runs consisted of eight working standards, followed by five unknown samples with
186 solvent blanks and continuing calibration checks (5 µg L^{-1}) in between. Runs never exceeded
187 80 determinations including analytical standards, blanks, calibration checks and samples.
188 Peak areas of target pesticides were obtained with Quantlynx v.4.1. Weighted (1/x) linear
189 least-squares regression curves were fitted to the observations and not forced through the
190 origin.

3. Results and discussion

Figure 2 shows an example total ion chromatogram (TIC) for the six pesticides in positive ion mode analysed over 18 min from a 10 µg L^{-1} standard of each pesticide in ultra-pure water.

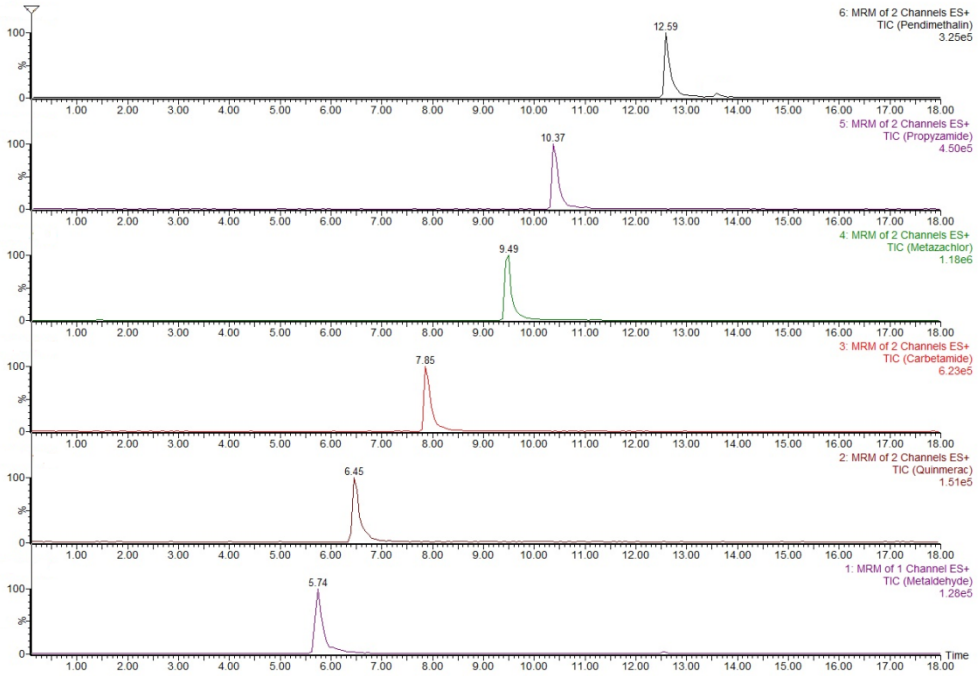

Figure 2. Example chromatograms of six pesticides at 10 µg L^{-1} in ultra-pure water by direct aqueous injection

3.1. Optimisation of the MS/MS parameters.

For the MS operation, only ESI in positive mode was evaluated for the determination of the six pesticides. The optimum cone voltage and collision energies are reported in Table 2. Good peak shape and suitable signal-to-noise ratios were obtained with a dwell time of 0.25 s.

205

206 3.2. Optimisation of the LC conditions

207 Optimisation of mobile phase composition and elution gradient was very important to achieve
208 good separation, high sensitivity, good ionization and resolution, particularly for trace
209 analysis. Results (see example in Figure 2) showed that higher sensitivity and good peak
210 shape could be achieved with 0.1% acetic acid in both eluents. The gradient was optimised to
211 obtain improved resolution and shorter analysis time.

212

213 3.3. Validation procedures

214 The analytical method was validated according to the performance criteria established by ICH
215 guidelines [20]. The validation parameters evaluated were linearity, accuracy, precision,
216 LODs, limits of quantification (LOQs) and matrix effect.

217

218 3.3.1. Linearity

219 Method linearity was evaluated by analysing the response for the seven concentration levels
220 prepared from the working standard solution described in Section 2.2 (0.2, 0.5, 1.0, 2.0, 5.0,
221 8.0 and 10 μg L^{-1}). Linear regression analysis of calibration data was performed by plotting
222 the peak areas of the quantitative ion versus the corresponding standard concentrations. Good
223 linearity was achieved with coefficients of determination between 0.994 to 0.999 (Table 3).
224 The method provided acceptable precision, accuracy and linearity over the range of 0.2 to
225 10.0 μg L^{-1}.

226

227 3.3.2. Accuracy and Precision

228 Inter-day and intra-day accuracy and precision (RSD) were assessed. Inter-day comparisons
229 express within laboratory across-day variations while intra-day comparisons express within
230 laboratory within-day variations. The intra-day test consisted of five consecutive analyses,
231 while the inter-day variations were assessed on different days for a 5 μg L^{-1} standard. Intra-
232 day precision (RSD) varied from 17.4% (pendimethalin) to 3.1% (metaldehyde), while the
233 inter-day precision varied from 11.4% to 24.3% (pendimethalin). Intra and inter-day accuracy
234 values were close to 100%..

235

3.3.3. Detection and Quantification limits

Limits of detection (Equation 1) and quantification (Equation 2) were calculated using the standard deviation of the response and the slope, as described by ICH validation of analytical procedures [17]:

$$LOD = 3.3 \times \frac{\sigma_R}{m} \quad (1)$$

$$LOQ = 10 \times \frac{\sigma_R}{m} \quad (2)$$

where σ_R is the standard deviation of the response and m is the slope of the calibration curve. The standard deviation of the response was calculated from the standard deviation of y-intercepts in the regression lines fitted to the data. Limits of detection and quantification ranged from 0.05 to 0.3 µg L^{-1} and 0.2 to 1.0 µg L^{-1}, respectively (Table 3).

Table 3. Calibration curves, coefficient of determination (r^2), limit of detection (µg L^{-1}) and limit of quantification (µg L^{-1}).

Analyte	Calibration curve		r^2	*LOD* (µg L^{-1})	*LOQ* (µg L^{-1})
	Slope	Intercept			
Metaldehyde	2219.7 ± 15.3	168.9	0.9998	0.09	0.3
Quinmerac	2489.1 ± 17.3	45.9	0.9998	0.08	0.3
Carbetamide	5524.8 ± 33.9	289.9	0.9998	0.09	0.3
Metazachlor	11302 ± 47.1	584.1	0.9999	0.09	0.3
Propyzamide	4544.5 ± 72.9	628.3	0.9987	0.05	0.2
Pendimethalin	4636.1 ±154.8	223.7	0.9944	0.3	1.0

252 **3.3.5. Matrix effects**

253 To assess the matrix effect the slopes of the calibration curves for ultra-pure water (1) and
254 stream water (2) were compared using a Student's *t* test (95%). The calculated value of *t*, $t_{cal,}$
255 is defined by :

256 $$t_{cal} = \frac{|b_1 - b_2|}{\sqrt{S_{b1}^2 - S_{b2}^2}} \quad (3)$$

257

258 where *b* is the slope of the calibration line and S_b is the deviation of the slope.
259 The null hypothesis (there is no significant difference between the two calibration lines) was
260 rejected when t_{cal} was greater than the theoretical value t_{theo} 2.306 (p = 0.05). Values of t_{cal}
261 ranged from 0.5 to 1.3 for the different pesticides so that no significant matrix effect was
262 found. After approximately 80 samples, the mass spectrometer sensitivity was observed to
263 gradually decrease over time, probably because of deposition and accumulation of salts on
264 the cone surface. Analytical controls were used to identify when this problem occurred.
265 When sensitivity reduced by 15%, the run was interrupted and maintenance was carried out.
266

267 **3.3.6. Blanks**

268 Ultra-pure water and methanol were used as solvent blanks during method validation and
269 field sample analysis. No carryover or system peaks were found. Additionally, target analytes
270 were undetected in field blanks.
271

272 ## 4. Applications of the method

273

274 Data for stream discharge and stream water concentrations of the six pesticides analysed in
275 water samples collected from the study stream are shown in Figure 3, between August and
276 December 2014. Daily rainfall data are also displayed. Pesticide concentrations tended to
277 increase sharply during rainfall events with the highest concentrations typically occurring in
278 the first storm event after application. This is consistent with observations reported elsewhere
279 from catchments with under-drained heavy clay soils [2]. The highest concentrations were
280 observed for metaldehyde over an event in late August which triggered a relatively low
281 hydrograph peak. For quinmerac, which is applied later than metaldehyde, the first peak
282 concentrations occur in an event around the 13th of October. Metaldehyde concentrations
283 also increase in this event but with lower peaks. Other notable increases in concentration

284 occur for carbetamide in a series of hydrographs starting on the 14th of November and for
285 propyzamide in the event of the 11th of December, which also resulted in increases in
286 pendimethalin concentrations. Both propyzamide and carbetamide tend to be applied a little
287 later than some of the other herbicides due to the specific requirements of weed control
288 timing for blackgrass on oilseed rape. Concentrations of metazachlor were consistently low,
289 peaking at 0.37 μg L^{-1} on the 29th of October. The magnitude of peak concentrations will
290 reflect a combination of factors including usage rate and the physico-chemical properties of
291 the compound. Compounds with high values of K_{OC} (such as pendimethalin) will tend to
292 bind to soil solids and hence have a lower propensity to leach than compounds which are
293 more hydrophilic (such as metazachlor, quinmerac and carbetamide). For most compounds,
294 peak concentrations were observed at the same time as the hydrograph peak or slightly after
295 the peak flow (i.e. on the falling limb of the hydrograph), although apparent delays in the
296 appearance of peak pesticide concentration may be artefacts of the relatively low sampling
297 frequency adopted (8 h).
298
299 Concentrations for all the pesticide compounds examined tended to decrease in hydrograph
300 recession periods in parallel with falling flow. Again, this is consistent with previous
301 observations of pesticide behaviour during storm events [2]. Clearly, peak concentrations of
302 all six pesticides were periodically greater than the maximum admissible concentration for
303 drinking water. Although this stream is not directly abstracted for water supply, it does feed
304 into the River Great Ouse system, which is used for municipal abstraction downstream. The
305 important point to note for the purposes of this paper is that the temporal pattern and
306 magnitude of observed concentrations is consistent with expectations under the
307 environmental conditions experienced over the study period.
308

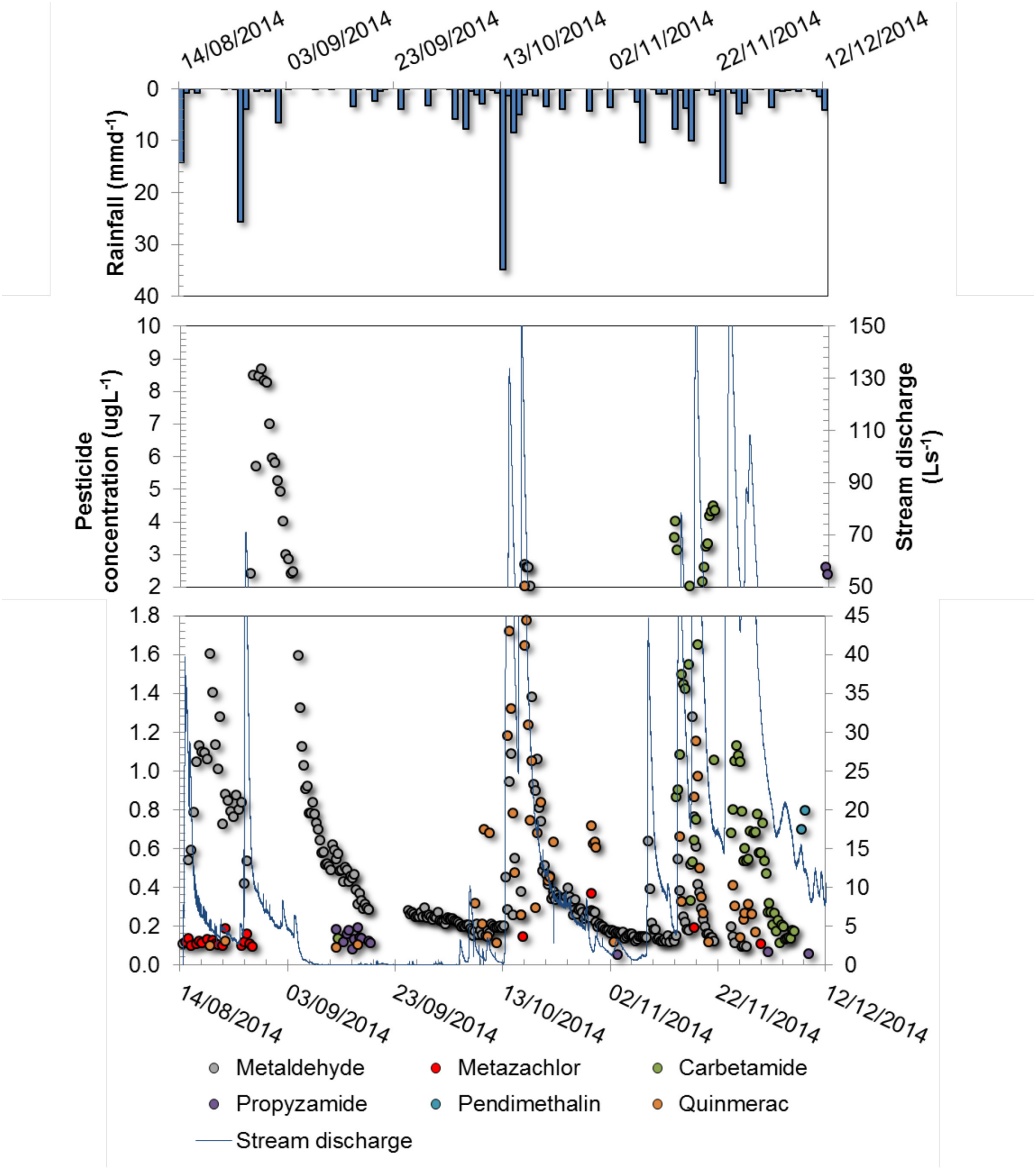

Figure 3. Rainfall (top panel), stream discharge (right axis) and pesticide concentrations (left axis) in the Hope Farm stream from August to December 2014.

5. Conclusions

An LC-MS/MS method for the simultaneous multi-residue analysis of six pesticide active ingredients in natural waters is presented in this paper. This DAI method is rapid and accurate and can be used for quantification and confirmation of metaldehyde, quinmerac, carbetamide, metazachlor, propyzamide and pendimethalin in water samples from ground and surface waters. The omission of a concentration and clean-up step means that sample processing is fast and straightforward. The method showed a good range of linearity (R^2 ranged from 0.995 to 0.999), accuracy (84 to 100%) and RSD precision (4 to 15%) and there was negligible apparent matrix effect compared to the same pesticides in ultra-pure water.

The LOQs obtained ranged from 0.2 to 1.0 µg L^{-1}. This is acceptable for detecting concentrations in natural water samples from many agricultural catchments where pesticide concentrations are high (edge of field concentrations often exceed 100 µg L^{-1}) but would be of limited value in assessing DWD compliance. The use of a multi-residue method with rapid and simple sample preparation reduces analysis time and improves laboratory efficiency. The temporal pattern and magnitude of concentrations in samples from a headwater arable stream were consistent with expectations for the environmental conditions experienced over the study period, suggesting that the method can yield a realistic description of pesticide exposure in natural waters.

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343

344 6. References

345

346 [1] J. Tournebize, E. Passeport, C. Chaumont, C. Fesneau, a. Guenne, and B. Vincent,
347 "Pesticide de-contamination of surface waters as a wetland ecosystem service in agricultural
348 landscapes," Ecol. Eng., vol. 56, pp. 51–59, 2013.

349 [2] A. Tediosi, M. J. Whelan, K. R. Rushton, T. R. E. Thompson, C. Gandolfi, and S. P.
350 Pullan, "Measurement and conceptual modelling of herbicide transport to field drains in a
351 heavy clay soil with implications for catchment-scale water quality management.," Sci. Total
352 Environ., vol. 438, pp. 103–12, Nov. 2012.

353 [3] C. Li, Y.-L. Wu, T. Yang, and Y. Zhang, "Determination of Metaldehyde in Water by
354 SPE and UPLC–MS–MS," Chromatographia, vol. 72, no. 9–10, pp. 987–991, 2010.

355 [4] M. J. Whelan, R. Van Egmond, I. Guymer, J. O. Lacoursiere, L. M. B. Vought, C.
356 Finnegan, K. K. Fox, C. Sparham, S. O'Connor, M. Vaughan, and J. M. Pearson, "The
357 behaviour of linear alkyl benzene sulphonate under direct discharge conditions in Vientiane,
358 Lao PDR," Water Res., vol. 41, no. 20, pp. 4730–4740, 2007.

359 [5] J. Fenoll, P. Hellín, C. M. Martínez, M. Miguel, and P. Flores, "Multiresidue method
360 for analysis of pesticides in pepper and tomato by gas chromatography with nitrogen-
361 phosphorus detection," Food Chem., vol. 105, no. 2, pp. 711–719, 2007.

362 [6] R. Romero-González, A. G. Frenich, and J. L. M. Vidal, "Multiresidue method for
363 fast determination of pesticides in fruit juices by ultra performance liquid chromatography
364 coupled to tandem mass spectrometry," Talanta, vol. 76, no. 1, pp. 211–225, 2008.

365 [7] A. Stachniuk and E. Fornal, "Analytical considerations on the use of a fruit-specific
366 and representative matrix in pesticide residue analysis by LC-ESI-MS/MS," Cent. Eur. J.
367 Chem., vol. 11, no. 7, pp. 1112–1131, 2013.

368 [8] M. T. Wan, J. Kuo, and J. Pasternak, "Residues of endosulfan and other selected
369 organochlorine pesticides in farm areas of the Lower Fraser Valley, British Columbia,
370 Canada.," J. Environ. Qual., vol. 34, no. 4, pp. 1186–1193, 2005.

371 [9] C. Hao, D. Morse, X. Zhao, and L. Sui, “Liquid chromatography/tandem mass
372 spectrometry analysis of neonicotinoids in environmental water,” Rapid Commun. Mass
373 Spectrom., vol. 29, no. 23, pp. 2225–2232, 2015.

374 [10] P. Kay and R. Grayson, “Using water industry data to assess the metaldehyde
375 pollution problem,” Water Environ. J., vol. 28, no. 3, pp. 410–417, 2014.

376 [11] Ea, “Environment Agency The determination of metaldehyde in waters using
377 chromatography with mass spectrometric detection (2009),” 2009.

378 [12] Mamy, L., Barriuso, E., & Gabrielle, B. (2005). Environmental fate of herbicides
379 trifluralin, metazachlor, metamitron and sulcotrione compared with that of glyphosate, a
380 substitute broad spectrum herbicide for different glyphosate-resistant crops. Pest
381 Management Science, 61(9), 905–916.

382 [13] C. Crescenzi, A. Di Corcia, E. Guerriero, and R. Samperi, “Development of a
383 multiresidue method for analyzing pesticide traces in water based on solid-phase extraction
384 and electrospray liquid chromatography mass spectrometry,” Environ. Sci. Technol., vol. 31,
385 no. 2, pp. 479–488, 1997.

386 [14] J. Quintana, I. Martí, and F. Ventura, “Monitoring of pesticides in drinking and
387 related waters in NE Spain with a multiresidue SPE-GC-MS method including an estimation
388 of the uncertainty of the analytical results,” J. Chromatogr. A, vol. 938, no. 1–2, pp. 3–13,
389 2001.

390 [15] S. Irace-Guigand, J. J. Aaron, P. Scribe, and D. Barcelo, “A comparison of the
391 environmental impact of pesticide multiresidues and their occurrence in river waters surveyed
392 by liquid chromatography coupled in tandem with UV diode array detection and mass
393 spectrometry,” Chemosphere, vol. 55, no. 7, pp. 973–981, 2004.

394 [16] University of Hertfordshire, “Pesticide Properties Database”, 2009

395 [17] ICH Harmonised Tripartite Guideline – “Validation of Analytical Procedures: Text and
396 Methodology”, 2005

397