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. In the EU, water companies are required to supply water to their customers with concentrations of individual pesticides no higher than 0.1 µg L^{-1}. However, concentrations in untreated water frequently exceed this limit for a number of different pesticides leading to occasional compliance challenges. 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

The use of pesticides is a necessary part of modern agriculture in order to keep up with increasing demands for food, fibre and energy from the growing global population. Nevertheless, pesticides can be transported from land to ground and surface waters by spray drift, leaching and surface runoff, where they can pose problems for aquatic ecosystems and for the quality of abstracted drinking water [1].

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 [2]. In the European Union (EU), the Drinking Water Directive (DWD: 98/83/EC) sets a limit for the concentration of individual pesticide active ingredients in drinking water at 0.1 µg L^{-1} and a limit of 0.5 µg L^{-1} for the detection of multiple pesticides[1]. To better understand the compliance risks, water companies and environmental regulatory agencies need to monitor abstracted water bodies, as well as treated water being supplied to consumers. Pesticide monitoring is a challenging task because a high number of active ingredients is typically used in 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) [3]. 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[4][5]. 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 [6] and analysis of

86 pesticides in potable water [7]. The main advantages of DAI are easy sample preparation/

87 manipulation, low consumable costs and reduced analysis time allowing high sample

88 throughput as well as low limits of detection (< 0.1 µg L^{-1}).

89 In this paper, we describe a DAI multi-component method for the determination of six

90 pesticides by LC-MS/MS in environmental waters. The specific requirements of the method

91 were to be accurate and rapid so as to allow the efficient processing of a large number of

92 samples. The pesticides analysed were metaldehyde, quinmerac, metazachlor, carbetamide,

93 propyzamide and pendimethalin. Molecular structures and relevant physico-chemical

94 properties are listed in Table 1. With the exception of pendimethalin, all the compounds

95 examined have organic carbon-water partition coefficient (K_{oc}) values less than 217 L kg^{-1},

96 which suggests that they will be moderately mobile in soil and, hence, prone to leaching

97 losses. All six pesticides are widely used in arable agriculture in Europe and have been

98 previously detected at concentrations of concern in UK water bodies [3][8]. Metaldehdye is a

99 particular problem for the UK water industry and has been responsible for the highest number

100 of compliance failures in recent years [9][10]. It is a selective molluscicide which is widely

101 used to control slugs and snails in several crops. It is only moderately mobile ($K_{oc} = 240$ L kg^{-1}

102) and has been observed to degrade in water-sediment interface with a median dissipation

103 time (DT_{50}) of 12.2 days (Table 1) which should, in principle reduce the risk of leaching loss

104 from soil. Nevertheless, it has a very stable structure which means that it is difficult to

105 remove in drinking water treatment (typically employing sand filtration, granulated activated

106 carbon filtration, ozonation and or chlorination) [9].

107 Quinmerac is used to control *Galium aparine*, *Veronica* spp and other broad leaved weeds in

108 cereals, oil seed rape and sugar beet. Carbetamide and propyzamide are herbicides used to

109 control black grass infestations predominantly in oil seed rape [11]. Metazacahlor and

110 pendimethalin are also herbicides used to control grass and broad-leaved weeds in a range of

111 crops including oil seed rape and Brussel sprouts [11]. Pendimethalin is not expected to be

112 particulary mobile and was included to provide a contrast to the other more mobile

113 compounds.

114 There are few published papers that report on the analysis of more than one of our target

115 pesticides. In general, these protocols only included 2 or 3 pesticides at the most with fruits

116 and vegetables being the studied matrices. Analysis in food stuffs requires an extraction step

117 before any determination can take place. A popular method is QuEChERS which includes

118 SPE followed by LC-MS/MS. Pesticides detected by this method include metazachlor,

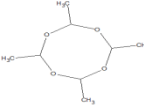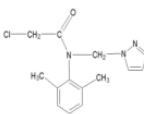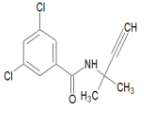119 pendimethalin and quinmerac [12], [13]. Others used homogenisation followed by
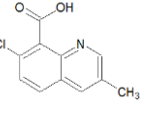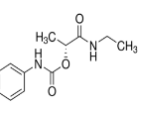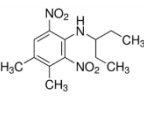
120 evaporation or supercritical fluid extraction as the extraction step followed by GC-MS or GC-
121 NPD (Nitrogen, Phosphorus Detection). Pesticides detected following these methods included
122 carbetamide, propyzamide and pendimethalin [14], [15]. Other protocols dealt with several of
123 our target pesticides in water samples, namely carbetamide, metazachlor, propyzamide [16]
124 metazachlor and pendimethalin [17]. These protocols involved SPE followed by LC-MS and
125 GC-MS retraspectively, although the method by Irace-Guigand (2004) required additional
126 UV-DAD detection.

127

128 Of the six target pestices, metaldehyde appears to be one of the more difficult compounds to
129 detect in complex samples containing several analytes. In fact, only one paper has reported
130 the analysis of metaldehyde in a multiresidue method alongside any of our target pesticides
131 (i.e. propyzamide) [18]. This approach used SPE prior to GC-MS for food extracts. To the
132 best of our knowledge, no method has been previously reported for the combined rapid
133 determination of these particular six pesticides with minimal sample preparation approach in
134 environmental water samples.

135

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

Pesticide	Type	Molecular mass (g/mol)	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

138 [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}) [19]

140

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 [18].

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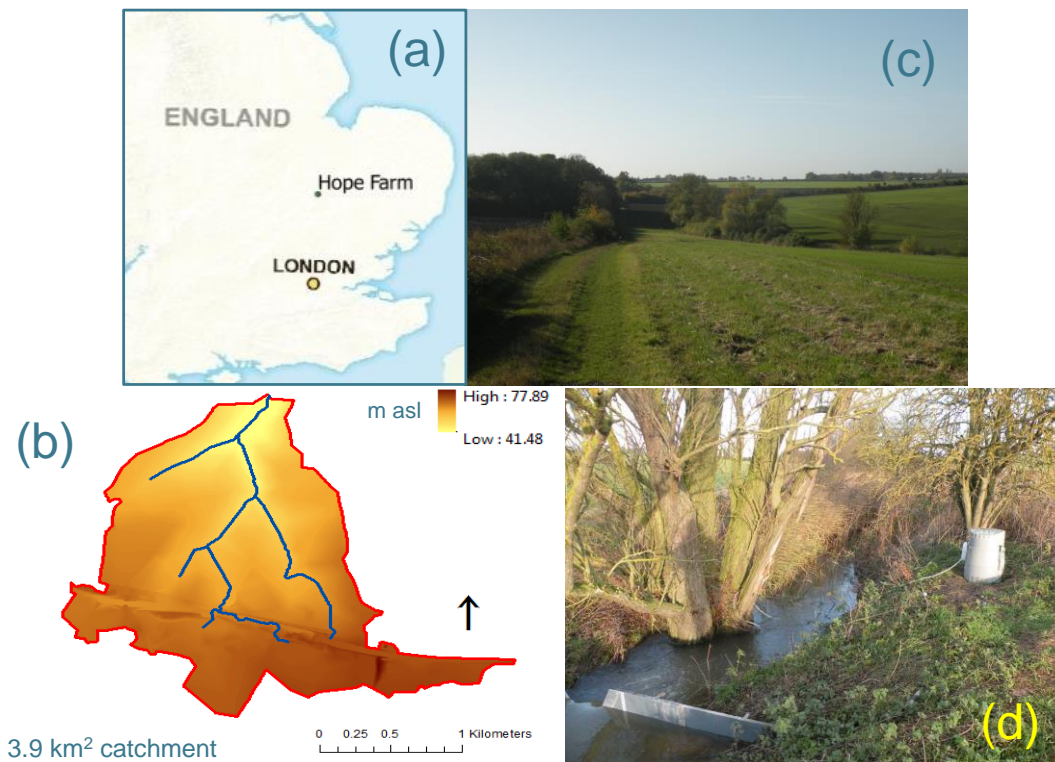169   **Table 2.** SRM transitions used for target compounds.

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

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2.4. Sample collection and Analysis

172   The method was tested on samples collected from a monitoring study in a small headwater

173   stream at Hope farm in Knapwell, Cambridgeshire, UK (Figure 1). The stream drains a low

174   relief catchment (elevation range 41-78 m above mean sea level) of approximately 3.9 km^2,

175   which is dominated by arable land.

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

183

184 The predominant crop rotation is wheat-oil seed rape and most of the soils belong to the

185 Hanslope Soil Association, which is a typically under-drained. Stream discharge is low (but

186 usually perennial) in summer, which suggests minimal baseflow contributions and is flashy in

187 winter with flows often exceeding 150 L s^{-1} during storm events. The stream was monitored

188 for five months between August 2014 and December 2015. Discharge was measured with a

189 90° v-notch weir, equipped with an ISCO AV2150 water level and a velocity sensor. Samples

190 were collected with an ISCO 6712 automatic water sampler at constant sampling intervals of

191 8 h, with a sample volume of 250 mL. Sample bottles were changed approximately every 7

192 days and replaced with fresh bottles which had been thoroughly pre-cleaned before each

193 change-over using water and methanol. Pesticide concentrations in field bottle blanks,

194 prepared with ultra pure water, were always less than the limits of detection (LOD) and often

195 not detectable. Samples were refrigerated immediately upon arrival to the laboratory

196   (typically less than 2 h after sample collection) and filtered through 0.2 µm syringe-mounted

197   disc filters (Milipore Millex[TM], Fisher Scientific, UK) within 24 h of collection.

198

199   **2.5. Sample injection and data processing**

200   Sample runs consisted of eight working standards, followed by five unknown samples with

201   solvent blanks and continuing calibration checks (5 µg L^{-1}) in between. Runs never exceeded

202   80 determinations including analytical standards, blanks, calibration checks and samples.

203   Peak areas of target pesticides were obtained with Quantlynx v.4.1. Weighted (1/x) linear

204   least-squares regression curves were fitted to the observations and not forced through the
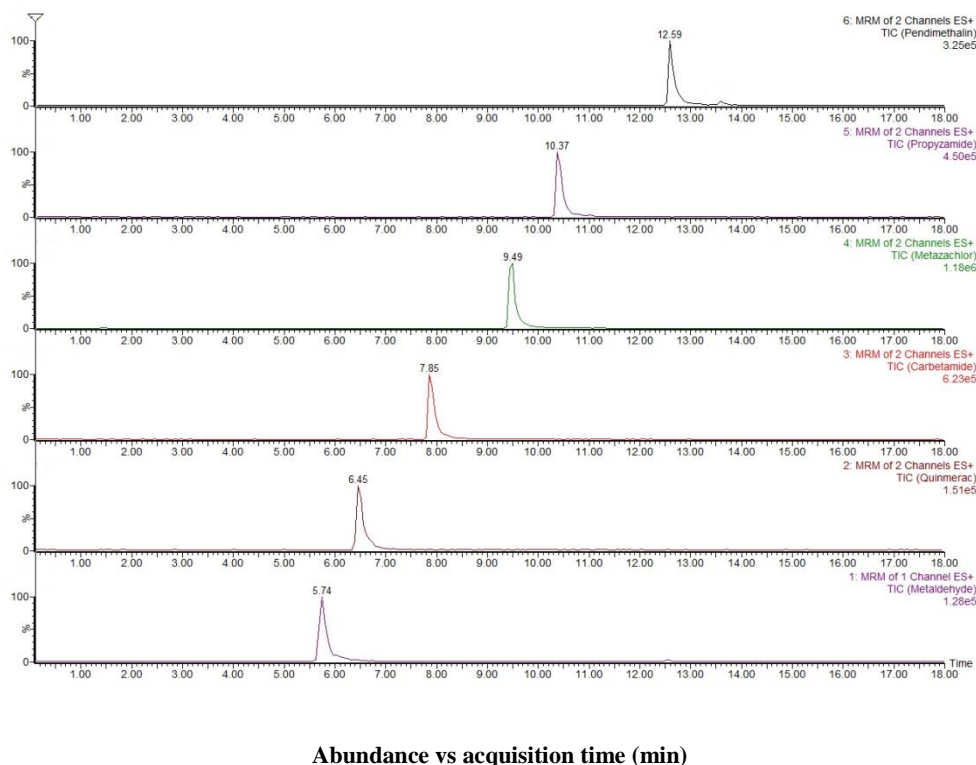
205   origin.

206

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.

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Abundance vs acquisition time (min)

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

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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.

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220

3.2. Optimisation of the LC conditions

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

227

3.3. Validation procedures

The analytical method was validated according to the performance criteria established by ICH guidelines [19]. The validation parameters evaluated were linearity, accuracy, precision, LODs, limits of quantification (LOQs) and matrix effect.

232

3.3.1. Linearity

Method linearity was evaluated by analysing the response for the seven concentration levels prepared from the working standard solution described in Section 2.2 (0.2, 0.5, 1.0, 2.0, 5.0, 8.0 and 10 µg L^{-1}). Linear regression analysis of calibration data was performed by plotting the peak areas of the quantitative ion versus the corresponding standard concentrations. Good linearity was achieved with coefficients of determination between 0.994 to 0.999 (Table 3). The method provided acceptable precision, accuracy and linearity over the range of 0.2 to 50.0 µg L^{-1}.

241

3.3.2. Accuracy and Precision

Inter-day and intra-day accuracy and precision (RSD) were assessed. Inter-day comparisons express within laboratory across-day variations while intra-day comparisons express within laboratory within-day variations. The intra-day test consisted of five consecutive analyses, while the inter-day variations were assessed on different days for a 5 µg L^{-1} standard. Intra-day precision (RSD) varied from 17.4% (pendimethalin) to 3.1% (metaldehyde), while the inter-day precision varied from 11.4% to 24.3% (pendimethalin). Intra and inter-day accuracy values were close to 100% (Table S1).

250

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:

$$LOD = 3.3 \times \frac{\sigma_R}{m} \tag{1}$$

$$LOQ = 10 \times \frac{\sigma_R}{m} \tag{2}$$

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

3.3.5. Matrix effects

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

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

where *b* is the slope of the calibration line and S_b is the deviation of the slope.

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

3.3.6. Blanks

Ultra-pure water and methanol were used as solvent blanks during method validation and field sample analysis. No carryover or system peaks were found. Additionally, target analytes were undetected in field blanks.
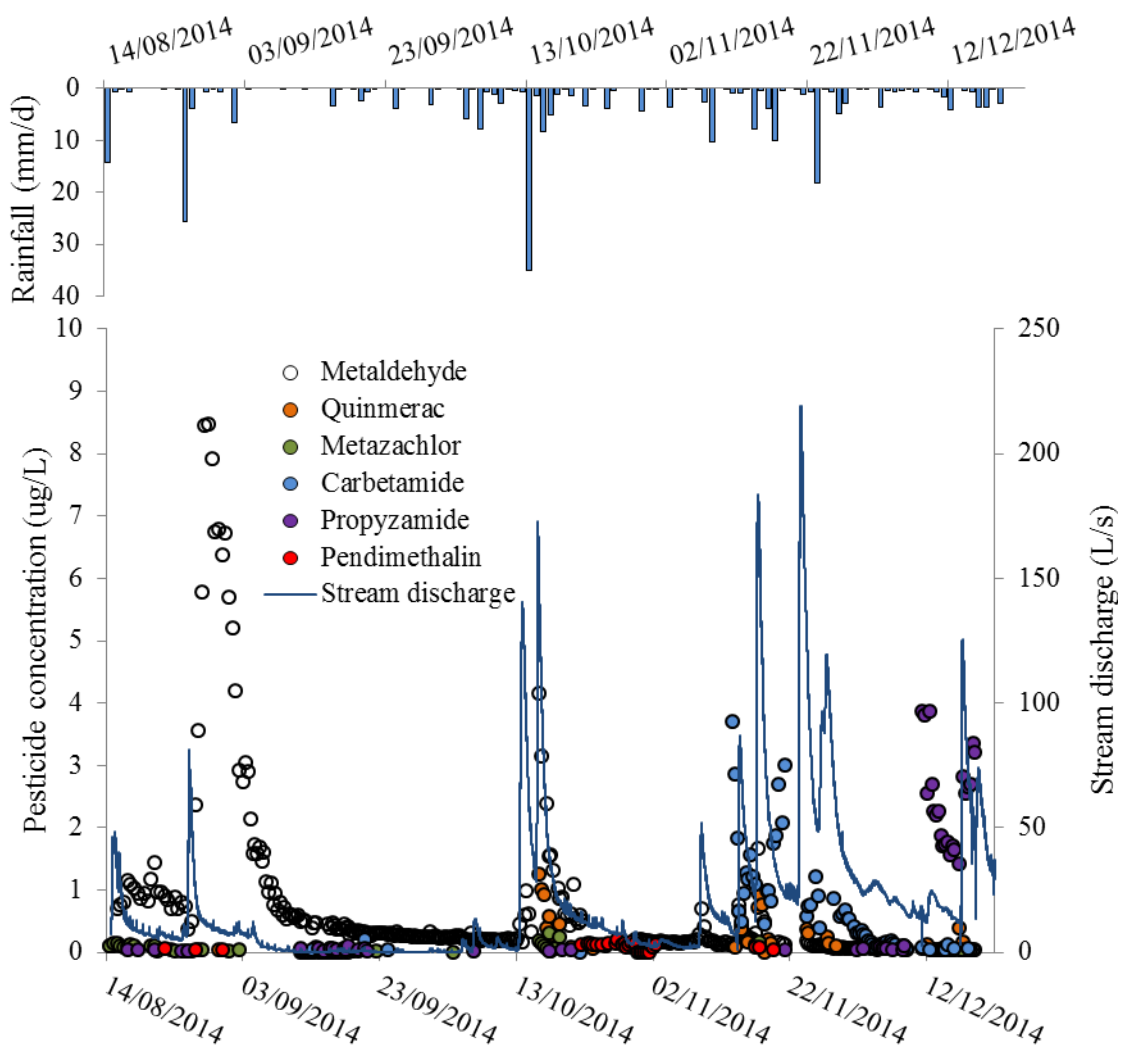
4. Applications of the method

The method developed here has similar aims to those previously mentioned [16,17] in that the main purpose is to detect multiple pesticides in environmental waters and to do this down to low levels around, 0.1µg/L. The main difference and indeed benefit of the method described in this paper is that an extraction is not needed and so large numbers of samples can be processed in a minimal timeframe, this also means that lower volumes of samples are needed resulting in less waste being developed and therefore a more efficient process. In addition to this, any potential errors that may occur during extraction processes are avoided. Data for stream discharge and stream water concentrations of the six pesticides analysed in water samples collected from the study stream are shown in Figure 3, between August and December 2014. Daily rainfall data are also displayed. Pesticide concentrations tended to

increase sharply during rainfall events with the highest concentrations typically occurring in the first storm event after application. This is consistent with observations reported elsewhere from catchments with under-drained heavy clay soils [3]. The highest concentrations were observed for metaldehyde over an event in late August which triggered a relatively low hydrograph peak. For quinmerac, which is applied later than metaldehyde, the first peak concentrations occur in an event around the 13th of October. Metaldehyde concentrations also increase in this event but with lower peaks. Other notable increases in concentration occur for carbetamide in a series of hydrographs starting on the 14th of November and for propyzamide in the event of the 11th of December, which also resulted in increases in pendimethalin concentrations. Both propyzamide and carbetamide tend to be applied a little later than some of the other herbicides due to the specific requirements of weed control timing for blackgrass on oilseed rape. Concentrations of metazachlor were consistently low, peaking at 0.37 μg L^{-1} on the 29th of October. The magnitude of peak concentrations will reflect a combination of factors including usage rate and the physico-chemical properties of the compound. Compounds with high values of K_{OC} (such as pendimethalin) will tend to bind to soil solids and hence have a lower propensity to leach than compounds which are more hydrophilic (such as metazachlor, quinmerac and carbetamide). For most compounds, peak concentrations were observed at the same time as the hydrograph peak or slightly after the peak flow (i.e. on the falling limb of the hydrograph), although apparent delays in the appearance of peak pesticide concentration may be artefacts of the relatively low sampling frequency adopted (8 h).

Concentrations for all the pesticide compounds examined tended to decrease in hydrograph recession periods in parallel with falling flow. Again, this is consistent with previous observations of pesticide behaviour during storm events [3]. Clearly, peak concentrations of all six pesticides were periodically greater than the maximum admissible concentration for drinking water. Although this stream is not directly abstracted for water supply, it does feed into the River Great Ouse system, which is used for municipal abstraction downstream. The important point to note for the purposes of this paper is that the temporal pattern and magnitude of observed concentrations is consistent with expectations under the environmental conditions experienced over the study period.

330
331 **Figure 3.** Rainfall (top panel), stream discharge (right axis) and pesticide concentrations (left axis) in the Hope Farm stream
332 from August to December 2014.

333

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} [3]) 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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