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Prevalence of neonicotinoids and sulfoxaflor in alluvial aquifers in a high corn and soybean producing region of the Midwestern United States

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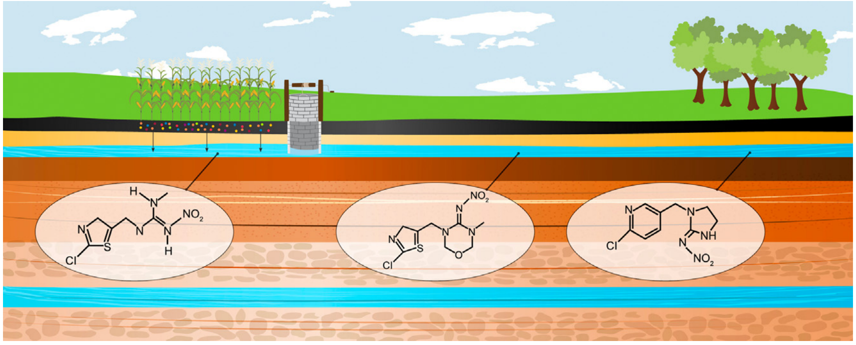
HIGHLIGHTS

- Neonicotinoids are prevalent in 73% of sampled alluvial aquifers.
- Clothianidin was the most commonly detected neonicotinoid.
- Neonicotinoid concentrations inversely related to well depth.
- Use in vulnerable hydrogeologic settings leads to transport into groundwater.
- Solid phase extraction method was more sensitive than direct aqueous injection.

GRAPHICAL ABSTRACT



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ABSTRACT

Neonicotinoids have been previously detected in Iowa surface waters, but less is known regarding their occurrence in groundwater. To help fill this research gap, a groundwater study was conducted in eastern Iowa and southeastern Minnesota, a corn and soybean producing area with known heavy neonicotinoid use. Neonicotinoids were studied in alluvial aquifers, a hydrogeologic setting known to be vulnerable to surface-applied contaminants. Groundwater samples were analyzed from 40 wells for six neonicotinoid compounds (acetamiprid, clothianidin, dinotefuran, imidacloprid, thiacloprid, thiamethoxam), and sulfoxaflor. Samples were analyzed using liquid chromatography tandem mass spectrometry (LC/MS/MS) with both direct aqueous injection and solid phase extraction methods. Neonicotinoids were prevalent in the alluvial aquifers with 73% of the wells having at least one neonicotinoid detection. Clothianidin (68%, max: 391.7 ng/L) was the most commonly detected, followed by imidacloprid (43%, max: 6.7 ng/L) and thiamethoxam (3%, max: 0.2 ng/L). Acetamiprid, dinotefuran, sulfoxaflor, and thiacloprid were not detected during the study. The solid phase extraction method was more sensitive than direct aqueous injection, where only clothianidin detected in 23% of samples. SPE is the preferred method for detecting low concentrations of hydrophilic pesticides in water. This study documented that the combination of heavy chemical use overlying a hydrogeologic setting vulnerable to surface applied contaminants leads to transport of neonicotinoids into an important groundwater resource.

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1. Introduction

Over the past decade there has been a three-fold increase in the use of treated seeds in the United States (U.S. Geological Survey, 2018a; Simon-Delso et al., 2015) with a particularly rapid increase in use between 2003 and 2011 with the applications of a pre-emptive insecticide applied as a seed coating for row crops, such as corn (maize), cotton, soybeans, and wheat (Tooker et al., 2017). By 2008, neonicotinoids (primarily imidacloprid, clothianidin, thiamethoxam) represented 80% of the seed-treatment market in the United States (Tooker et al., 2017; Elbert et al., 2008; Douglas and Tooker, 2015). Currently, 50% of soybeans (18.2 million hectares) (Hurley and Mitchell, 2017), nearly 100% of corn (>36.4 million hectares), and 95% of cotton (15 million hectares) are treated with neonicotinoids (Tooker et al., 2017; Douglas and Tooker, 2015). In 2014, the U.S. Geological Survey (USGS) estimated that over 3.5 million kg of neonicotinoids were applied to crops in the United States (U.S. Geological Survey, 2018a). This estimate included all methods of pesticide application, including aerial, foliar, and seed treatments.

Neonicotinoid use, particularly as a seed treatment, has become prominent in the “corn belt” states of Iowa, Illinois, Indiana, Michigan, Ohio, Nebraska, Kansas, Minnesota, and Missouri (U.S. Geological Survey, 2018a; Myers and Hill, 2014; Stokstad, 2013). In Iowa, annual neonicotinoid use has increased 4000 fold between 2001 and 2014, from 61.9 kg to almost 375,000 kg (U.S. Geological Survey, 2018a; Myers and Hill, 2014). The geographic use and intensity during the same time period for two other commonly used neonicotinoids, clothianidin, and thiamethoxam, mirrors the use of imidacloprid (U.S. Geological Survey, 2018a). Based upon USGS estimates, use of acetamiprid, dinotefuran, sulfoxaflor, and thiacloprid between 2014 and 2017 was limited in Iowa and Minnesota (Fig. 1) (U.S. Geological Survey, 2018a). It is believed that sulfoxaflor, a sulfoximine, has not traditionally been used in the upper Midwest, but USGS estimates from 2015 to 17 showed irregular, but potentially heavy use in northern Iowa and Minnesota (U.S. Geological Survey, 2018a). In 2014–15, sulfoxaflor was included as an analyte in a direct aqueous injection method developed by the Iowa State Hygienic Laboratory at the University of Iowa (SHL) to monitor environmental exposures.

Neonicotinoids have been frequently detected in surface water in the United States, but less is known about their potential to contaminate groundwater (Hladik et al., 2017; Hladik and Kolpin, 2015; Klarich et al., 2017; Hladik et al., 2014; Hladik et al., 2018a; Bradford et al., 2018; Starner and Goh, 2012) . The U.S. Environmental Protection Agency (USEPA) estimates peak surface water and groundwater concentration ranges between 40 and 269,000 ng/L for clothianidin and thiamethoxam (United States Food and Drug Administration, 2017; U.S. Environmental Protection Agency, 2017a; U.S. Environmental Protection Agency, 2017b; U.S. Environmental Protection Agency, 2017c; U.S. Environmental Protection Agency, 2017d; U.S. Environmental Protection Agency, 2017e). These two neonicotinoids are most prone to leaching due to their physio-chemical characteristics (Hladik et al., 2018b; Wood and Goulson, 2017; Goulson, 2013). Groundwater concentrations as high as 140 ng/L have been measured beneath areas planted with treated seeds (De Perre et al., 2015) and concentrations of up to 10,000 ng/L in areas with in-furrow applications for potatoes (Huseth and Groves, 2014). The state of Wisconsin has also documented neonicotinoid contamination in groundwater, but the study focused primarily on irrigation wells that are not generally used as a source of drinking water for humans (Bradford et al., 2018). Low concentrations of neonicotinoids have also been found at concentrations between 0.1 and 16 ng/L in shallow groundwater in agricultural regions in the state of Minnesota (Berens et al., 2021).

In the United States, 42.5 million people, or 13% of the population, rely on private wells for drinking water (Dieter et al., 2018). This reliance is more pronounced in Iowa, with 75% of the state's population using groundwater as their primary source of drinking water, and 275,000 to 300,000 people using private wells (Iowa Department of Natural Resources, 2018). Private well water is currently unregulated in the United States, with treatment left to individual households. In addition, such wells have been shown to be vulnerable to contamination from a variety of sources (U.S. Environmental Protection Agency, 2019a). A study of 2100 wells nationwide found that 23% of domestic wells contained one or more contaminants at concentrations greater than human-health benchmarks (Desimone and Hamilton, 2009). Seventy-three percent of wells contained multiple contaminants at concentrations greater than one-tenth of individual benchmarks. The study used concentrations of greater than one-tenth of a human-health benchmark as an indicator that contaminant concentrations may pose a potential human health concern (Desimone and Hamilton, 2009).

Despite neonicotinoids being documented in water sources and the contamination risks posed to wells, exposure from drinking well water have not been adequately assessed (Klarich et al., 2017; Klarich Wong et al., 2019). Based on previous research, it is likely that many shallow rural wells are similarly contaminated with neonicotinoids, but additional data are needed to better characterize groundwater contamination by these insecticides. This report explores groundwater contamination of neonicotinoid insecticides and sulfoxaflor in alluvial aquifers in an agricultural region of the United States (i.e., portions of Iowa and Minnesota) as a first step in a broader understanding of potential human exposure risks from drinking water. Neonicotinoids and sulfoxaflor were measured in 40 wells completed in alluvial aquifers that are part of an ongoing groundwater quality research by the USGS (U.S. Geological Survey, 2018b). Alluvial aquifers are considered susceptible and prone to contamination for surface-applied contaminants, such as pesticides and their degradates (Kolpin et al., 2000; Kolpin et al., 1997). Thus, the agricultural setting in combination with the vulnerable hydrogeology makes this region ideal for determining the prevalence of neonicotinoids in shallow groundwater. A secondary objective of this study was to validate a modified analytical method with previously published methods (Hladik and Calhoun, 2012; Vargo, 2015).

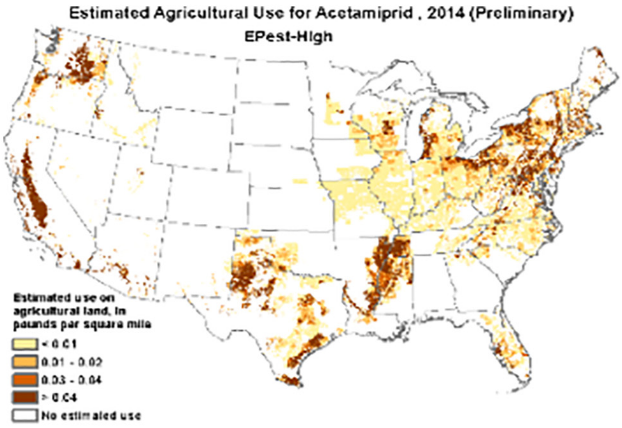
2. Materials and methods

2.1. Sample collection

Water samples were collected from 40 wells, a mixture of observation and private water wells, completed in alluvial aquifers in Holocene deposits across portions of Iowa and Minnesota from July to November 2017 (Fig. 2). Samples were collected from wells previously monitored by the USGS National Water Quality Assessment Program's Eastern Iowa Basins as part of the land-use (LUS) and study-unit surveys (SUS) as described in previous publications (Savoca et al., 2001; Kalkhoff et al., 2001; Sadorf and Linhart, 2000).

Sample collection took place directly at the well; thus, ambient groundwater samples were collected. All wells were initially purged for up to 30 min and/or until field properties were stabilized to remove any stagnant water prior to sample collection. This ensured that fresh, ambient groundwater was obtained for analysis. Field properties were measured periodically during pumping using USGS standard methods (United States Geological Survey, 2008) to ensure that water was representative of ambient groundwater. The properties measured included temperature (°C), dissolved oxygen (mg/L), specific conductance (μS/cm), and pH. The properties were measured at the time of sample collection using a multiprobe instrument. Forty untreated

Fig. 1. Estimated agricultural use for neonicotinoids and sulfoxaflor in the United States in 2014.
Figure from U.S. Geological Survey (2018a).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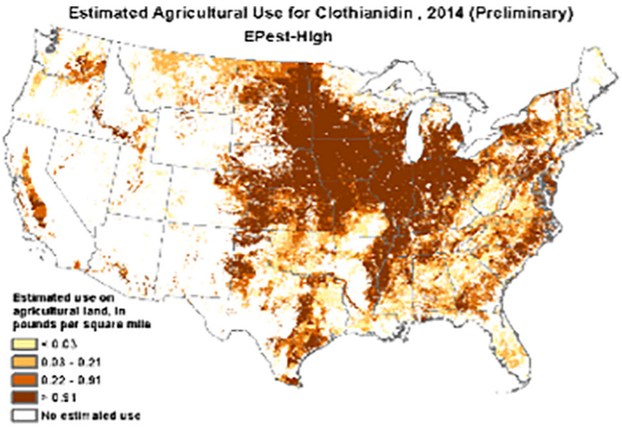
EPest-High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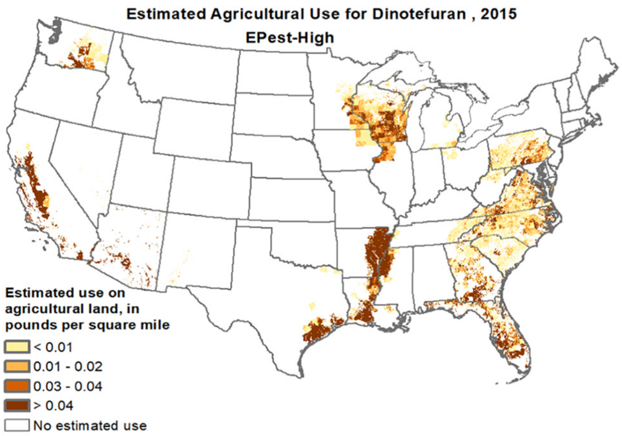
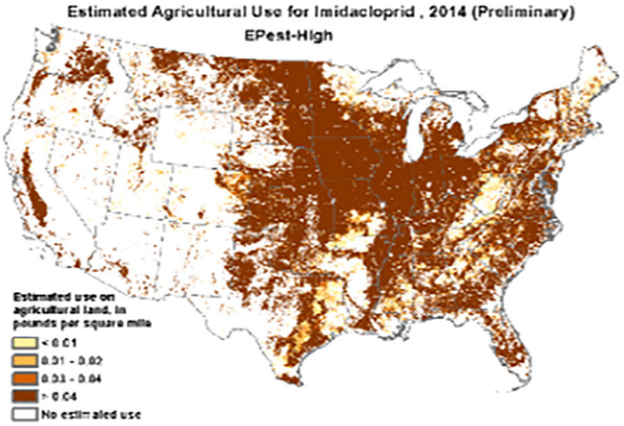
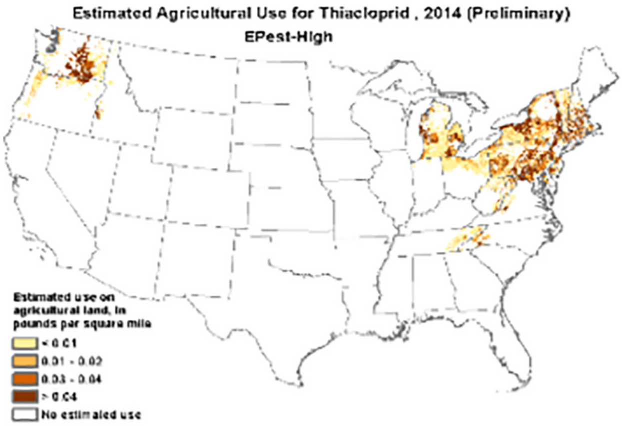
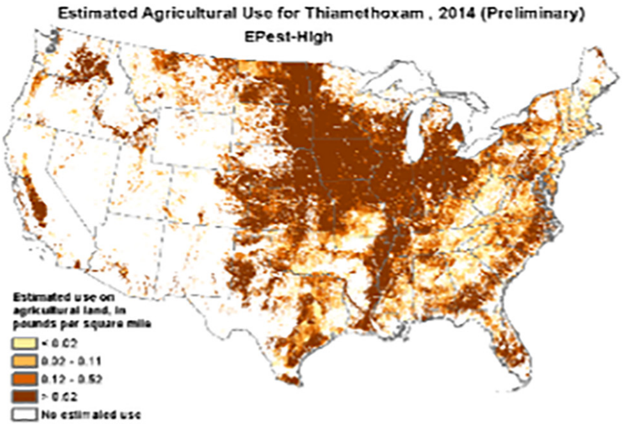
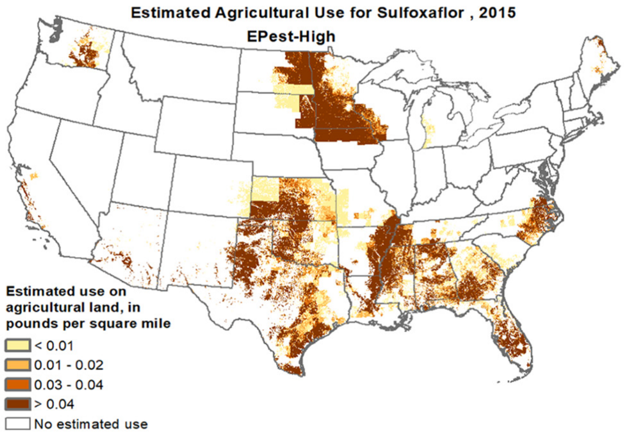

Estimated Agricultural Use for Dinotefuran , 2015
EPest-High


Estimated Agricultural Use for Imidacloprid , 2014 (Preliminary)
EPest-High


Estimated Agricultural Use for Thiacloprid , 2014 (Preliminary)
EPest-High


Estimated Agricultural Use for Thiamethoxam , 2014 (Preliminary)
EPest-High


Estimated Agricultural Use for Sulfoxaflor , 2015
EPest-High

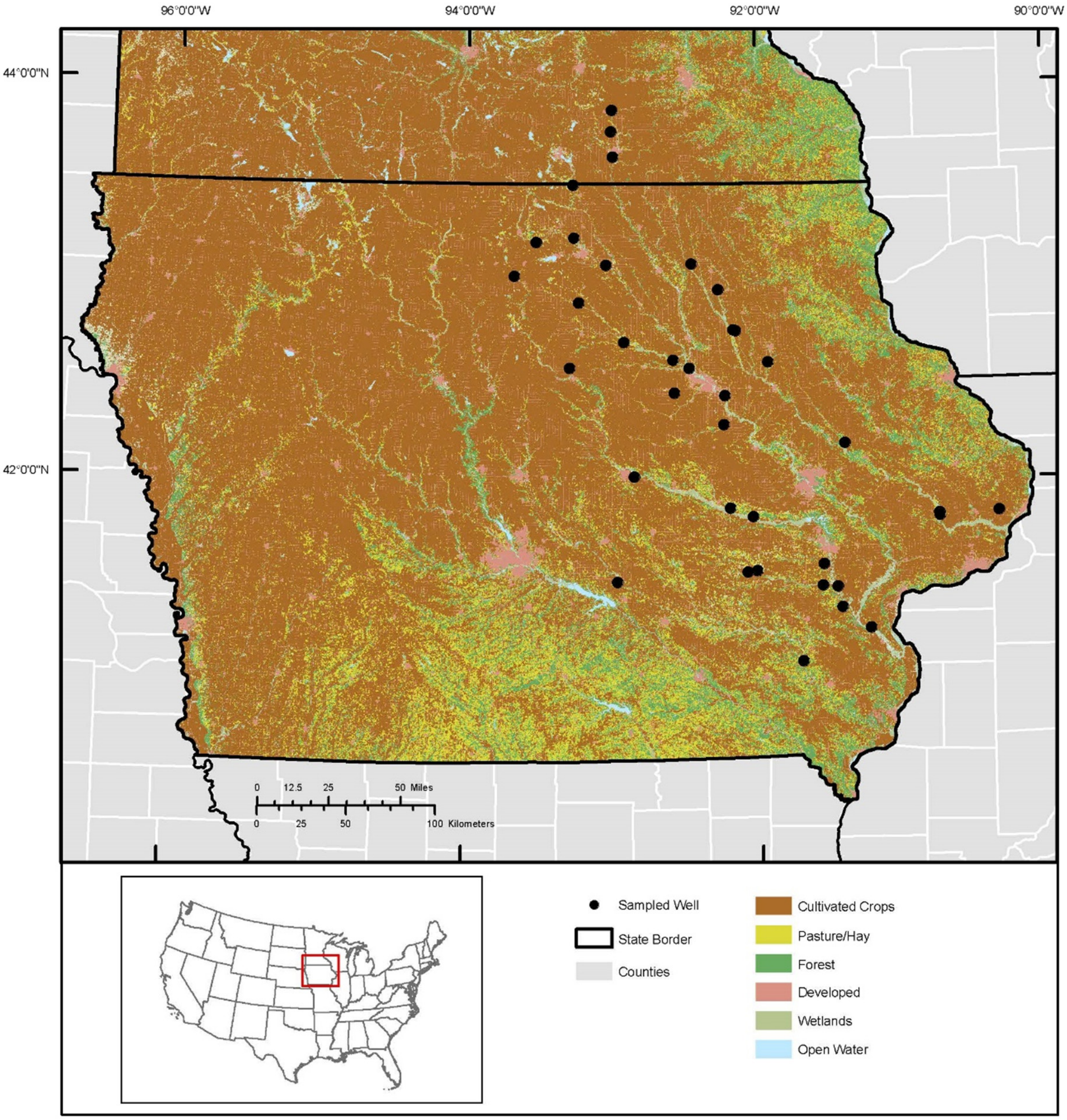


Fig. 2. Map of the alluvial aquifer wells sampled in Iowa and Minnesota. Land cover is courtesy of 2016 National Land Cover Database (Yang et al., 2018).

water samples and 11 replicates were collected directly into unpreserved, clean 1-L amber glass bottles with Teflon-lined lids. For nutrient samples, a 125-mL brown polyethylene bottle was rinsed with native water filtered through a 0.45-μm filter before being filled. All samples were chilled in the field immediately following collection, then refrigerated at about 4 °C until analysis. Primary samples were analyzed at the SHL and replicates were analyzed at USGS Organic Chemistry Research Laboratory in Sacramento, California, USA. Data from the University of Iowa and USGS are published in the Supplemental information section (Tables S-7–9).

2.2. Reagents and chemicals

Each sample was analyzed for six neonicotinoid compounds: acetamiprid (purity >99%), clothianidin (purity >99%), dinotefuran (purity >99%), imidacloprid (purity >99%), thiacloprid (purity >99%), and thiamethoxam (purity >99%), and sulfoxaflor (purity >99%). Target analytes were purchased from Chem Service (West Chester, Pennsylvania, USA). Isotope-labeled imidacloprid-d_4 and thiamethoxam-d_3 were obtained from C/D/N Isotopes (Pointe-Claire, Quebec, Canada). Imidacloprid-d_4 (purity >99%) was used as the internal standard and thiamethoxam-d_3 (purity >99%) as a recovery surrogate. High performance liquid chromatography (HPLC)-purity methanol and acetonitrile (Fisher Optima grade) were purchased from Fisher Scientific (Pittsburg, Pennsylvania, USA). Organic-free, HPLC-purity water was prepared in the laboratory using a MilliporeSigma Milli-Q Ultrapure system (Bedford, Massachusetts, USA). All reagents and standard materials were used without any additional purification. Concentrated stock solutions (1000 ng/mL) were prepared by dissolving neonicotinoid standards in acetonitrile (ACN). The concentrated stock was then further diluted to 100- and 10-ng/mL solutions. Standard solutions were stored at <−10 °C. Standard solutions were replaced every six months.

2.3. Analytical methods

Samples were filtered in the laboratory using baked 0.7-μm nominal pore size GF/F-grade glass-fiber filters (Whatman, Piscataway, New Jersey, USA). The primary samples were analyzed at SHL for six neonicotinoids (acetamiprid, clothianidin, dinotefuran, imidacloprid, thiacloprid, thiamethoxam) and a sulfoximine (sulfoxaflor) using both direct aqueous injection (DAI) and solid phase extraction (SPE). Sulfoxaflor was included in this analysis because it is sometimes considered as a neonicotinoid and has a similar mode of action (Watson et al., 2011; Sparks et al., 2013). A subset of 11 replicate samples sent to the USGS Organic Chemical Research Laboratory for extraction and analysis using a previously published SPE method (Hladik and Calhoun, 2012). The replicate subset was collected to compare the analytical methods between the two laboratories.

All nutrients sampled were analyzed at the USGS National Water Quality Laboratory in Denver, Colorado. Analysis of whole water nutrients included total nitrogen, analyzed using an alkaline persulfate digestion (with a reporting limit (RL) = 0.05 mg/L (Patton and Kryskalla, 2003), and total phosphorus, analyzed using semi-automated colorimetry (RL = 0.004 mg/L; USEPA method 365.1 (O'dell, 1993). Dissolved nutrient analysis included ammonia (RL = 0.01 mg/L), nitrite (RL = 0.001 mg/L), nitrate (NO3-N; RL = 0.04 mg/L), and ortho-phosphorus (RL = 0.004 mg/L) analyzed using colorimetry (Fishman, 1993; Patton and Kryskalla, 2011).

2.3.1. SHL direct aqueous injection

The DAI process used followed an established method developed by SHL (Vargo, 2015). This method has been previously used to investigate the occurrence of neonicotinoids in drained wetlands in Iowa (Evelsizer and Skopec, 2018). Filtered sample water (10 mL) was used for preparation of DAI analysis. This sample water was added to a pre-cleaned, 10-mL glass volumetric flask until approximately half-full. Each sample was then spiked with 25 μL of a 1000-ng/mL internal standard solution, imidacloprid-d_4. Each sample was then diluted to 10-mL calibration mark using the remaining 10 mL of sample. The volumetric flask was then capped and inverted to mix contents. Sample water (2.5 mL) was then transferred to a labeled amber glass HPLC vial and capped for analysis using a disposable glass pipet.

2.3.2. SHL solid phase extraction

The SPE method used is based upon a previously published method (Hladik and Calhoun, 2012), but was adapted for this study. Filtered water samples (1 L) were spiked with a recovery surrogate, thiamethoxam-d_3 (100 μL of a 1000-ng/mL solution) and extracted using a precleaned Oasis HLB SPE cartridge (6 cc, 500 mg; Waters Corporation, Milford, Massachusetts, USA). Cartridges were precleaned with 2 column volumes (~10 mL) of methanol and 2 column volumes of organic-free water. The sample water (1 L) was then pumped through the cartridges using Resprep Sample Delivery system (Restek, Bellefonte, Pennsylavnia, USA) at a rate of approximately 10 mL/min using a Prep Sep vacuum manifold (Fisher Scientific, Pittsburg, Pennsylvania, USA). After extraction, cartridges were left on the manifold to dry for approximately 30 min or until the SPE sorbent was visibly dry. The analytes were eluted from the SPE cartridge into a clean glass concentrator tube using 10 mL of methanol. The eluant was evaporated using dry nitrogen in an N-evap to 1 mL in a fume hood. Sample eluent were then stored in a freezer at −20 °C (up to 30 days).

Prior to analysis, a disposable glass pipet was used to remove the eluate from the glass concentration tube (step described in preceding paragraph). The eluate was placed into a clean 10-mL volumetric flask, spiked with an internal standard, imidacloprid-d_4 (C/D/N Isotopes, Pointe-Claire, Canada) (100 μL of a 1000-ng/mL solution) and diluted to the final calibration mark of 10 mL with organic-free lab water. This dilution step was added so that extracted samples could be analyzed using the same Zorbax Eclipse Plus C18, 1.8 μm, 2.1 × 50 mm column used for DAI. This dilution step in lab water was required as initial attempts to directly analyze the sample in pure methanol resulted in unacceptable deterioration of the chromatographic peak shapes and separation. A disposable glass pipet was then used to transfer the sample to a labeled amber glass HPLC vial and cap for analysis.

2.3.3. SHL LC/MS/MS

Samples were analyzed using a liquid chromatography tandem mass spectrometry (LC/MS/MS) system with a reversed phase HPLC column with acetonitrile/methanol/water/acetic acid gradient and an electrospray interface in positive ion monitoring mode (ESI+). The systems include an Agilent 1290 Infinity Autosampler (Santa Clara, California, USA) and an AB Sciex Instruments Linear Ion Trap Quadrupole LC/MS/MS Mass Spectrometer (Model AB Sciex 5500 QT) (Concord, Ontario, Canada). Aliquots of the sample extracts (40 μL) were injected into the HPLC system utilizing Zorbax Eclipse Plus C18 column (1.8 μm, 2.1 × 50 mm; Agilent) for chromatographic separation of the target analytes.

The column flow rate was 0.40 mL/min, and the column temperature 30 °C. The mobile phases were 0.15% acetic acid (glacial, HLPC grade, Fisher Scientific) in organic-free water (Channel A) and 0.15% acetic acid in 50% acetonitrile/methanol (Channel B). Data were collected in the multiple-reaction-monitoring (MRM) mode (Table 1). Additional instrument details are provided in the supplementary materials. Each neonicotinoid insecticide has a chlorine atom in its molecular structure and the mean molecular weight is based on the isotopic abundance of 35Cl and 37Cl isotopes. The precursor ion monitored is the more abundant 35Cl isotope.

2.4. Data analysis

LC/MS/MS data were processed using Analyst and MultiQuant software (AB Sciex, Concord, Ontario, Canada). The presence of a test analyte was confirmed by: (1) the retention times matched the analytical standards with no more than 2% variation, (2) peak shapes were consistent with analytical standards, and (3) detected peaks had the correct precursor/product ions for both the quantitation and confirmation ions. The ratio of the quantitative precursor/product ion pair to the qualitative precursor/product ion pair in the sample did not vary by more than ±30% from the ratio observed in calibration standards.

Statistical analysis was performed using SAS 9.4. The distribution of data was examined for normality using the Shapiro-Wilk test. The continuous variables were assessed and were not normally distributed. A natural log transformation of these continuous variables was also assessed, but the log-transformed data were also not normally distributed. In addition to the mean, values for the variables were also reported as median, maximum, and minimum to account for the skewed distribution. Non-detects of clothianidin, imidacloprid, and thiamethoxam were set at half the limit of detection. The USEPA recommends this approach be used for chemicals when they may be present below the limit

Table 1
Experimental parameters for multiple-reaction-monitoring (MRM) in ESI+.

Analyte	MW	t_R (min)	Ion type	Ions (m/z)	DP (V)	CE (V)
Acetamiprid	222.7	3.91	Quantitation	223 → 126	85	31
			Confirmation	223 → 73	85	77
Clothianidin	249.7	3.25	Quantitation	250 → 132	55	26
			Confirmation	250 → 169	55	19
Dinotefuran	202.2	1.40	Quantitation	203 → 129	65	17
			Confirmation	203 → 43	65	70
Imidacloprid	255.7	3.40	Quantitation	256 → 175	65	28
			Confirmation	256 → 209	65	24
Sulfoxaflor	277.3	4.62	Quantitation	278 → 174	55	14
			Confirmation	278 → 154	55	14
Thiacloprid	252.7	4.71	Quantitation	253 → 126	90	31
			Confirmation	253 → 73	90	82
Thiamethoxam	291.7	2.57	Quantitation	292 → 211	65	19
			Confirmation	292 → 131	65	35
Imidacloprid-d_4	259.69	3.40	Internal standard	260 → 179	65	26
Thiamethoxam-d_3	294.73	2.57	Recovery surrogate	295 → 214	65	20

MW = molecular weight; t_R = retention time; min = minutes; m/z = mass to charge ratio; DP = declustering potential; CE = collision energy; V = volts.

of detection (U.S. Environmental Protection Agency, 2017f). Acetamiprid, dinotefuran, sulfoxaflor, and thiacloprid were not detected in any samples (U.S. Environmental Protection Agency, 2017f). A review of LC/MS/MS data indicates that neonicotinoids were present in some samples, but at levels below the level of detection (LOD). The value of non-detects for these four compounds were set at zero. This approach for handling left-censored concentrations (i.e., non-detects) is also recommended by USGS when nonparametric statistical tests are used for data interpretation (Helsel and Hirsch, 1992). Non-parametric tests, Wilcoxon Rank-Sum Test ($N = 2$) or Kruskal-Wallis Test ($N = 3$), were used to compare differences in neonicotinoid results by various ancillary data, including testing method, physical and chemical properties of water, and well depth. Spearman's rank correlation analyses were used to measure the strength and direction of association between neonicotinoid concentrations, well depth, and physical and chemical properties of water. Water and properties, such as pH and depth, were categorized into discrete groups to assess their relation to the occurrence of neonicotinoids. Chi-square tests were used to assess relations between categorized variables. Two-tailed p-values were considered statistically significant if they were < 0.05.

3. Results and discussion

3.1. Method validation

A storage stability study was conducted to determine the length of time that the seven analytes could be stored in water before substantial degradation of the target analytes occurred. Stability of target analytes in groundwater showed that all target analytes were stable over a 64-day period (Table 2). Two 1-L amber glass bottles of well water were collected from a volunteer household. Each bottle was spiked with 100 ng/L (nominal concentration) of each analyte. One bottle was stored at room temperature (20–25 °C) and the other was stored in a refrigerator (2–6 °C). The accuracy of recovered analytes had a range within ±30%, with a mean recovery of 110% (SD, ±10%) for room temperature samples and 115% (SD, ±10%) for refrigerated samples. The precision, relative standard deviation (RSD), of detected concentrations during the stability test averaged 5% (standard deviation (SD), ±3%; range, 2–15%) for the room temperature sample and 5% (SD, ±1%; range, 2–6%) for the refrigerated sample. The precision varied the most for thiamethoxam at room temperature with detected concentrations varying about 15% compared to about 3% in the refrigerated sample (Table 2). Compared to all analytes, the precision for dinotefuran differed the most in refrigerated samples at about 6%. A similar study, conducted by SHL using refrigerated wetland surface water samples, indicated the accuracy of detections ranged from 80 to 120% 31 days after initiation of the study (Vargo, 2015).

Table 2
Recovery (%) of target analytes over 64-day stability study.

Compound ion	Mean	Std Dev	RSD	Mean	Std Dev	RSD
	Room temp sample			2–6C sample		
Quantitation						
Acetamiprid	116.6	0.04	3.7	118.9	0.04	3.4
Clothianidin	107.4	0.06	5.6	116.9	0.06	5.3
Dinotefuran	118.0	0.08	7.1	118.3	0.05	4.4
Imidacloprid	107.8	0.06	5.3	111.0	0.05	4.3
Sulfoxaflor	109.4	0.04	3.7	113.4	0.03	2.6
Thiacloprid	118.4	0.04	3.3	121.3	0.06	4.7
Thiamethoxam	104.7	0.15	14.5	111.8	0.03	2.7
Confirmation						
Acetamiprid	112.6	0.04	3.4	115.2	0.04	3.1
Clothianidin	106.5	0.03	2.9	111.9	0.06	5.6
Dinotefuran	104.7	0.06	5.5	106.1	0.06	6.0
Imidacloprid	106.3	0.02	1.7	112.2	0.03	2.4
Sulfoxaflor	112.0	0.04	4.0	113.7	0.04	3.8
Thiacloprid	111.0	0.04	3.2	114.0	0.05	4.3
Thiamethoxam	103.8	0.14	13.4	112.1	0.03	2.6
Imidacloprid-d_4 ISTD	99.7	0.03	2.7	99.7	0.03	2.7

Std Dev = standard deviation; RSD = relative standard deviation.

The modified SPE method was also evaluated prior to sampling to test recovery. Three 1-L amber glass bottles filled with organic-free water were spiked with the seven analytes, internal standard, and surrogate. The cartridges were then eluted with 10 mL of methanol. Recovery accuracy for all analytes ranged from 95 to 105% with a precision (RSD) of <10%. Based upon the SHL DAI method, a recovery of 70–130% was considered acceptable (Vargo, 2015).

A seven-point external calibration curve between 0.01 and 2.5 ng/mL was run with each set of samples. Calibration standards were generated by diluting the 100- and 10-ng/mL concentrated stock solutions with organic-free lab water. Each calibration standard was spiked with internal standard, imidacloprid-d_4 (25 μL of 1000-ng/mL solution). The calibration standards had a mean accuracy of 110% (SD ± 0.5) and precision of 5% (SD ± 5.0). Both linear and quadratic fits were evaluated for the calibration curves. Both fits had mean R-square values >0.99. The quadratic and linear fits were not statistically different. SHL uses a quadratic curve, and USGS uses a linear curve with 1/x weighting. To ease comparison between methods, the quadratic fit has been selected for this study. Concentrations detected above the highest calibration standard were diluted and retested to confirm the result. Method detection limit (MDL) was calculated based upon a prior study by Hladik and Calhoun that used guidance from the USEPA (Hladik and Calhoun, 2012; U.S. Environmental Protection Agency, 1997). The MDL on the LC-MS/MS without sample enrichment ranged from 2.6–17.8 ng/L. Following SPE, the MDL was between about 0.03 and 0.2 ng/L, respectively (Table S-6).

Concentrations of the seven analytes in samples were validated against lab blanks ($n = 5$), matrix spikes ($n = 15$), and replicate samples ($n = 11$). SHL DAI samples ($n = 40$) were also used for quality control to confirm SHL SPE results. At least one laboratory blank was run with each set of samples. Lab blank samples were prepared by spiking 10 mL of organic-free water with imidacloprid-d_4 (25 μL of 1000-ng/mL solution). The blank was then transferred (2.5 mL) to a labeled amber glass HPLC vial and cap for analysis. No contamination was observed in any of the laboratory blanks tested. Matrix samples consisted of 8 high (25 μL of 100-ng/mL solution, 250 ng/L) and 7 low (25 μL of 10-ng/mL solution, 25 ng/L). Each matrix was spiked with internal standards (25 μL of 1000 ng/mL). Recoveries for all target analytes in these spikes were 105 ± 15%. Recovery of the surrogate used with the SPE samples, thiamethoxam-d_3, had a mean recovery 100% (±10 SD, ± 10%). The recovery in one sample was adjusted because it was spiked with half of the surrogate. No other recovery correction has been made to the reported data.

Clothianidin was also the most frequently detected analyte with both the USGS and SHL DAI tested samples, 36% and 23% respectively. For samples with concentrations above the respective method MDLs, the mean RSD was 20% with a range of 16–25%. This study documented the SHL SPE method was generally much more sensitive than either the USGS or SHL DAI methods with the differences in detection frequencies being driven by the differences in their respective method MDLs. SHL SPE detection results were validated by both the USGS and SHL DAI methods when normalized using a common MDL. In addition, the majority of the concentrations were also within analytical variability (further validating the SHL SPE results) (Table 3).

A direct comparison of the SHL SPE and SHL DAI methods showed that detected concentrations of clothianidin varied by 7%. Only 9 samples had a detection for clothianidin. No other analytes were found in any samples. The highest reported concentration was 401 ng/L, which differed by 2.4% from the concentration detected in the same sample using SHL SPE. Clothianidin concentrations ranged from 12 to 401 ng/L. Results of the Wilcoxon Rank-Sum Test showed that median

Table 3
Comparison of analyte concentrations (ng/L) in replicate samples by test type.

Sample	Clothianidin			RSD	Imidacloprid			RSD	Thiamethoxam			RSD
	SPE	DAI	USGS		SPE	DAI	USGS		SPE	DAI	USGS	
Sample 1	17.7	18.4	13.5	**16.0**	<	<	<	–	0.2	<	<	–
Sample 2	0.3	<	<		0.2	<	<		<	<	<	
Sample 3	<	<	<		<	<	<		<	<	<	
Sample 4	0.2	<	<		<	<	<		<	<	<	
Sample 5	<	<	<		<	<	<		<	<	<	
Sample 6	<	<	<		<	<	<		<	<	<	
Sample 7	391.7	401.2	259.8	**22.5**	6.5	<	<	–	<	<	<	
Sample 8	[a]	<	<		[a]	<	<		<	<	<	
Sample 9	11.7	12.9	9.2	**16.7**	4.1	<	<	–	<	<	<	
Sample 10	0.2	<	<		<	<	<		<	<	<	
Sample 11	5.1	<	3.6	**24.9**	0.1	<	<	–	<	<	<	
MDL	**0.05**	**5.40**	**3.90**		**0.09**	**8.90**	**3.80**	–	**0.03**	**2.60**	**3.40**	–

[a] SPE = SHL solid phase extraction; DAI = SHL direct aqueous injection; USGS=U.S. Geological Survey's SPE method; RSD = relative standard deviation.

detection of imidacloprid and clothianidin were significantly different (Imidacloprid, two-sided $p \leq 0.001$; Clothianidin, two-sided $p = 0.002$) between the two methods. This difference is likely due to enrichment using SPE cartridge.

In Table 3 the results for SHL SPE, SHL DAI and USGS SPE are shown. The results demonstrate the modified SPE method had greater sensitivity than the other two methods. SHL SPE was more likely to detect neonicotinoids, especially imidacloprid and thiamethoxam at very low levels. The SHL DAI extraction was the least sensitive of the compared methods, as the minimum detected concentration of clothianidin was 12.1 ng/L (Table 4). The lowest detect clothianidin concentration by the other two methods was 3.6 ng/L (USGS SPE) and 0.1 ng/L (SHL SPE) (Table 4).

SHL DAI only detected clothianidin in 9 samples (22%) and no other compounds. However, the SHL SPE method found an additional 16 wells also contained clothianidin residues. Imidacloprid (43%, $n = 16$) and thiamethoxam (3%, $n = 1$) were also found. This indicates that surveys using DAI likely underestimate the extent of neonicotinoid contamination in the environment. For example, a well water survey conducted in 2017–2018 by SHL only found quantifiable concentrations of neonicotinoids in 4 of the 280 wells tested (1%) (State Hygienic Laboratory at the University of Iowa, 2018). SHL used a reporting limit of 25 ng/L for the six neonicotinoids it looked for during that study (Vargo, 2015). If this study relied on DAI and a comparable reporting limit, clothianidin would have only been detected in 3 samples. For fiscal year 2018, SHL tested over 2300 samples for neonicotinoids using DAI (State Hygienic Laboratory at the University of Iowa, 2019). It is likely that low levels of neonicotinoids were present but were undetected in many of these wells.

Table 4
Concentration (ng/L) of neonicotinoids detected in untreated well water.

	SHL SPE[a] (n = 37)			SHL DAI (n = 40)			USGS (n = 11)		
	CLO	IMI	THX	CLO	IMI	THX	CLO	IMI	THX
Detects	25	16	1	9	ND	ND	4	ND	ND
Frequency	68%	43%	3%	23%	<	<	36%	<	<
Mean	15.3	1.2	<	13.8	<	<	27.3	<	<
Median	0.4	<	<	<	<	<	<	<	<
Min Detect	0.1	0.1	0.2	12.1	<	<	3.6	<	<
Max Detect	391.7	6.7	0.2	401.2	<	<	259.8	<	<

ND = not detected. < = Less than MDL. Acetamiprid, dinotefuran, sulfoxaflor, and thiacloprid were not detected using any of the analytical methods. Sulfoxaflor is not included in the USGS analytical method.

[a] SPE = SHL solid phase extraction; DAI = SHL direct aqueous injection; USGS=U.S. Geological Survey's SPE method; CLO = clothianidin; IMI = imidacloprid; THX = thiamethoxam.

3.2. Analytes in groundwater

Neonicotinoids were found in the majority of alluvial aquifers sampled. Using the SPE method, 73% of the wells had at least one and 38% had at least two neonicotinoids detected. The most frequently detected neonicotinoid was clothianidin (68%, maximum concentration: 391.7 ng/L), followed by imidacloprid (43%, maximum concentration: 6.7 ng/L) and thiamethoxam (3%, maximum concentration: 0.2 ng/L) (Table 4). The clothianidin detection frequency in alluvial aquifers was similar to that documented previously in midwestern U.S. streams (75%) (Hladik et al., 2014), while results for imidacloprid and thiamethoxam were substantially different. Prior studies found imidacloprid (23%) was more commonly detected in groundwater and thiamethoxam (47%) was detected less compared to surface water (Hladik et al., 2014). Other studies have found that while pesticides were less common in groundwater than streams they were still prevalent, with detections typically less than 1 μg/L (Kolpin et al., 1998; Gilliom, 2007). The prevalence of clothianidin in both streams and alluvial aquifers is likely due to a combination of its heavy use, physical/chemical properties, and its occurrence as a major metabolite of thiamethoxam degradation (Hilton et al., 2016). The dramatic difference in detection frequencies for thiamethoxam between streams and alluvial aquifers documents its differential persistence along surface and subsurface transport pathways. Acetamiprid, dinotefuran, sulfoxaflor, and thiacloprid were not detected in alluvial aquifers for this study possibly due to limited or no agricultural application during the study (U.S. Geological Survey, 2018a). This aligns with the USGS's 'predicted' usage of these compounds (Fig. 1) where none of these compounds were believed to be used in Iowa. The prevalence of neonicotinoids in alluvial aquifers indicates that neonicotinoids are being transported from the soil following application to groundwater in this vulnerable hydrogeological setting. This application is primarily due to seed treatment application, but based upon USGS estimate after 2014 other methods such as foliar or direct soil application are also used, but less common (U.S. Geological Survey, 2018a). Starting in 2015, the provider of the surveyed pesticide use data stopped making estimates for seed treatment application available because of complexity and uncertainty U.S. Geological Survey, 2018a. While previous research has documented the prevalence of contaminants including nitrate, herbicides, and herbicide-transformation products in alluvial aquifers (Berens et al., 2021; Kolpin et al., 2000; Kolpin et al., 1998; Hruby et al., 2015), this study documents the prevalence of neonicotinoids in this aquifer type.

The study also indicates that private wells may be a pathway of human exposure to neonicotinoids. This exposure has previously been documented in finished water samples from municipal systems. Studies in the United States, Canada, and China have all detected these insecticides with peak concentrations for individual neonicotinoids as high as 8622 ng/L (Klarich et al., 2017; Klarich Wong et al., 2019; Craddock et al., 2019; Wan et al., 2019; Sultana et al., 2018; Montiel-León et al., 2018; Mahai et al., 2020). In the United States, a cross-sectional study detected imidacloprid in untreated and treated water samples at concentrations between 0.008 and 0.202 ng/L from 1999 to 2015, with detection frequency increasing between 2004 and 2011 (Craddock et al., 2019). In 2016, Klarich et al. found clothianidin, imidacloprid, and thiamethoxam at concentrations up to 57 ng/L in finished water samples at the University of Iowa water treatment facility in Iowa City, Iowa, USA (Klarich et al., 2017) and a follow-up study detected two metabolites of imidacloprid, desnitro-imidacloprid and imidacloprid-urea, in concentrations up to 0.60 ng/L (Klarich Wong et al., 2019). A nationwide Chinese study found multiple neonicotinoids in tap and drinking water samples, with median concentrations ranging between 0.14 and 0.86 ng/L (Mahai et al., 2020). In Canada, thiamethoxam, clothianidin, and imidacloprid have been detected in water systems. In Ontario, the mean concentrations were below the limits of detection but had a peak value of 91.7 ng/L for thiamethoxam (Sultana et al., 2018). In Quebec, tap water from four samples had maximum concentrations for these three neonicotinoids ranging from 1.0–10 ng/L (Montiel-León et al., 2018). These median concentrations are comparable to the results of this study and are below the limits recommended by the European Union for single pesticides in drinking water (< 100 ng/L) (European Parliament and Council, 1998; European Parliament and Council, 2000; European Parliament and Council, 2006; European Parliament and Council, 2013; European Parliament and Council, 2008). In this study only one sample, with a concentration of 391.7 ng/L, exceeded this level. No samples had concentrations of neonicotinoid mixtures that exceeded the EU's total pesticide residue limit of 500 ng/L (European Parliament and Council, 1998; European Parliament and Council, 2000; European Parliament and Council, 2006; European Parliament and Council, 2013; European Parliament and Council, 2008). Neonicotinoids are not regulated in drinking water in China, Canada or the United States (Mahai et al., 2020; Health Canada, 2019; U.S. Environmental Protection Agency, 2019b).

To determine if hydrologic residence time was an important factor in the transport of neonicotinoids in alluvial aquifers, concentrations of clothianidin and imidacloprid were compared to well depth and dissolved oxygen concentration. Both variables are general indicators of groundwater age, with shorter residence time associated with shallower wells ($<$50 m) and higher concentrations of dissolved oxygen ($>$5 mg/L) (Kolpin et al., 2000; Kolpin et al., 1997; Kolpin et al., 1995a; Kolpin et al., 1995b). Previous research has documented an inverse relation between groundwater age and the pesticide detection frequencies (Kolpin et al., 2000; Kolpin et al., 1997; Kolpin et al., 1998; Gilliom, 2007; Kolpin et al., 1995a; Kolpin et al., 1995b; Barbash, 1999). This is one of the first studies, however, to determine if this inverse relation also holds true for neonicotinoids. The well depths for this study ranged from 3.5 to 61 m with median well depth of 6.9 m, with only one sample having a depth greater than 50 m. Spearman's correlation analyses to evaluate the relation between depth and clothianidin and imidacloprid concentrations documented a statistically significant inverse relation between well depth and imidacloprid ($p = 0.04$) and clothianidin ($p = 0.05$) concentrations. This was further confirmed using the Wilcoxon Two-Sample Test which showed that shallower wells with depths below the median ($<$6.9 m) were significantly associated with higher concentrations of both clothianidin ($p = 0.017$), imidacloprid ($p = 0.005$), the total number of detected neonicotinoids ($p = 0.01$) and total neonicotinoid concentration ($p = 0.01$). Wells with depths less than 6.9 m were 7.3 times (unadjusted Odds Ratio = 7.3; 95% Confidence Interval (CI) (1.7–31.1, $p = 0.01$)) more likely to have a concentration over the median, 0.41 ng/L, of clothianidin and 2.6 times (unadjusted Odds Ratio = 2.6; 95% CI (1.0–6.7), $p = 0.01$) more likely to have a total neonicotinoid concentration, including clothianidin, imidacloprid and thiamethoxam, above the median, 0.7 ng/L. Neither dissolved oxygen or aquifer vulnerability, a categorized variable combining depth and dissolved oxygen (DO), were found to be significantly correlated with analyte concentrations. Vulnerability has previously been defined as low (well depth $>$ 50 m and DO $<$0.5 mg/L); intermediate (well depth $>$ 50 m and DO $>$0.5 mg/L OR well depth $\leq$ 50 m and DO $<$0.5 mg/L); and high (wells depth $\leq$ 50 m and DO $\geq$5 mg/L) (Kolpin et al., 2000). None of the wells sampled during this study were classified as low vulnerability. Given the shallow depths of the wells, DO concentrations likely did not vary enough to observe a statistically significant correlation with neonicotinoid concentrations. In Iowa, the state's drinking water typically comes from six major aquifer groups - alluvial aquifers, sand and gravel aquifers, Cretaceous (Dakota) sandstone, Silurian-Devonian bedrock, Mississippian bedrock, and Cambrian-Ordovician bedrock (Iowa Department of Natural Resources, 2018). A larger sample size with wells from different aquifer types and a wider range of depths would help to better characterize any potential relation on a statewide basis to both dissolved oxygen and aquifer vulnerability.

Additional available ancillary data included field properties and nutrients, such as ammonia, organic nitrogen, nitrate, orthophosphate, and organic carbon. pH was significantly correlated with clothianidin (pH $p = 0.03$), total neonicotinoid concentration (pH $p = 0.03$) and total neonicotinoid detection rate (pH $p = 0.01$). The median pH for samples was neutral with a range from 5.5 to 7.9. Water with an acidic pH was 2.8 (unadjusted Odds Ratio = 2.8; 95% CI (0.7–11.1), $p = 0.1$) times more likely to have clothianidin concentrations above the median ($>$0.41 ng/L), and 2 times (unadjusted Odds Ratio = 2.0; 95% CI (0.46–8.7), $p = 0.4$) as likely to have at least one detect compared to samples above a pH of 7. The presence of neonicotinoids in acidic waters is not surprising as these pesticides are resistant to hydrolysis at neutral or acidic pH.

Imidacloprid and thiamethoxam are both stable at pH ranging from 4 to 7 (Bonmatin et al., 2015). Clothianidin has the longest half-life in soil, up to 19 years, of any of the analytes studied (Wood and Goulson, 2017; Goulson, 2013; Bonmatin et al., 2015; Thompson et al., 2020). It has been found to be stable at the observed environmental pH and temperature conditions (Wood and Goulson, 2017; Goulson, 2013; Bonmatin et al., 2015; Thompson et al., 2020). The half-lives of imidacloprid and thiamethoxam in soil range from 7 days to 3.5 years (Wood and Goulson, 2017; Goulson, 2013; Bonmatin et al., 2015; Thompson et al., 2020). Photolysis is also a common degradation pathway for neonicotinoids, but because well water is not typically exposed to direct sunlight, documented contamination has the potential to persist (Bonmatin et al., 2015). The half-life for acetamiprid, dinotefuran, sulfoxaflor and thiacloprid are much shorter ranging from 1.6 days to 2.5 years (Thompson et al., 2020). This partially explains the more frequent occurrences of clothianidin and imidacloprid. If their current use continues or increases, we expect to see more frequent occurrences and higher concentrations in groundwater. Statistically significant correlations between the occurrence of neonicotinoids and nutrients and organic carbon were not observed (Table 5).

Sampled wells came from two USGS studies: the land-use (LUS) and study-unit surveys (SUS) (Table S-8, USGS Site ID) (U.S. Geological Survey, 2018b). Land use in the vicinity of the two well types was also different. Land-use wells were monitoring wells located at the edge of a field. Study-unit wells were generally located in rural areas more distant from cropped fields. Theoretically, the flow path to observation wells from the site of application was shorter than the study-unit wells. The study-unit wells are generally screened at the base of the aquifer to obtain the maximum amount of water. Monitoring wells were generally screened in the mid to upper part of the aquifer to document transport from the fields. Despite land use differences the median concentrations of individual neonicotinoids, total neonicotinoid concentration and number of detections did not signifcantly vary by study type ($p > 0.05$). Furthermore, over 40% of samples were from private wells. A comparison of monitoring and private wells revealed that

Table 5
Spearman correlation between concentrations of analytes detected using SPE method with variables in alluvial wells.

	CLO	IMI	THX	Total concentration	Total detection
Clothianidin	1.000	0.497 *0.002*	0.222 *0.186*	0.978 *<.0001*	0.777 *<.0001*
Imidacloprid	0.497 *0.002*	1.000	−0.132 *0.437*	0.612 *<.0001*	0.764 *<.0001*
Thiamethoxam	0.222 *0.186*	−0.132 *0.437*	1.000	0.205 *0.224*	0.208 *0.217*
Well depth (m)	−0.324 *0.050*	−0.341 *0.039*	−0.063 *0.713*	−0.349 *0.034*	−0.319 *0.054*
Water temperature (C)	0.062 *0.713*	0.216 *0.199*	−0.141 *0.406*	0.077 *0.651*	0.169 *0.318*
Air temperature (C)	0.314 *0.062*	−0.043 *0.802*	0.285 *0.092*	0.248 *0.144*	0.238 *0.162*
Specific conductance (MS/CM)	−0.086 *0.612*	0.007 *0.969*	−0.281 *0.092*	−0.046 *0.787*	−0.019 *0.912*
Hydrogen ion (mg/L)	0.341 *0.039*	0.283 *0.089*	0.266 *0.112*	0.344 *0.037*	0.391 *0.017*
Dissolved oxygen (mg/L)	0.172 *0.316*	0.172 *0.317*	0.179 *0.296*	0.162 *0.346*	0.075 *0.662*
Dissolve oxygen % saturation	0.148 *0.389*	0.187 *0.274*	0.179 *0.295*	0.146 *0.394*	0.063 *0.715*
pH	−0.353 *0.032*	−0.292 *0.080*	−0.267 *0.111*	−0.355 *0.031*	−0.402 *0.014*
Carbon dioxide (mg/L)	0.229 *0.179*	0.250 *0.142*	0.122 *0.478*	0.249 *0.143*	0.323 *0.054*
Carbonate	−0.326 *0.052*	−0.199 *0.246*	−0.242 *0.156*	−0.309 *0.067*	−0.307 *0.068*
Bicarbonate	−0.205 *0.230*	−0.125 *0.467*	−0.268 *0.113*	−0.186 *0.278*	−0.152 *0.376*
Organic nitrogen (mg/L)	−0.067 *0.721*	−0.060 *0.749*	0.143 *0.443*	−0.091 *0.628*	−0.010 *0.958*
Ammonia (NH3 and NH4+) (mg/L) as nitrogen	−0.171 *0.312*	−0.134 *0.430*	−0.138 *0.415*	−0.165 *0.329*	−0.133 *0.434*
Nitrite (mg/L as nitrogen)	−0.030 *0.861*	−0.024 *0.887*	−0.080 *0.638*	−0.057 *0.737*	0.048 *0.780*
Nitrate (mg/L as nitrogen)	0.276 *0.099*	0.204 *0.225*	0.142 *0.401*	0.259 *0.121*	0.213 *0.206*
Nitrate plus nitrite (mg/L as nitrogen)	0.240 *0.152*	0.192 *0.256*	0.144 *0.394*	0.219 *0.192*	0.190 *0.260*
Orthophosphate (mg/L as PO4)	0.041 *0.810*	−0.035 *0.837*	−0.125 *0.462*	0.033 *0.848*	−0.041 *0.809*
Orthophosphate (mg/L as phosphorus)	0.041 *0.810*	−0.032 *0.850*	−0.133 *0.434*	0.033 *0.847*	−0.041 *0.809*
Organic carbon	−0.093 *0.585*	0.015 *0.931*	−0.281 *0.092*	−0.066 *0.696*	−0.083 *0.625*

The numbers in each cell indicate the correlation coefficients (above) and the p values (below, in italics). CLO = clothianidin; IMI = imidacloprid; THX = thiamethoxam. Shaded boxes indicate a significant correlation ($p<0.05$).

there was no statistical difference between the median individual neonicotinoid concentrations, total neonicotinoid concentration, or the number of neonicotinoids detected in the two types of wells ($p > 0.05$).

4. Conclusions

Neonicotinoids were documented to be prevalent in alluvial aquifers sampled across an area of intense crop production in eastern Iowa and southeast Minnesota, with 73% of the sampled wells having at least one neonicotinoid detected. Clothianidin (68%) was the most frequently detected, followed by imidacloprid (43%) and thiamethoxam (3%). Acetamiprid, dinotefuran, sulfoxaflor, and thiacloprid were not detected in alluvial aquifers for this study. These pesticides were likely not detected because their use is limited in the study area. Neonicotinoids were found more often in shallower wells and in environmental conditions (i.e., low pH) that may limit their degradation, potentially driving persistence. This finding indicates that neonicotinoid contamination of alluvial wells is likely driven by the overlapping combination of land use and hydrogeological setting. Iowa and Minnesota are both areas where intense neonicotinoid use via treated seeds is prevalent and where alluvial aquifers have previously been shown to be vulnerable to surface applied contaminants.

The study also showed that the modified SPE method was more sensitive than two other methods, a SPE method used by USGS and a DAI method by SHL. Clothianidin was detected in 68% of wells using SHL SPE compared to 36% and 23% by the two other methods, respectively. Imidacloprid and thiamethoxam were not found by either of these methods, but very low levels were found in 43% and 3% of wells. The finding indicates that occurrence of neonicotinoids in water could be underestimated by DAI methods. SPE is the preferred method for detecting low concentrations in water.

In Iowa, over 75% of the population relies on groundwater, either from private wells or municipal systems (Iowa Department of Natural Resources, 2018); therefore additional research would be useful to characterize the exposure risks from other major aquifers in the Midwest and to better understand the comparative risks between municipal users and private wells from neonicotinoid exposure via drinking water.

CRediT authorship contribution statement

Darrin A. Thompson: Conceptualization, Methodology, Investigation, Formal analysis, Validation, Writing – original draft. **Dana W. Kolpin:** Data curation, Writing – review & editing. **Michelle L. Hladik:** Investigation, Validation, Writing – review & editing. **Kimberlee K. Barnes:** Investigation, Writing – review & editing. **John D. Vargo:** Methodology,

Validation, Supervision. **R. William Field:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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