Pharmaceuticals and pesticides in rural community drinking waters of Quebec, Canada – a regional study on the susceptibility to source contamination

Barry Husk, Juan Sebastian Sanchez, Roland Leduc, Larissa Takser, Olivier Savary and Hubert Cabana

ABSTRACT

In Canada, the presence of pharmaceuticals and pesticides in municipal drinking water has been examined primarily in larger urban centres which draw their supplies from surface water. However, few studies have examined this issue in smaller and rural communities, which represent nearly one-third of the Canadian population and which draw their drinking water mainly from groundwater. This study presents a regional-scale assessment of the presence of these contaminants in the drinking waters of 17 smaller rural communities, compared with two larger urban communities, in south-central Quebec. From a total of 70 chemicals examined, 15 compounds (nine pharmaceuticals and six pesticides) were detected. The three most frequently detected contaminants were caffeine, atrazine and naproxen, respectively, in 29%, 24% and 21% of the samples. Detections reported here for the first time in Quebec drinking water include the known human carcinogen cyclophosphamide and the fungicide thiabendazole. Maximum concentrations of pharmaceuticals ranged from 30 to 1,848 ng L^{-1} and of pesticides from 21 to 856 ng L^{-1}. This study provides direct evidence that drinking water in smaller, rural communities of Quebec, Canada, whether sourced from groundwater or surface water, can contain measurable levels of pharmaceuticals and pesticides, indicative of their susceptibility to source contamination.

Key words | drinking water, groundwater, pesticides, pharmaceuticals, rural communities, source vulnerability

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INTRODUCTION

Anthropogenic contaminants in drinking water

Sources of drinking water are increasingly subjected to a wide range of trace organic contaminants of anthropogenic origin. Aided by improved analytical methods, such contaminants are now commonly detected in aquatic environments in many countries, including Canada. They are found in both surface water and groundwater (Segura *et al.* 2011; Manamsa *et al.* 2016; Bradley *et al.* 2018), as well as in municipal and domestic wastewater effluent (Kostich *et al.* 2014; Ghoshdastidar *et al.* 2015).

The presence of such trace organic contaminants in aquatic environments is of concern both due to their potential impact on aquatic ecosystems, where sub-lethal effects have been found in aquatic organisms at environmentally relevant concentrations (Brausch *et al.* 2012; Hayes & Hansen 2017), as well as to their potential to influence human health by exposure through consumption of drinking

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water (Daughton 2010; Brender & Weyer 2016; Goodson 2016; Bondy & Campbell 2017; Stayner *et al.* 2017).

Groundwater-sourced drinking water and rural communities

Groundwater, in particular, is a critically important source of drinking water. The quality of groundwater in Canada is increasingly threatened by changes brought about through urbanization, climate change, increasing energy production, intensification of agriculture and subsequent contamination (Council of Canadian Academies 2009; Arnold *et al.* 2016). Nearly a third of the Canadian population, some 12 million people, use groundwater for drinking water, and over 80% of the Canadian rural population depends on groundwater for its entire water supply (Environment & Climate Change Canada 2013). In the province of Quebec, Canada, groundwater enables water supply to nearly 90% of inhabited territory, supplying about 20% of the population, including over 700 municipal drinking water distribution networks, making it the Canadian province with the most municipalities in this situation (Nowlan 2007). Approximately 25% of these Quebec municipal groundwater supply networks apply no treatment to the drinking water before its distribution (MDDELCC 2016).

Rural areas differ from most urban areas in that they source drinking water primarily from groundwater. Consequently, with few exceptions (e.g., Benotti *et al.* 2008; Kozuskanich *et al.* 2014), the majority of studies of treated municipal drinking water systems have, by implication, examined surface water systems which are the primary source of drinking water in larger urban environments. However, anthropogenic contaminants, including human pharmaceuticals, are known to contaminate natural aquatic environments in rural areas with lower population densities (Nebot *et al.* 2015) and groundwater contamination by rural septic system effluents has been recognized as a potential health concern (Withers *et al.* 2014). Also, due to the concentration of agricultural activities in rural areas, these less populous regions are disproportionately at greater risk of exposure to pesticide contamination through drinking water (Hallberg 1989; Starner & Goh 2012; Sultana *et al.* 2018). In addition, in some jurisdictions, regulatory requirements for drinking water testing frequency and number of parameters are less demanding for smaller municipalities, including in this study region where municipalities of less than 5,000 people have lower such requirements due to the cost of analyses (Gouvernement du Québec 2017). This essentially creates a two-tier system of drinking water supply, split roughly along an urban/rural divide, and potentially places populations of smaller rural municipalities at higher risk than those of larger urban municipalities where regulatory requirements are more stringent (Hrudey *et al.* 2008).

Research gaps and challenges

As a preventative measure, public health and environmental authorities in Canada are requiring drinking water suppliers to examine the vulnerability of their sources of drinking water to contamination from anthropogenic pollutants (Government of Ontario 2006; Government of Quebec 2014). However, in spite of the regulatory measures put in place, gaps persist in reaching a full understanding of the vulnerability of treated drinking water to the presence of trace organic contaminants in many parts of Canada, particularly in rural communities using groundwater supplies. Some of those gaps and research challenges include the following:

- Determining sufficient frequency and duration of sampling in order to permit the evaluation of temporal variations.
- Emphasizing regional versus local studies, in order to capture land use, geological and other variables over wider areas.
- Conducting simultaneous sampling of all sites within regional studies to permit accurate temporal comparison between sites.
- Selecting which compounds to analyse from the vast number of potential contaminants, including both regulated and non-regulated contaminants, as well as their degradation by-products and metabolites.
- Achieving acceptable analytical limits of detection (LD) for targeted compounds.

As a result of these combined challenges, there is a limited evidence base available to policymakers, drinking water regulators, suppliers and consumers to enable a better understanding of the presence and susceptibility of treated

drinking water to contamination by trace organic contaminants, especially in smaller, rural communities, including in Quebec, Canada. Taking these situations into account, this study was structured to respond to as many of these research gaps and challenges as possible, while examining the presence of markers of anthropogenic contamination in rural community drinking waters of south-central Quebec.

MATERIALS AND METHODS

Choice of contaminant compounds

While drinking water supplies may be contaminated by trace organic contaminants from a multitude of sources, in order to undertake efficient prevention and remediation programmes it is essential to identify the primary sources of contamination in any particular watershed. To aid in that process, we have identified and structured our search around two major sources of pollutants of anthropogenic origin found in aquatic environments, particularly in rural areas: (a) agricultural products and (b) human wastewater from septic or municipal wastewater effluent.

In order to evaluate exposure of drinking water sources to these two categories of contaminants, a select group of products representative of each category have been chosen in this study as 'markers' (or 'proxies') of the presence of that category. Detection of such markers would thereby indicate the vulnerability of source water exposure to contaminants of that origin, as well as the potential for the presence of other products from the same category. Typically, as markers representative of potential agricultural contamination in drinking water, agronomic pesticides are chosen (Ongley 1996; Snow *et al.* 2009), and in the case of potential contamination by human wastewater, pharmaceuticals are commonly used (Lim *et al.* 2017). Contaminants from both categories were included in this study so as to permit a greater understanding by individual municipalities of specific sources of pollutants susceptible to being found in their region.

The choice of individual compounds selected for analysis is outlined in Table 1. This selection was based on a combination of the volumes of pesticides used in Quebec and the volumes of pharmaceuticals consumed in Canada, as well as the analytical method used and analytical standards available. Products of various sub-categories were included while ensuring that they could be analysed simultaneously according to the multi-residue analytical techniques employed.

Study area and site selection

In order to examine the presence of anthropogenic trace organic contaminants in drinking water supplies on a regional scale, a series of 17 municipalities sourcing their drinking water from groundwater in the south-central region of Quebec was selected. In addition, for comparison purposes, two municipalities sourcing their drinking water from surface water were included, for a total of 19. This group of 19 municipalities covers a geographical area of 2,662 km^2 and includes portions of three Quebec administrative regions (Estrie, Centre-du-Québec and Montérégie) and three surface watersheds (St. Francis, Yamaska and Nicolet Rivers) (Figure 1).

The total population served by all municipal drinking water systems involved in this study is approximately 300,000 (Table 2). The 17 groundwater-sourced municipalities are composed primarily of smaller, rural communities (average population approximately 3,600), whereas the two municipalities sourcing their drinking water from surface water, Sherbrooke and Drummondville, are relatively larger municipalities (populations of 162,000 and 75,000, respectively). Municipal drinking water treatment methods employed by individual municipalities, as well as their population and geographical area, are shown in Table 2.

Sampling methods

The study was conducted in two stages, the first in one rural community sourcing its drinking water from individual private groundwater wells (St-François-Xavier-de-Brompton, 'SFXB'), over two years (2013–2014), every two weeks between May and November, for a total of 26 campaigns. The second stage was conducted on a regional scale in 16 additional rural communities sourcing their municipal drinking water from groundwater, as well as two larger municipalities (Sherbrooke and

Table 1 | List of pharmaceuticals and pesticides examined and related information

Product Pharmaceuticals	Category ATC code[d]	Classification ATC classification[d]	CAS no.[a]	LD[b] ng l^{-1}	LQ[c]
Acetaminophen	–	Anti-inflammatory-antirheumatic	103-90-2	3.58	12.40
Amoxicillin	J01	Systemic antibacterial	26787-78-0	4.90	24.10
Atenolol	C07	Beta-blocker	29122-68-7	1.92	9.44
Bezafibrate	C10	Lipid modifier	41859-67-0	1.94	9.08
Caffeine	N06	Stimulant	58-08-2	4.93	13.50
Carbamazepine	N03	Antiepileptic	298-46-4	10.50	24.40
Cyclophosphamide	L01	Antineoplastic	50-18-0	4.26	11.10
Fenofibrate	C10	Lipid modifier	49562-28-9	1.00	9.20
Ibuprofen	M01	Anti-inflammatory-antirheumatic	15687-27-1	6.94	27.00
Ifosfamide	L01	Antineoplastic	3778-73-2	4.42	12.50
Indomethacin	M01	Anti-inflammatory-antirheumatic	53-86-1	3.46	12.30
Ketoprofen	M01	Anti-inflammatory-antirheumatic	22071-15-4	1.70	6.07
Mefenamic acid	M01	Anti-inflammatory-antirheumatic	61-68-7	1.55	7.51
Naproxen	M01	Anti-inflammatory-antirheumatic	22204-53-1	2.05	11.50
Ofloxacin	J01	Systemic antibacterial	82419-36-1	1.50	10.50
Trimethoprim	J01	Systemic antibacterial	738-70-5	1.23	10.70
Pesticides	**Category**	**Chemical class**			
Acetamiprid	Insecticide	Neonicotinoid	135410-20-7	3.74	9.08
Aldicarb	Insecticide, nematicide	N-methyl carbamate	116-06-3	3.95	13.90
Aldicarb-sulfone	Insecticide, degradation product	N-methyl carbamate	1646-88-4	7.72	19.70
Aldicarb-sulfoxide	Insecticide, degradation product	N-methyl carbamate	1646-87-3	2.04	8.82
Atrazine	Herbicide	Triazine	1912-24-9	4.29	11.90
Azinphos-methyl	Insecticide	Organophosphate	86-50-0	6.50	11.80
Bendiocarb	Insecticide	N-methyl carbamate	22781-23-3	4.78	9.80
Bentazon	Herbicide	Thiadiazine	25057-89-0	6.12	19.70
Boscalid	Fungicide	Anilide	188425-85-6	4.59	14.30
Carbaryl	Insecticide, nematicide	N-methyl carbamate	63-25-2	2.32	6.78
1-Naphthol	Insecticide, degradation product	Organic compound	90-15-3	2.63	6.41
Carbendazim	Fungicide, degradation product	Benzimidazole	10605-21-7	2.52	6.41
Carbofuran	Insecticide, nematicide	N-methyl carbamate	1563-66-2	2.56	6.28
Chlorfenvinphos	Insecticide	Organophosphate	470-90-6	1.32	4.84
Chlorotoluron	Herbicide	Urea	15545-48-9	3.57	8.60
Chlorpyrifos	Insecticide, nematicide	Organophosphate	2921-88-2	1.32	4.84
Clothianidin	Insecticide	Neonicotinoid	205510-53-8	4.63	15.20
Coumaphos	Insecticide	Organophosphate	56-72-4	5.46	12.30
Cyanazine	Herbicide	Triazine	21725-46-2	3.68	9.97
Diazinon	Insecticide	Organophosphate	333-41-5	2.64	6.04
Dimethoate	Insecticide	Organophosphate	60-51-5	2.24	5.86

(*continued*)

Table 1 | continued

Product Pharmaceuticals	Category ATC code[d]	Classification ATC classification[d]	CAS no.[a]	LD[b] ng l^{-1}	LQ[c]
Dinotefuran	Insecticide	Neonicotinoid, guanidine	165252-70-0	5.15	11.10
Diuron (DCMU)	Herbicide	Urea	330-54-1	4.66	9.45
Fludioxonil	Fungicide	Non-classified	131341-86-1	7.21	22.10
Hexazinone	Herbicide	Triazine	51235-04-2	2.65	6.54
Imazethapyr	Herbicide	Imidazolinone	81335-77-5	2.16	5.99
Imidacloprid	Insecticide	Neonicotinoid	105827-78-9	5.56	14.10
Iprodione	Fungicide	Dicarboximide	36734-19-7	10.00	22.60
Isoproturon	Herbicide	Urea	34123-59-6	3.71	8.90
Kresoxim-methyl	Fungicide	Strobin	143390-89-0	8.90	23.60
Linuron	Herbicide	Urea	330-55-2	7.50	25.10
Malathion	Insecticide	Organophosphate	121-75-5	12.80	25.80
Methibenzuron	Herbicide	Urea	18691-97-9	3.60	7.92
Metobromuron	Herbicide	Urea	3060-89-7	7.94	22.80
Metolachlor	Herbicide	Chloroacetanilide	51218-45-2	2.78	6.20
Metoxuron	Herbicide	Urea	19937-59-8	3.06	6.76
Monolinuron	Herbicide	Urea	1746-81-2	2.56	9.42
Nitenpyram	Insecticide	Neonicotinoid	150824-47-8	2.89	7.38
Omethoate	Insecticide	Organophosphate	1113-02-6	7.03	21.40
Parathion	Insecticide	Organophosphate	56-38-2	5.84	19.20
Pendimethalin	Herbicide	2,6-Dinitroaniline	40487-42-1	2.55	7.41
Permethrin	Insecticide	Pyrethroid	52645-53-1	3.10	7.43
Phosmet	Insecticide	Organophosphate	732-11-6	3.76	9.27
Piperonyl butoxide	Synergist for insecticides	Non-classified	1951-03-06	2.09	5.39
Pyraclostrobin	Fungicide	Strobin	175013-18-0	3.32	8.92
Pyrimethanil	Fungicide	Pyrimidine	53112-28-0	6.46	14.60
Sebuthylazine	Herbicide	Triazine	7286-69-3	2.71	5.82
Simazine	Herbicide	Triazine	122-34-9	3.46	8.84
Spinosad A	Insecticide	Spinosyn, macrocyclic lactone	131929-60-7	2.77	8.29
Terbuthylazine	Algaecide, herbicide, microbiocide	Triazine	5915-41-3	2.73	7.05
Thiabendazole	Fungicide	Benzimidazole	148-79-8	2.08	5.59
Thiacloprid	Insecticide	Neonicotinoid	111988-49-9	2.34	5.13
Thiamethoxam	Insecticide	Neonicotinoid	153719-23-4	3.54	9.54
Trifloxistrobin	Fungicide	Strobin	141517-21-7	3.50	7.92

[a]Chemical Abstracts Service number (American Chemical Society 2018).
[b]Analytical method limits of detection.
[c]Analytical method limits of quantification.
[d]Anatomic Therapeutic Chemical Classification (World Health Organization Collaborating Centre for Drug Statistics Methodology 2018).

Drummondville) sourcing their drinking water from surface water. Sampling for this second stage was carried out monthly over two years (2014–2015), between May and November, for a total of 12 campaigns. The December to April period was excluded from sampling of both stages for logistical reasons. Discrete (grab) samples were

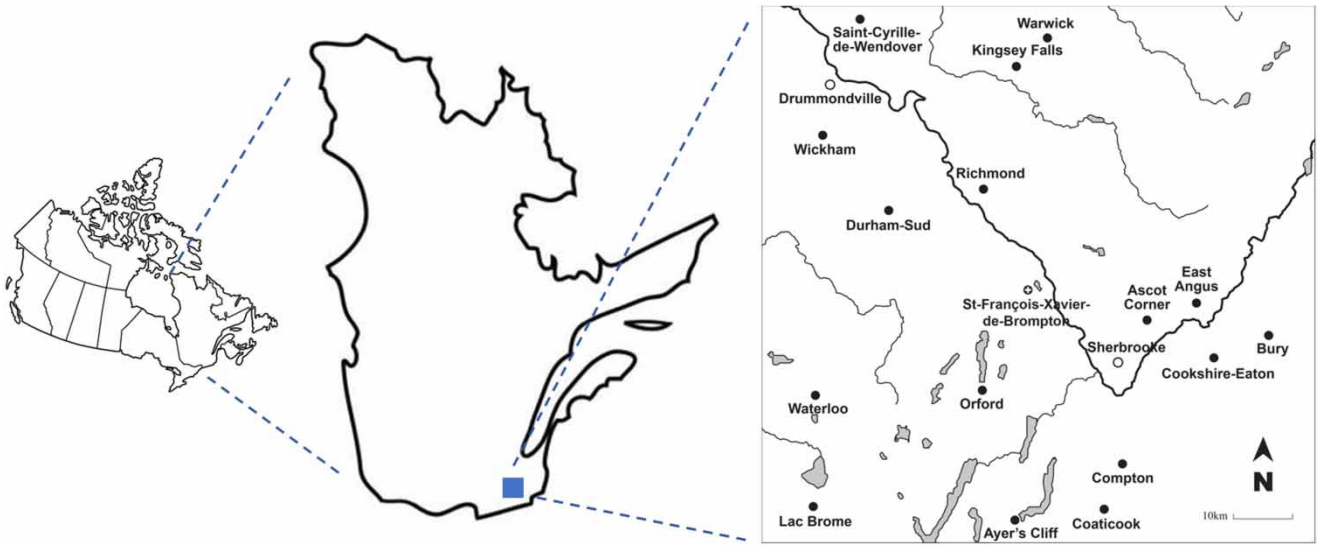

Figure 1 | Map illustrating the study area located in south-central Quebec, Canada.

collected from each municipality in 1 litre, trace-cleaned, amber glass bottles, at drinking water points available to the public (e.g., public washrooms) within the areas served by each municipal drinking water distribution system. In the case of SFXB, samples were collected in five individual residences at drinking water point-of-use. For each sampling campaign municipalities were all sampled on the same date within a period of 8 hours, and individual municipalities were always sampled at the same location (with the exception of SFXB). In all cases, water was allowed to run from the taps for 2 to 3 min before collecting the sample. The water samples were transported on ice and stored the same day at 4 °C in the dark until sample preparation and analysis, according to standard sampling procedures (MDDEP 2011; CEAEQ 2014).

Analytical methods

The analytical methods for pharmaceuticals and pesticides used in this project were performed according to Ba *et al.* (2014) and Haroune *et al.* (2014, 2015). Analysis was performed on an Acquity UPLC XEVO TQ mass spectrometer (Waters Corporation, Milford, MA, USA) using an Acquity UPLC HSS-T3 column (100 mm × 2.1 mm, 1.8 μm) equipped with a fritted 0.2 μm pre-filter (Waters Corporation). The solvent flow rate was set to 0.40 mL min^{-1} and the column temperature was kept at 35 °C. The sample volume injected was 5 μL. The mobile phase was (A) 0.20% formic acid/water and (B) 0.20% formic acid/methanol acetonitrile (80:20 v/v). In the case of pharmaceuticals, the elution gradient started with 5% of eluent B, increasing to 90% in 8 min and then back to initial conditions in 4 min. For pesticides, the elution gradient started with 5% of eluent B for 1 min, increased to 80% in 5 min, increased to 90% in 1 min, held for 2 min and then back to 5% in 1 min. A positive electrospray ionization (ESI+) source in multi-reaction monitoring mode was used. The optimized parameters were obtained by direct infusion of analytical standard solutions at 10 μg mL^{-1} as follows: desolvation gas (N_2) at 800 L h^{-1}; cone gas (N_2) at 50 L h^{-1}; collision gas (N_2) at 0.22 mL min^{-1}; capillary voltage 2.5 kV; source temperature of 150 °C and desolvation temperature of 550 °C. Two daughter traces (transitions) were used. The most abundant transition was used for quantification, whereas the second most abundant was used for confirmation. Calibration was done according to the calibration curve method. The matrix effects were determined by comparing the slope of a calibration curve (6-point regression curves from 0.10 to 30.0 ng mL^{-1}) acquired in the matrix (drinking water) and the slope of a calibration curve acquired in the solvent (acidic aqueous methanol). Both calibration curves were performed in triplicate. The recovery was between 90% and 110% (data not shown).

Table 2 | Municipalities studied, indicating the population, geographical area and drinking water treatment methods

Municipalities	Population[a]	Geographical area[a] (km^2)	Drinking water treatment methods[b,c]
Groundwater sourced private wells ($n = 5$)			
St-François-Xavier-de-Brompton	2,325	98.7	Softening
Groundwater sourced municipalities			
Ascot Corner	3,090	85.0	Chlorination
Ayer's Cliff	1,111	7.3	Chlorination
Bury	1,219	235.0	(No treatment)
Coaticook	9,224	222.7	Other
Compton	3,198	207.6	Chlorination
Cookshire-Eaton	5,250	298.0	Chlorination
Durham-Sud	1,017	92.6	(No treatment)
East Angus	3,773	8.3	Chlorination
Kingsey Falls	2,038	70.5	Chlorination, softening
Lac-Brome (Knowlton)	5,611	222.9	Chlorination
Orford	3,949	148.2	(No treatment)
Richmond	3,293	6.9	Chlorination, filtration, iron/manganese
St-Cyrille-de-Wendover	4,651	109.8	Chlorination, filtration, iron/manganese
Warwick	4,699	110.4	Chlorination
Waterloo	4,446	13.3	Chlorination, filtration, iron/manganese
Wickham	2,500	98.9	Chlorination, filtration, iron/manganese, softening
Subtotal	59,069	1,937.3	
Surface water sourced municipalities			
Drummondville	74,540	259.7	Chlorination, filtration, charcoal
Sherbrooke	162,163	366.2	Chlorination, ozonation, micro-straining
Subtotal	236,703	625.9	
Grand total	298,097	2,661.9	

[a]Répertoire des municipalités (Ministère des Affaires municipales et Occupation du territoire du Québec 2018).
[b]Répertoire des stations municipales de production d'eau potable approvisionnées en eau souterraine (Ministère du Développement durable Environnement et Lutte contre les changements climatiques du Québec 2018b).
[c]Répertoire des stations municipales de production d'eau potable approvisionnées en eau de surface (Ministère du Développement durable Environnement et Lutte contre les changements climatiques du Québec 2018a).

No significant matrix effect was observed. The tandem mass spectrometry (MS/MS) acquisition and data processing were performed with Masslynx 4.1 software (Waters Corporation).

Quality assurance

The analytical method LD and limits of quantification (LQ) were determined in matrix regression using five replicates from independent calibration solutions to minimize systematic errors and six levels of concentration ranging from 0.10 to 30.0 ng mL^{-1}. The LD and LQ were calculated as three and 10 times the standard deviation of y-intercepts of regression lines (ICH Harmonised Tripartite Guideline 2005) and the LD and LQ values for each analyte are as listed in Table 1. Standard concentrations were prepared and analysed for every 12 samples to confirm percentage recovery. In order to minimize the sorption of target contaminants on glassware during experiments, all glassware was deactivated using 5% (v/v) dimethyldichlorosilane in toluene (soaked for 1 h). Glassware was then rinsed with two volumes of toluene and then with three volumes of methanol and water until reaching a neutral pH.

A field quality assurance protocol was used to determine the effect, if any, of field procedures on concentrations of contaminants in water samples. Field blank samples were taken on a rotating basis of municipalities (for municipal wells: two per sampling date, 12% of samples; for SFXB private wells: one per sampling date, 20% of samples) using laboratory grade, organic-free water and were processed and analysed for all analytes as described for the other samples. No specific trend in blank contamination as to compound, municipality or date was observed. A conservative approach was chosen for data censorship by discarding all field sample results for any compound that was detected in blank samples, for each sampling date.

RESULTS AND DISCUSSION

Detections, quantifications and concentrations

Of the 70 compounds evaluated in 314 samples, 15 products (nine pharmaceuticals and six pesticides) were detected in at least one sample over the three-year period of the study.

Results are presented in Table 3, indicating the number of detections and quantifications, the frequency of detection, as well as the maximum concentrations detected per molecule, and are compared to the Quebec regulatory drinking water standards (also Appendix, Figure A1, available with the online version of this paper). All quantification results were statistically non-normally distributed according to the Shapiro–Wilk test ($p < 0.01$), histogram, kurtosis and skewness evaluations. Tabulation and statistical analysis of results were performed in Microsoft Excel (Microsoft Corporation), incorporating RealStats Resource Pack (Real Statistics).

The three most frequently detected contaminants were caffeine, atrazine and naproxen, respectively, in 29%, 24% and 21% of the samples. The highest concentrations of single contaminants found were for mefenamic acid (1,848 ng L^{-1}), cyclophosphamide (1,233 ng L^{-1}), and metolachlor (856 ng L^{-1}) (Table 3). To the best of our knowledge, this is the first reporting of the known human carcinogen cyclophosphamide and the fungicide thiabendazole in treated municipal drinking water in Quebec, Canada.

Thirty-one per cent of samples contained multiple contaminants, with a maximum of 13 contaminants being detected in 15 samples. Total mean detections per sample were slightly more than double for pharmaceuticals (16 compounds analysed) over pesticides (54 compounds analysed) at 1.50 and 0.70 detections per sample, respectively, for the total study period (Table 4).

Temporal variation

The results of monthly temporal variation as determined by the number of detections per sample, per month, per molecule, are illustrated in Table 4 (also Appendix, Figure A2, available online). Temporal presence of pesticides per sample increased steadily from May until peaking in August and September, followed by a downward trend in

Table 3 | Contaminant detection and concentration results for all study years, all samples combined, compared to regulatory drinking water standards for Quebec

Product	Total samples	Number of results		Frequency of detection	Maximum concentration ng L^{-1}	Quebec regulatory standard[c]
		> LD[a], <LQ	> LQ[b]			
Pharmaceuticals						
Caffeine	314	62	29	29%	285	*
Naproxen	314	57	9	21%	404	*
Ofloxacin	314	59	2	19%	177	*
Acetaminophen	314	47	8	18%	147	*
Cyclophosphamide	314	37	12	16%	1,233	*
Ibuprofen	314	44	1	14%	97	*
Mefenamic acid	314	38	7	14%	1,848	*
Carbamazepine	314	27	3	10%	30	*
Bezafibrate	314	26	3	9%	79	*
Pesticides						
Atrazine	314	45	30	24%	606	3,500
Metolachlor	314	38	16	17%	856	35,000
Hexazinon	314	32	1	11%	21	*
Terbuthylazine	314	32	2	11%	287	*
Thiabendazole	254	20	3	9%	125	*
Carbendazim	254	0	1	<1%	71	*

[a]Analytical method limit of detection.
[b]Analytical method limit of quantification.
[c]Quebec regulatory standards for drinking water (Ministère du Développement durable Environnement et Lutte contre les changements climatiques du Québec 2017).
*Product unregulated in Quebec.

Table 4 | Temporal variation of detections, indicating the number of detections by month, by category and molecule, as well as mean detections per sample, for all samples combined

	May	June	July	August	Sept.	Oct.	Nov.	Total
No. samples	38	43	71	48	43	38	33	314
Pharmaceuticals								
Caffeine	1	16	19	29	11	11	4	91
Naproxen	2	6	15	10	11	16	6	66
Ofloxacin	2	4	13	10	12	10	10	61
Acetaminophen	4	8	13	10	12	8	0	55
Cyclophosphamide	0	7	11	0	10	10	11	49
Ibuprofen	0	2	7	6	10	10	10	45
Mefenamic acid	4	1	9	0	10	12	9	45
Carbamazepine	3	0	9	0	10	8	0	30
Bezafibrate	0	0	0	0	10	10	9	29
Sub-total detections-Pharmaceuticals	16	44	96	65	96	95	59	471
Mean detections/sample	0.42	1.02	1.35	1.35	2.23	2.50	1.79	1.5
Pesticides								
Atrazine	0	6	24	18	15	5	7	75
Metolachlor	0	6	13	14	10	5	3	51
Terbuthylazine	0	2	4	8	10	5	5	34
Hexazinon	0	2	5	10	10	6	0	33
Thiabendazole	3	3	0	4	6	10	0	26
Carbendazim	0	0	0	1	0	0	0	1
Sub-total detections-Pesticides	3	19	46	55	51	31	15	220
Mean detections/sample	0.08	0.44	0.65	1.15	1.19	0.82	0.45	0.7
Combined totals								
Detections	19	63	142	120	147	126	74	691
Mean detections/sample	0.5	1.47	2.0	2.50	3.42	3.32	2.24	2.2

detections until November. This trend corresponds to findings elsewhere of minimum values occurring before, and maximum values after, spring applications of agricultural herbicides (United States Geological Survey 1996). Detections of pharmaceuticals per sample increased from May through to the end of October, then reduced in November.

As previously noted, sampling during the winter period of December to April was not conducted during this study. However, research has shown that aquatic concentrations of pharmaceuticals, and the consequent risk for contamination of drinking water, can severely increase during cold seasons in boreal regions (Vieno *et al.* 2005). It is therefore strongly recommended that future studies in this region include sampling during the winter period, particularly for pharmaceuticals.

Sources of contaminants by municipality

In many jurisdictions, including this study region, municipalities are required to evaluate potential risks to public drinking water supplies from sources of anthropogenic contamination (Government of Ontario 2002; MDDELCC 2014). Moreover, the World Health Organization recommends that municipalities implement water safety plans (WSPs), a comprehensive approach for risk assessment and risk management of drinking water (World Health Organization 2008). However, many of these studies do not examine sources of contaminants or do not include anthropogenic contaminants.

In this study, we have categorized contaminants according to their source, either from human waste

(pharmaceuticals) or agriculture (pesticides). In Figures 2 and 3, we show the relative influence of each of these categories of contaminant, by municipality, as expressed by the mean number of detections per sample, by category (also Appendix, Figure A3, available online). In the context of evaluating the vulnerability of drinking waters' sources to anthropogenic contaminants, such analyses could allow municipalities to more accurately target sources of contamination for their individual conditions. For example, the municipality of Ayer's Cliff indicates relatively stronger contamination from human waste markers (Figure 2), but no contamination from agricultural markers (Figure 3). Conversely, the municipality of Waterloo indicates relatively high detections of agricultural pesticides (Figure 3), but no detections of human waste markers (Figure 2). However, the municipality of Drummondville, sourcing its drinking water from river surface water, indicates relatively important influences by both human waste (Figure 2) and agriculture (Figure 3) markers.

Although private well owners, such as in the municipality of SFXB, are not required to determine sources of contamination in their drinking water, the strong presence of both categories of these contaminants (especially pharmaceuticals) in their water supply weighs in favour of further examination of this issue.

Eighteen of the 19 municipalities evaluated were affected by contamination of either pesticides or pharmaceuticals, or both. Three municipalities (Sherbrooke, Richmond, Waterloo) were affected only by agricultural influence (pesticides) and six municipalities (Kingsey Falls, Ascot Corner, East Angus, Coaticook, Ayer's Cliff, Lac-Brome) were affected only by pollutants linked to human wastewater (pharmaceuticals). Finally, the municipalities of Wickham, Durham-Sud, Orford, Compton, Drummondville, Warwick, St-François-Xavier-de-Brompton and Cookshire are affected by pollutants from both human wastewater and agricultural contaminants.

Three of the 18 municipalities – Bury, Durham-Sud and Orford – do not treat their drinking water. Of these three, results for Bury indicated no presence of any of this study's contaminant markers. However, the other two – Durham-Sud and Orford – showed the presence of both pesticides and pharmaceutical products.

Although this study was not designed to directly answer questions regarding how differing land uses affect the

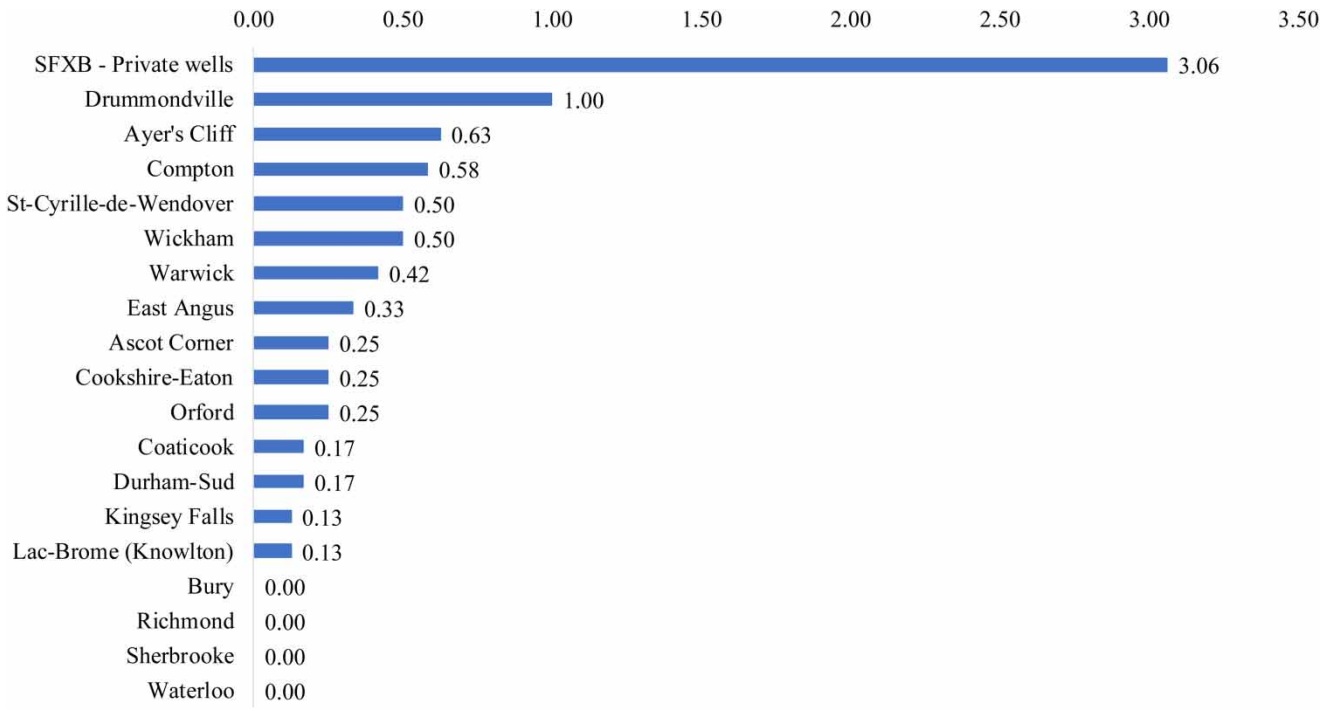

Figure 2 | Human wastewater influence (i.e., presence of pharmaceuticals). Mean number of detections of pharmaceuticals per sample, by municipality, all samples combined.

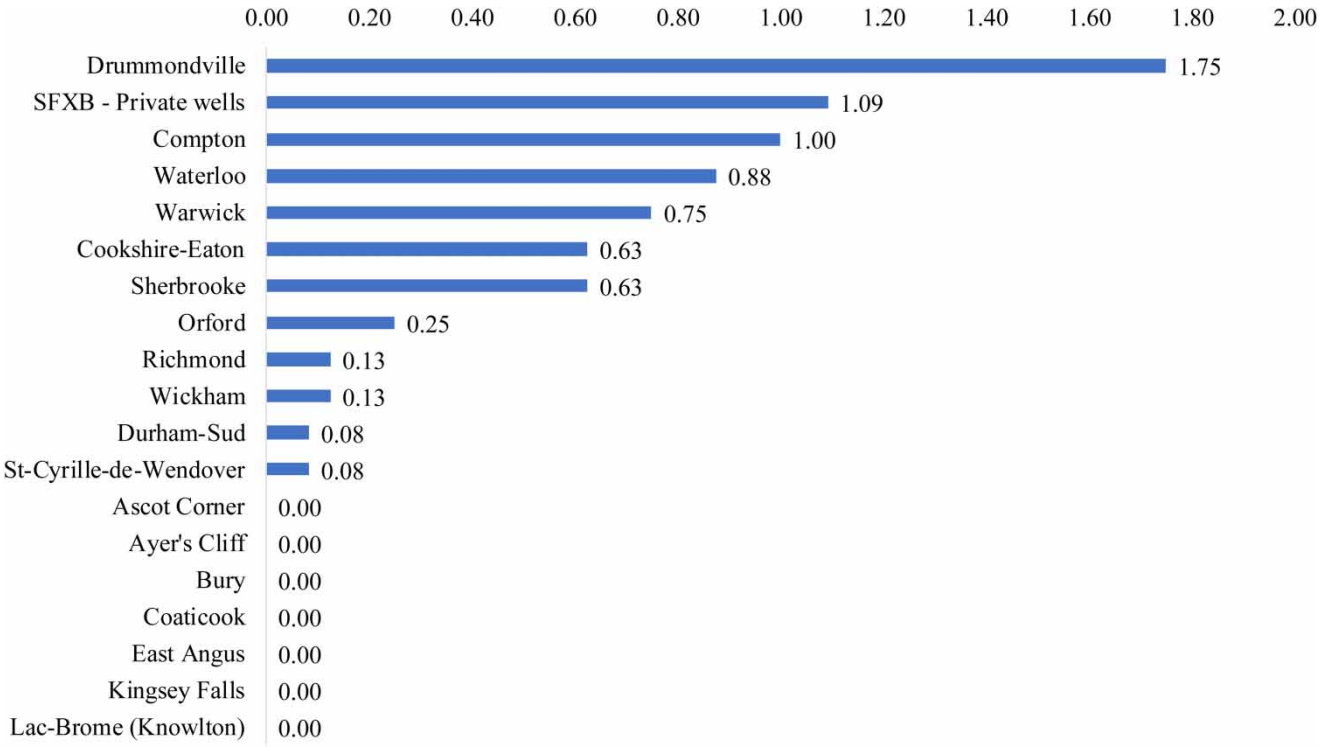

Figure 3 | Agricultural influence (i.e., presence of pesticides). Mean number of detections of pesticides per sample, by municipality, all samples combined.

presence of contaminants in groundwater-sourced drinking water, other aquifer research conducted in this same region determined that landscape-scale contaminant data were not a predictor of groundwater pollution (Saby *et al.* 2017). Also, research conducted elsewhere has determined that concentrations of pharmaceuticals in aquatic systems are correlated with human population density in the drainage area, volume of the receiving waterbody and technologies used in wastewater treatment systems (Hughes *et al.* 2012).

Significant differences exist between the two surface water-sourced municipalities, both in terms of source of water as well as treatment methods (Table 2 and Appendix, Table A1, available online). Sherbrooke's water source is a major lake close to watershed headwaters (Lake Memphremagog) with relatively little municipal human wastewater influence, whereas Drummondville's water source is the St. Francis River near its outlet, situated downstream of several other municipalities, agricultural areas, industries and landfill sites. In this respect, Drummondville's source water is likely subject to greater anthropogenic contamination than that of Sherbrooke. While Drummondville's drinking water contains the highest level of mean detections of both pesticides and pharmaceuticals per sample of municipal water, that of Sherbrooke is comparable to those of all groundwater-sourced municipalities combined. As the municipal treatment methods of Drummondville water are equivalent or superior to those of the other municipalities (Table 2), the higher contaminant results in treated water for this municipality are likely related primarily to a greater presence of contaminants in its source water, although this would require further verification.

These results illustrate how such analysis could assist municipal water resource managers in the determination of sources of anthropogenic contamination for each municipality and in their water sanitation programmes. It is also an indication that private groundwater wells can be equally or more affected by these contaminants than municipal drinking water sources.

Potential human health issues and concerns

While human health issues are not the primary focus of this study, it is important to place the findings of this study in the

overall context of potential health risks and regulatory considerations. Of the toxic substances included within Canadian and Quebec drinking water guidelines, several relate to pesticides, but none relates to pharmaceuticals (Government of Canada 1999; Gouvernement du Québec 2017). Only 16 pesticides are currently required to be evaluated by municipalities according to the drinking water regulations of the jurisdiction of this study. In contrast, the European Commission in its Drinking Water Directive specifies that concentrations of any pesticides may not exceed 0.1 μg L^{-1} for a single pesticide and 0.5 μg L^{-1} for total pesticides (European Commission 1998). Our study confirms the presence of several pesticides in treated drinking water, some of which have been reported to be linked to birth defects, fetal development or preterm delivery (Brender & Weyer 2016; Bondy & Campbell 2017; Hayes & Hansen 2017; Stayner *et al.* 2017).

In addition to the findings in this study, pharmaceuticals are frequently detected in treated drinking water elsewhere (Benotti *et al.* 2008; Daughton 2010). In this study, the finding of cyclophosphamide, detected in 49 samples, or 16%, is of particular concern. Cyclophosphamide is a medication used as chemotherapy and to suppress the immune system. It is a known human carcinogen and is a cytotoxic, genotoxic, anti-neoplastic drug, even at low concentrations (Zounková *et al.* 2007). It was detected repeatedly and consistently in five out of seven months of the May to November period of this study, in multiple municipalities, confirming its regular presence in these drinking waters. Its levels of detection surpassed concentrations of 1.2 μg L^{-1}, far exceeding concentrations of such cytotoxic drugs found in drinking water elsewhere (Aherne *et al.* 1990; Johnson *et al.* 2008). Based on 1.5 L day^{-1} of adult water consumption, exposure to this chemical could exceed the suggested 1,500 ng $person^{-1}$ day^{-1} threshold of toxicological concern (Kroes *et al.* 2000). An additional potential concern with such cytotoxic drugs is the possibility that carcinogenic effects could exist at any level of exposure (i.e., there is no threshold dose below which no carcinogenic effects may occur). Of particular concern are any special subgroup populations which may be more vulnerable to developmental concerns, such as pregnant women, their fetuses and breast-fed infants (Johnson *et al.* 2008; Rowney *et al.* 2009). Therefore, when considering potential indirect exposure via drinking water supplies, the use of a benchmark based on therapeutic dose may not be applicable to any pharmaceuticals that may be non-threshold genotoxins (Webb *et al.* 2003). Also detected at high concentrations is mefenamic acid, a member of the nonsteroidal anti-inflammatory class of drugs (NSAIDs) and which is used to treat mild to moderate pain.

The results of our study also indicate that drinking water in this region is a vector of exposure to complex mixtures of chemicals, with as many as 13 separate compounds of the 70 tested being detected in individual samples (Appendix, Table A2, available online). However, the compounds targeted in this study are only a fraction of the estimated 80,000+ parent compounds in commercial production (Monteiro & Boxall 2010), in addition to an unknown number of associated environmental metabolites and degradants potentially present (Vasquez *et al.* 2014). The standard protocol for deriving toxicity values uses single chemical exposure under controlled settings, a situation that is not realistic in everyday life (Ducey & Sapkota 2010). Exposure to such mixtures can result in cumulative, additive and synergistic effects on health (the so-called 'cocktail effect'), regardless of whether each individual contaminant is below its maximum acceptable regulatory concentration (Kortenkamp *et al.* 2007). This situation calls for a systematic risk assessment of exposure to these chemicals as mixtures, instead of as individual compounds (Carpenter *et al.* 2002; Zeliger 2003).

In addition, other studies have found certain environmental contaminants to have potential endocrine disrupting properties (Kortenkamp *et al.* 2011; Vandenberg *et al.* 2012; Vandenberg 2014), including atrazine and carbamazepine (Benotti *et al.* 2008), both of which are found in this study. Furthermore, pregnant women may be exposed through drinking water to several drugs that are teratogenic and in the post-natal period to drugs that are contraindicated during breastfeeding, including carbamazepine and cyclophosphamide, both present in this study (Mirkes 1985; Matalon *et al.* 2002).

All drinking water treatment plants in this study use chlorine-based disinfection methods which are subject to the unintentional production of disinfection by-products. Although not evaluated in this study, the presence of these by-products is a growing health

concern due to their acknowledged carcinogenic/genotoxic potential (Richardson *et al.* 2007).

CONCLUSIONS AND RECOMMENDATIONS

This study examined the presence of markers for two categories of anthropogenic contamination of rural community drinking waters in south-central Quebec, Canada. By sampling at point-of-use, simultaneously in several municipalities, on a regional scale and over three seasons and three years, this study provides significant baseline data concerning the presence of pesticides and pharmaceuticals in finished drinking water in this region. We find that treated drinking water at point-of-use in rural municipalities of Quebec can contain measurable levels of pharmaceuticals and pesticides, an indication of the vulnerability of drinking water sources to contamination by either human wastewater or agricultural practices, as well as the inability of drinking water treatment systems to completely remove these contaminants. The results further demonstrate both temporal and spatial variations in the presence of these contaminants on a regional basis. Municipalities and other government agencies must consider the implementation of drinking water treatment systems capable of further reducing or eliminating the presence of these contaminants. In addition, smaller, rural municipalities should be subject to regulatory contaminant monitoring at least equal to that of larger municipalities, such that their populations benefit from equal knowledge and protection from contaminant exposure. Our research calls for prompt evaluation of the potential effects on human health by exposure through drinking water to such detected trace organic contaminants and their metabolites – individually as well as in mixtures – especially with regard to more vulnerable populations. In particular, the finding of the carcinogen cyclophosphamide in this study emphasizes the need for research into the occurrence of pharmaceuticals in the environment and the presence of high-risk compounds such as this, especially in drinking waters. We call on policymakers and scientists to cooperate in the establishment of a combination of monitoring, regulation and management measures to address the growing issue of trace organic contaminants in drinking water as established in this and other studies.

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