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Chemical contaminants in Brazilian drinking water: a systematic review

Luciano Barros Zini and Mariliz Gutterres

ABSTRACT

The goals of this research are to evaluate which chemical contaminations were detected in Brazil's drinking water reported in papers published from 2012 to 2019, to propose guideline values for emerging contaminants and assess which are the priority parameters from a health risk perspective. The methodology used was a systematic review. The chemical contaminants quantified were evaluated according to Brazilian drinking-water standards, and Guideline Values were proposed for emerging pollutants using conservative endpoints from NOAEL and LOAEL available in literature. From 1351 articles evaluated, 15 reached the research goal. Seventy-seven parameters were quantified in Brazilian drinking water from underground, surface and rainwater sources. Soil composition, mining, sewage and agricultural activities were the main sources for the seven classes framed: pesticides, metals, organic, endocrine disruptors, drugs, personal care products and illicit drugs. Twenty-two parameters are listed in the current Brazilian drinking water quality standard and 54 are not. Water was not considered appropriate to drink due to cadmium, aluminum, iron, nickel, mercury, atrazine, propionaldehyde, beryllium, acetone and 17 α-ethinyl estradiol (carcinogenic). Measures to reduce chemical contamination in drinking water need to be taken such as the expansion of sewage treatment and upgrading to tertiary treatment, and controlling and reducing the application of pesticides.

Key words | chemical contaminant, drinking water, emerging pollutants, guideline value, health-based target, health risk assessment

HIGHLIGHTS

- 77 parameters were evaluated in Brazilian drinking water from 15/1351 articles.
- 10 parameters exceeded the health limits for potability.
- Soil components, mining, sewage and agricultural activities were the main sources.
- Improve sewage treatment and reduced pesticide use are required.
- New guideline values are proposed for 49 emerging pollutants.

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GRAPHICAL ABSTRACT

INTRODUCTION

Chronic diseases such as cancer can be associated with several variables like chemical contamination, complex mixtures, occupational exposures, physical and biological agents, lifestyle and genetic disposition of each individual, in addition to the fact that some studies point to a correlation between environmental contaminants and cancer (Siddique *et al.* 2016; Evans *et al.* 2019; Yin *et al.* 2020). The 69th World Health Assembly's report, with delegations from 194 member states, indicates that about 25% of the global burden of morbidity in humans is linked to environmental factors, in particular exposure to chemical substances, and that the annual global sales of chemical products doubled between 2000 and 2009. The forecast is that they will multiply by six between 2010 and 2050 (OMS 2016). In Brazil, for the 2018–2019 biennium, 600,000 new cases of cancer were estimated to occur each year (INCA 2017). One of the hypotheses for the cause of chronic diseases such as cancer is long-term exposure to chemical contaminants through drinking water in low concentrations, and the work presents a systematic review to study what has been detected in terms of chemical contaminants in Brazilian drinking water, to propose guideline values (GV) for emerging contaminants and assess which are the priority parameters from a health risk perspective.

The world estimate shows that in 2018 there were 18.1 million new cases of cancer and 9.6 million deaths. In general, the highest incidence rates were observed in developed countries (North America, Western Europe, Japan, South Korea, Australia and New Zealand). Intermediate rates are seen in South and Central America, Eastern Europe and much of Southeast Asia (including China) (Bray *et al.* 2018). Governments recognize the importance of the rational management of chemicals for the protection of human health. This is recorded in the World Sustainable Development Goals, goal 3.9: by 2030, the number of deaths and illnesses caused by dangerous chemicals, air contamination, water and soil to be considerably reduced; and goal 6.3: by 2030 to improve water quality and minimize chemical emissions and hazardous materials (UN 2015). However, what are these chemical contaminants, what are the priorities and what health risk do they pose to the population?

Brazil has about 210 million inhabitants, 5570 municipalities distributed in 26 states and a federal district. Agriculture is the main base of Brazilian's economy and pesticide use has increased by 83%, rising from 300,000 to 549,000 tons from 2009 to 2018 (IBAMA 2020). It is estimated that more than 100 million Brazilians do not have access to sewage treatment (SNIS 2019). Untreated sewage represents a risk for waterborne diseases, or acute diseases, that are transmitted by microbial pathogens, with the causal link being the presence of viruses, bacteria

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(removed by disinfection) or protozoa detected in drinking water. Microbiological contamination in drinking water has acute effects and there are published reviews about outbreaks caused by protozoa (Baldursson & Karanis 2011; Murphy *et al.* 2014; Efstratiou *et al.* 2017), with registered outbreaks since 1954 (Karanis *et al.* 2007). However, what are the chemical risks for untreated sewage?

Regarding chemical contamination in drinking water, there are systematic reviews related to arsenic (Celik *et al.* 2008; Argos *et al.* 2010; Esteban *et al.* 2014; Saint-Jacques *et al.* 2014; Tsuji *et al.* 2014), fluoride (Taghipour *et al.* 2016), heavy metals (Razak *et al.* 2015), sodium (Talukder *et al.* 2017), hardness (Gianfredi *et al.* 2017) and some of the papers try to study the impacts they have on health through meta-analyzes or epidemiological studies.

Brazil's drinking water quality standard is provided in Annex XX Health's Ministry n° 5/2017 and the framework has to be met by those responsible for supplying drinking water (municipality, municipal or state public company, or private company) and for assuring quality control purposes to be accomplished in the semi-annual analysis of 89 parameters distributed in inorganics, organics, pesticides and disinfection by-products. Each parameter has a health-based target (HBT) to classify water potability. These parameters have been valid in Brazil since December 2011 and there is a review in progress by the Brazilian Ministry of Health, scheduled for publication in 2021, so the present study will serve as a tool to support this and future governmental review processes.

Emerging pollutants are defined by the lack of regulation and are not commonly monitored but they have the potential to cause adverse effects on the environment and humans (Geissen *et al.* 2015). Although analytical methods have already been developed for emerging pollutant detection like drugs, hormones, personal care products (PCP) or even illicit drugs like cocaine and its metabolites (Torres *et al.* 2015; Caldas *et al.* 2016; Campestrini & Jardim 2017), they do not have HBT in drinking water compliance. Authors reviewed the literature on emerging contaminants in aquatic matrices in Brazil from 1997 to 2016 (Montagner *et al.* 2017), however a review about chemical contaminants from a public health perspective about drinking water is not available to the best of our knowledge.

This study differs from others because it is a systematic review from a drinking water and health risk perspective, based on chemical contaminations reported in published papers from 2012 to 2019, a period that coincides with the Brazilian potability standard valid since December 2011, and proposes guideline values for non-regulated parameters. Disinfection by-products, fluoride contents, arsenic concentrations and cyanobacterial flowering toxins were not included in the present study. This study does not intend to reach all contamination detected in Brazilian drinking water, just that which can be found by the proposed methodology.

METHODS

The search of the scientific literature was performed based on review protocol Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) (Liberati *et al.* 2009). The first step for conducting the review consisted of the definition of relevant research question, databases and appropriate search terms according to keywords and a search algorithm for the review objective. The next step comprised a database search and preliminary selection based on the title. Then the abstracts were assessed in order to identify papers that helped to answer the research question: what chemical contaminations were detected in Brazil's drinking water?

The interfaces of Science Direct, Pub Med and Scopus were selected to search the published scientific papers in journals. The search algorithm used was: (potable water OR drinking water) AND (chemical contaminant OR contaminants) AND (water analysis) AND (Brazil). Filters were applied from 2012 to 2019 only for scientific articles. Articles that met the criteria of having chemical contamination in drinking water's detection or quantification from samples collected in Brazilian territory were previously selected and subsequently evaluated in full.

The parameters quantified were evaluated from a health risk perspective according to Brazil's drinking-water quality standards, and a guideline value (GV) was proposed for emerging pollutants. Drinking water was classified as potable or not according to the HBT in Brazil's drinking-water quality standards. For the unforeseen parameters, guideline

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values were elaborated according to Guidelines for Drinking-Water (WHO 2017) based on a literature review regarding toxicological data and subsequently evaluated if the emerging pollutant's quantified concentration was below or above the GV proposed.

RESULTS AND DISCUSSION

The total number of articles found was 1351; 1190 in the Science Direct database, 33 in Pub Med and 128 in Scopus. There were 33 surveys conducted in Brazil involving analyses of raw water, sludge from the decanter, effluent and spring, and 27 articles met the criteria for analyzing drinking water's chemical contaminants in Brazilian territory after reading the title and abstract. After detailed reading of the 27 articles, it was observed that in fact 15 fully met the criteria according to the systematic review selection process shown in Figure 1.

Table 1 shows the systematic review's results. Chemical contaminants in drinking water were found in 18 cities from six states, besides a nationwide survey in 22 capitals (Machado *et al.* 2016) and two studies in the states of Rio Grande do Sul (Oliveira *et al.* 2019) and Minas Gerais (Reis *et al.* 2019) that did not mention the cities. From the 15 articles that met all criteria, 77 different parameters were quantified in drinking water. They were organized in seven different classes with the respective number of parameters quantified: pesticide, 21; metal, 15; drug, 16; endocrine disruptor, 11; organic, eight; PCP, three; and illicit drugs, two. Caffeine and phenolphthalein were also found. The analytical methods were LC-MS/MS, GC-qMS, LC-UV and ICP-MS. The limits of quantification ranged from 0.5 ng/L to 125 μg/L. Drinking water samples

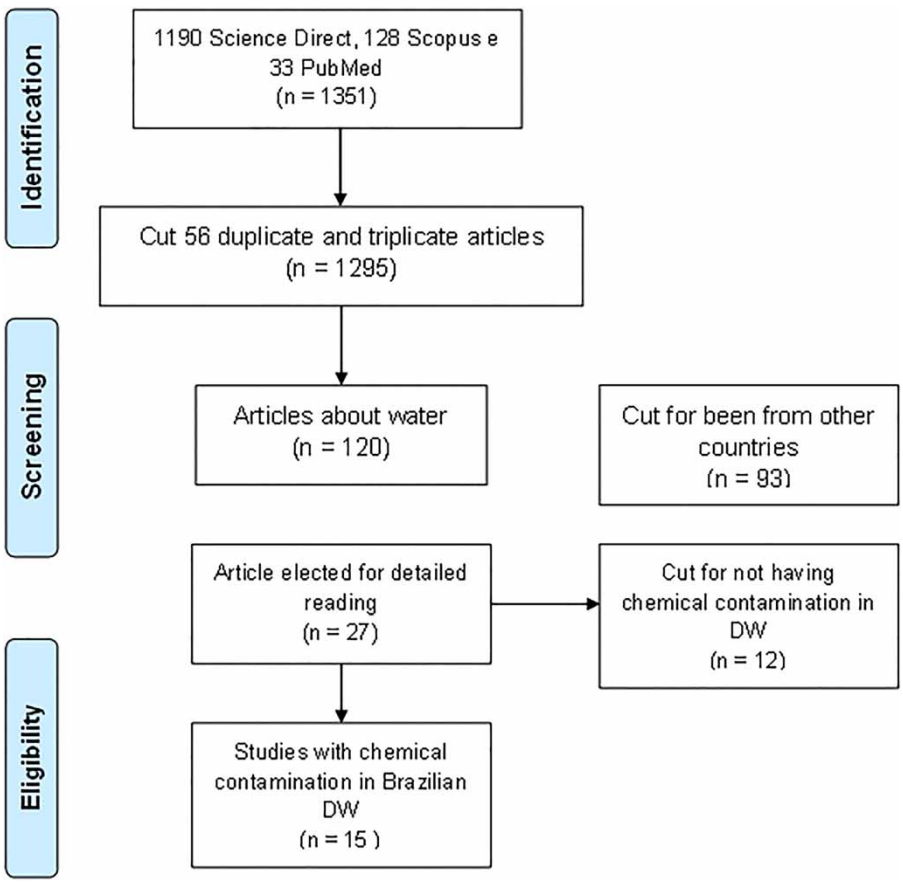

Figure 1 | Systematic review selection process.

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Table 1 | Chemical contamination in Brazilian drinking water, from 2012 to 2019

Parameter	Class	N	Result (μg/L)	DL μg/L	QL μg/L	Analytical Method	Source	City – FU	HBT[a] μg/L	Reference
Atrazine	Pesticide	2/62	0.01–0.02	n.i.	n.i.	SPE + CG/MS	Subterranean	Lucas do Verde – MT	2	Moreira *et al.* (2012)
Deethylatrazine		1/62	0.02						No	
Chlorpyrifos		3/62	0.01–0.04						30	
Endosulfan alpha		13/62	0.01–0.82						20	
Endosulfan beta		12/62	0.02–0.26							
Flutriafol		12/62	0.03–0.34						60[b]	
Metolachlor		8/62	0.01–0.59						10	
Permethrin		1/62	0.19						20	
Atrazine		2/62	0.25–9.33				Subterranean	Campo Verde – MT	2	
Endosulfan alpha		3/62	0.45–0.56						20	
Endosulfan beta		2/62	0.18–0.54							
Flutriafol		5/62	0.23–57.11						60[b]	
Metolachlor		3/62	0.26–1.48						10	
Bisphenol A	Endocrine Disruptor	3/5	<1,200	400	1,200	LC-MS/MS	Superficial	Campinas, Atibaia e Baurueri – SP	No	Jardim *et al.* (2012))
4-n-octylphenol		2/5	<100	40	100			Campinas – SP	No	
4-n-nonylphenol		1/5	<100	40	100			Campinas e Atibaia – SP	No	
Atenolol	Drug	n.i.	<60	0.1	60	SPE + LC-MS/MS	Superficial	Capinas – SP	No	Maldaner & Jardim (2012)
Paracetamol			<40	0.067	40				No	
Ibuprofen			<125	0.208	125				No	
Carbofuran	Pesticide		<10	0.028	10				7	
Diuron			<15	0.043	15				90	
Atrazine	Pesticide	1	0.0923	n.i.	0.004	SPE + LC-MS/MS	Superficial	Morro Redondo – RS	2	Caldas *et al.* (2013)
Carbofuran		3	0.0089		0.008				7	
Clomazone		4	0.04–0.124		0.04				No	
Diuron		1	0.0958		0.04				90	
Epoxiconazole		2	0.0456–0.083		0.04				18[b]	
Irgarol		1	0.0072		0.004				No	
Tebuconazole		2	0.053–0.0797		0.04				180	
Mebendazole	Drug	1	0.0185		0.008				No	
Propylparaben	PCP	1	0.1355		0.008				No	

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Parameter	Class	N	Result (μg/L)	DL μg/L	QL μg/L	Analytical Method	Source	City – FU	HBT[a] μg/L	Reference
Cadmium	Metal	56	0.06–32.8	n.i.	0.05	ICP-MS	Subterranean	Conceição das Alagoas – MG	5	Cardoso *et al.* (2014)
Manganese			0.35–21.9		0.05				100	
Lead			0.42–7.7		0.05				10	
Nickel			1.19–221		0.1				70	
Tin			<0.1–1.26		0.1				No	
Copper			1.18–70.4		0.2				2,000	
Mercury			<0.2–3.38		0.2				1	
Chrome			<0.5–7.34		0.5				50	
Zinc			10.5–556		0.5				5,000	
4-Tert-Octylphenol	Endocrine Disruptor	4	1.53	0.14	0.62	SPE + GC-qMS	Subterranean	Novo Hamburgo – RS	No	Furtado & Mühlen (2015)
4-nonylphenol			5.62	0.12	1.11				No	
Estrone			1.93–2.28	0.09	0.68		Superficial and Subterranean	Novo Hamburgo and São Leopoldo – RS	No	
17-alpha-ethinylestradiol			2.16–2.68	0.32	0.63				No	
Atrazine	Pesticide	75	0.002–0.015	0.001	0.002	SPE + LC-MS/MS	Superficial	16 capitals	2	Machado *et al.* (2016)
Caffeine	–	93	0.005–2.769	0.0001	0.004			22 capitals	No	
Triclosan	PCP	1	<0.009	0.003	0.009			Porto Alegre – RS	No	
Phenolphithalein	–	1	<0.003	0.001	0.003			Palmas – TO	No	
Cocaine	Illicit drug	12	<6–22	2	6	LC-MS/MS	Superficial	Limeira, Campinas, Santa Bárbara do Oeste, Piracicaba and Espírito Santo do Pinhal – SP	No	Campestrini & Jardim (2017)
Benzoylecgonine			<5–652	2	5				No	
Acrolein	Pesticide	36	<3.71–115	n.i.	3.71	HPLC-UV	Rainwater	São Domingos – BA	No	Moura *et al.* (2018)
Formaldehyde	Organic		<7.65–40.8		7.65				No	
Acetaldehyde			<8.7–100		8.7				No	
Propianaldehyde			< 0.002–160		0.002				No	
Hexaldehyde			n.i.–518		n.i.				No	
Valeraldehyde			n.i.–283		n.i.				No	
Acetone			n.i.-170		n.i.				No	
Butyraldehyde			<0.0003		0.0003				No	
Benzaldehyde			<0.0005		0.0005				No	
Methylparaben	PCP	1	<0.08	0.024	0.08	LC-MS/MS	Superficial	Rio Grande – RS	No	Marta-Sanchez *et al.* (2018)
Paracetamol	Drug	1	0.016	0.003	0.01	SPE-UHPLC-MS/MS	Superficial	cities n.i. – RS	No	Oliveira *et al.* (2019)
Atenolol	Drug	1	0.026	0.003	0.01		Superficial		No	
Carbamazepine	Drug	2	0.013–0.027	0.003	0.01		Superficial and Subterranean		No	

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Androstano	Endocrine Disruptor	10	0.018–0.027	n.i.	0.005	SPE-GC/MS	Superficial and Subterranean	Rosário do Catete – SE	No	Maynard *et al.* (2019)
Bisphenol A			0.013–0.043		0.001				No	
Cholesterol			0.005–0.053		0.002				No	
Dibutyl phthalate			0.0020–0.034		0.002				No	
Diethyl phthalate			0.019		0.002				No	
Caffeine			0.14–0.19		0.003				No	
Aluminum	Metal	23	141.4–788.8	2.9	9.9	ICP-OES	Subterranean	Itaporã and Caarapó – MS	200	Francisco *et al.* (2019)
Cobalt			13.30–56.20	3	10				No	
Chrome			9.2–10.2	2.2	9.2				50	
Copper			6.1–28	0.36	1.2				2,000	
Iron			42.8–1,124	14	47				300	
Manganese			9.2–1,632	1.1	5.2				100	
Nickel			91.8	16.3	54.3				70	
Zinc			2–90.8	0.25	0.85				500	
Caffeine			0.0225–0.1	0.006	0.0198	LC-MS/MS			No	
Imidacloprid	Pesticide		0.023–0.188	0.0053	0.0174				300[b]	
Carbendazim			0.009	0.0027	0.0088				120	
2-Hydroxyatrazine			0.016–0.08	0.0027	0.009				No	
Hexazinone			0.018	0.0025	0.0081				No	
Clomazone			<0.0048	0.0015	0.0048					
Tebuthiuron			0.021	0.003	0.0099				No	
Malathion			0.0115–0.013	0.0029	0.0095				No	
Aluminum	Metal	10	3.9–176.8	1	n.i.	ICP-MS	Subterranean	RIbeirão Preto – SP	200	Alves *et al.* (2019)
Arsenic			<0.2–0.38	0.2					10	
Chrome			0.73–3.36	0.5					50	
Lead			0.14–25.22	0.05					10	
Copper			0.54–1453.57	0.2					2000	
Manganese			1.03–48.09	0.05					100	
Nickel			0.2–6.21	0.2					70	
Zinc			4.98–1393.97	0.5					5000	
Cadmium			<0.05–0.63	0.05					5	
Beryllium			0.12–0.28	0.1					No	
Tin			0.12–2.08	0.1					No	
Vanadium			1.3–2.53	1					No	

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Table 1 | continued

Parameter	Class	N	Result (µg/L)	DL µg/L	QL µg/L	Analytical Method	Source	City – FU	HBT[a] µg/L	Reference
Betamethasone	Drugs	72	<0.008–2.62	0.0024	0.008	LC-MS/MS	Superficial	cities n.i. – MG	No	Reis *et al.* (2019)
Fluconazole			<0.0087–0.75	0.0026	0.0087				No	
Loratadine			<0.0136–0.055	0.0136	0.0136				No	
Prednisone			<0.008–6.32	0.0024	0.008				No	
Atorvastatin			<0.0128–0.657	0.0128	0.2553				No	
Danofloxacin			<0.0009–0.042	0.0009	0.0171				No	
Enoxacin			<0.401–0.219	0.01	0.4016				No	
Enrofloxacin			<0.0005–0.219	0.0005	0.005				No	
Norfloxacin			<0.0393–0.210	0.001	0.0393				No	
Ketoprofen			<0.0065–0.561	0.0065	0.0646				No	
Gemfibrozil			<0.0085–0.293	0.0085	0.085				No	

a: health based target; b: SES RS 320/2014.

analyzed were from surface water bodies, underground sources and rainwater. Research that evaluated the filter bed from residential filters was also included. Twenty-two chemical contaminants found are listed in the Brazilian drinking water quality standard with respective HBT, where three pesticides are listed from Rio Grande do Sul ordinance. Fifty-five parameters assigned with 'No' in the HBT column in Table 1 are not regulated in Brazil and consequently are not routinely monitored.

It is important to assess contamination sources from all parameters found in drinking water and evaluate what could be done to prevent them from reaching water sources. The transport of contaminants to the water sources can occur by soil or air and will depend on a series of physical and chemical properties of each compound, such as half-life in soil, in air, in water, volatility, solubility, among others. The contaminant classes found are derived from the main sources: soil composition, mining, domestic sewage and agricultural activities. The contamination sources are illustrated in Figure 2. The pesticide with 21 quantified parameters was the class with the highest number of pesticides. The classes from domestic sewage total 34 parameters (drugs, endocrine disruptor, illicit drugs, PCP, caffeine and phenolphthalein, as shown in Table 1).

It would be more rational to prevent contamination from reaching water sources than to implement advanced technologies to remove the pollutants, since large-scale application to supply cities could be economically impractical. Domestic sewage is treated, or even released raw into water sources. However, to what extent is the sewage treatment not only an accumulation point for chemical contaminants in sludge? What could be done to prevent these chemical contaminations from reaching drinking water, since knowledge about their health risks is limited?

The results in Table 1 are discussed separately regarding drinking water quality standards, emerging pollutants and relevant considerations.

Chemical contaminants predicted in Brazilian drinking water quality standards

Twenty-three of the chemical contaminants found are listed in Brazilian drinking water quality standard. Twelve are pesticides (atrazine, chlorpyrifos, endosulfan alpha and

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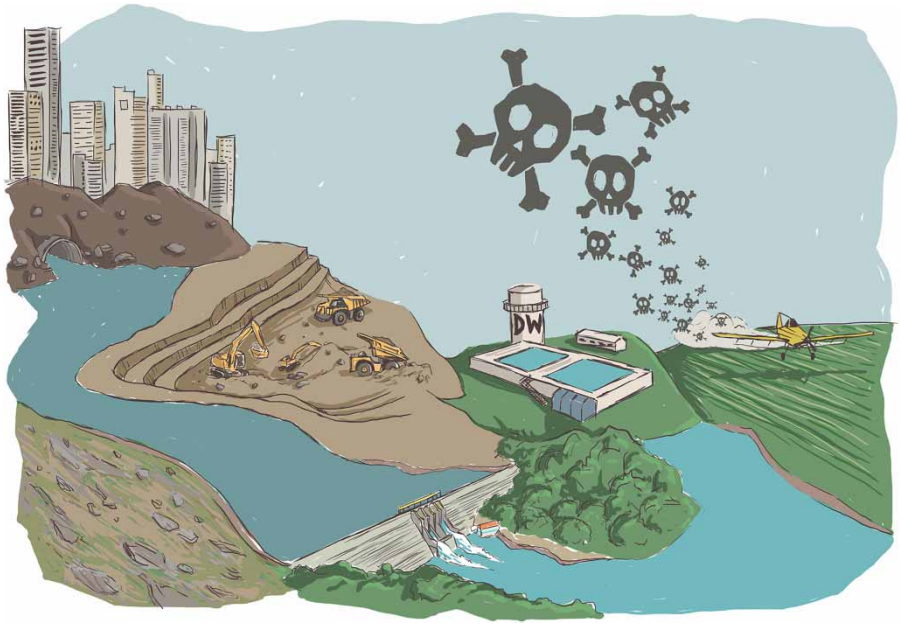

Figure 2 | Soil composition, mining, domestic sewage and agricultural activities: the main sources of chemical contamination in Brazilian drinking water (DW).

beta (HBT applies to the sum), flutriafol, metolachlor, permethrin, carbofuran, diuron, epoxiconazole, tebuconazole, and metolachlor); and 11 are metals (aluminum, arsenic, iron, cadmium, manganese, lead, nickel, copper, mercury, chrome and zinc). Twenty-one chemical contaminants are regulated throughout the Brazilian territory, through Annex XX in Ordinance Consolidation n° 5/2017 and two (flutriafol and epoxiconazole) only in Rio Grande do Sul territory, through state ordinance SES RS 320/2014.

In the health risk evaluation for the pesticide carbofuran in Campinas – SP (Maldaner & Jardim 2012) it was not conclusive because the HBT (7 μg/L) was lower than the quantification limit (QL) (10 μg/L). Analytical methods with lower QL than HBT should be used to evaluate health risk in this case. Six parameters were quantified above HBT with the following times above HBT: cadmium 6.56, aluminium 3.94, iron 3.75, nickel 3.15, mercury 3.38, and atrazine 4.65. These results define which water is not fit to drink. In addition, the pesticide flutriafol was quantified with 57.77 μg/L, a result close to the HBT of 60 μg/L. HBT is defined based on the amount of a substance in drinking water, expressed on a body mass basis, which can be ingested for a lifetime without appreciable risk to health and with a safety margin (WHO 2017). As in Brazil the body mass used to define HBT is 60 kg for a water consumption of 2 L per day, when analyzing the result of flutriafol close to HBT, people with a body mass below 60 kg are at greater risk, especially children. Moreover, there is also a variation in volume of water consumed per day. Despite this, tolerable daily intakes are regarded as representing a tolerable intake for a lifetime; they are not so precise that they cannot be exceeded for short periods of time (WHO 2017). However, if confirmed chemical pollution above HBT beyond consecutive analysis it is necessary to adopt advanced water treatment technologies or use other water sources. As flutriafol and atrazine are pesticides, their sources of contamination are possibly seasonal. In this sense, water quality must be monitored frequently and measurements to reduce the pesticides application surrounding the watershed should be considered.

Considering the time it takes to receive a laboratory report, usually the results will refer to water that has been already consumed by the population. In this sense, what could be done to know previously if people could be exposed to the risks of non-potable water due to chemical contamination above HBT? Perhaps an alternative is water quality monitoring in the watershed. A historical series by São Paulo's State Environmental Agency made it

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possible to assess the water quality from basic monitoring parameters, cheaper and faster analytical results, and was correlated with the presence of chemical contamination in drinking water (Jardim *et al.* 2012).

A limitation on Brazilian drinking water quality standards for not considering synergistic effects from multiple compounds chemical mixtures, based on the toxicity of each component individually, has been reported (Jardim *et al.* 2012). The Brazilian standard considers quantified risk, as opposed to the European Union, which considers precautionary principles, in which the risk is minimal. To quantify the risks, bases needed are supported by epidemiological evidence and toxicological studies. Risk assessment based on a combination of two or more components in experimental toxicological studies can be costly and slow; in this sense, one must move on to toxicological modeling by advanced computational methods. HBTs are calculated separately for individual substances, without specific consideration of each potential interaction of the substances with other compounds. Synergistic interactions among substances are generally selective and very limited. The toxicity mechanisms are different for many chemical pollutants, therefore there is no reason to suppose that interactions exist. There may, however, be occasions when a number of contaminants with similar toxicological mechanisms are present at levels close to the respective health-based target. Unless there is evidence against it, it is appropriate to assume that compounds' toxic effects are additive (WHO 2017).

Emergent pollutants

In this research, 54 parameters found were classified as emerging pollutants (those without HBT in Table 1), that is, they are not regulated by the Brazilian drinking-water quality standard, see Table 2. Sixteen were drugs (atenolol, atorvastatin, betamethasone, carbamazepine, danofloxacin, enoxacin, enrofloxacin, fluconazole, gemfibrozil, ibuprofen, ketoprofen, loratadine mebendazol, paracetamol, prednisone, norfloxacin), 11 endocrine disruptors (17 α-ethinyl estradiol, 4-n-nonylphenol, 4-n-octylphenol, 4-nonylphenol, 4-tert-octylphenol, androstano, bisphenol A, cholesterol, dibutyl phthalate, diethyl phthalate, estrone), eight pesticides (2-hydroxyatrazine and deethylatrazine – subproduct of atrazine, acrolein, clomazone, irgarol, hexazinone, malathion, tebuthiuron), eight organics (acetaldehyde, acetone, benzaldehyde, butyraldehyde, formaldehyde, hexaldehyde, propionaldehyde and valeraldehyde), four metal (beryllium, cobalt, tin and vanadium), three PCP (propylparaben, methylparaben and triclosan), and two illicit drugs (cocaine and its degradation by-product benzoylecgonine) besides caffeine and phenolphthalein.

Pesticides are used in agricultural production and regulation for monitoring does not keep pace with the speed at which new compounds are developed. The Brazilian drinking water quality standard is used as the criterion for inclusion of a new pesticide appropriate environmental parameter, such as the physical-chemical characteristics according to the risk of the parameter reaching surface or underground sources, or the volume of pesticide's commercialization in Brazil and the toxicological class. As the ordinance applies to the entire national territory, specific features should be regulated according to the local/regional economic activities. In this regard, Rio Grande do Sul (RS) has the Ordinance 320/2014, which adds 46 parameters of pesticides to determine whether the water is potable, in addition to the 27 provided for the national standard. One of these parameters, epoxiconazole, was found in Morro Redondo – RS (Caldas *et al.* 2013), where it is regulated, and another, flutriafolm, was quantified in Campo Verde and Lucas Verde – MT (Moreira *et al.* 2012), being an emergent pollutant in that state.

The other classifications (drugs, illicit drugs, endocrine disruptors, PCP and caffeine) have sewage discharge as the major source. Although there are alternatives available as advanced treatment systems, including membrane filtration, granular activated carbon, and advanced oxidation processes for the effective removal of emergent pollutants (Yang *et al.* 2017), the designs of existing treatment facilities are not suited to remove emerging contaminants and their transformation products (Gogoi *et al.* 2018). Municipal wastewater treatment facilities in Brazil treat up to the secondary (biological) stage, leading to limited removal of contaminants of emerging concern. It is an urgent priority to improve the sanitation infrastructure implementing tertiary treatment (Starling *et al.* 2018). Moreover, more than 100 million Brazilians who do not have access to sewage treatment (SNIS

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Table 2 | Proposed guideline values for emerging pollutants quantified in Brazilian drinking water

Parameter	Class	Dose Descriptor	(mg/kg)	UF	TDI	GV (μg/L)	MAX (μg/L)	Reference
Acetaldehyde	Organic	LOAEL	400	1,000	0.4	12,000	100	SCCS (2012)
Acetone		LOAEL	2,258	1,000	0.002258	67.74	170	IRIS-EPA (2001)
Benzaldehyde		NOAEL	143	100	1.43	42,900	5	EPA (1988)
Butyraldehyde		LOAEL	75	1000	0.075	2250	3	OXEA (2018)
Formaldehyde		NOAEL	82	100	0.82	24,600	40	ECHA (1996)
Hexanaldehyde		–	–	–	–	–	518	ECHA (1962a)
Propionaldehyde		LOAEL	1.5	1,000	0.0015	45	160	IRIS-EPA (2008)
Valeraldehyde		NOAEL	1,000	100	10	300,000	283	ECHA (1962b)
17-alpha-ethinyl estradiol	ED	NOAEL	1.70×10^{-7}	100	1.70×10^{-9}	5.10×10^{-5}	2.68	EPHC (2008)
4-n-nonylphenol		LOAEL	15	1000	0.015	450	5,62	Bontje *et al.* (2004)
4-n-octylphenol		NOAEL	22	100	0.22	6600	< 100	EPA (2020)
4-nonylpynol		NOAEL	15	100	0.15	4500	< 100	Bontje *et al.* (2004)
4-tert-octylphenol		NOAEL	22	100	0.22	6600	1,53	Tyl *et al.* (1999)
Androstano		–	–	–	–	–	0.027	–
Bisphenol A		NOAEL	5	100	0.05	1,500	< 1,200	WHO (2009b)
Cholesterol		–	–	–	–	–	0.053	–
Dibutyl phthalate		NOAEL	19	1,000	0.019	570	0.034	ECHA (2016)
Diethyl phthalate		NOAEL	150	1,000	0.15	4.500	0.019	SCCNFP (2002)
Estrone		NOAEL	1	100	0.01	3.00×10^{-2}	2.28	EPHC (2008)
2-hydroxyatrazine	Pesticide	NOAEL	5.8	1,000	0.0058	174	0.08	WHO (2011)
Acrolein		NOAEL	7.50×10^{-1}	100	7.50×10^{-3}	2.25×10^{-2}	115	Gomes & Meek (2002)
Clomazone		NOAEL	50	100	0.5	1.50×10^{-4}	0.124	Soatz *et al.* (2005)
Deetilatrazina		NOAEL	1.8	100	0.018	540	0.02	WHO (2017)
Hexazinone		NOAEL	0.05	1,000	0.00005	2	0.018	EPA (1994)
Irgarol		NOAEL	7.62	100	0.0762	2.286	72	WFD–EU (2011)
Malathion		NOAEL	0.3	1,000	0.0003	9.00×10^{-0}	0.013	WHO (2004)
Tebuthiuron		NOAEL	40	1,000	0.04	1,200	0.021	EPA (1991)
Atenolol	Drug	LOAEL	0.8	1,000	0.0008	24	< 60	Snyder *et al.* (2008)
Atorvastatin		NOAEL	8.00×10^{-1}	1,000	0.08	2.40×10^{-3}	0.657	Walsh *et al.* (1996)
Betamethasone		NOAEL	0.2	1,000	0.0002	6.00×10^{-0}	2.62	Norman *et al.* (2014)
Carbamazepine		NOAEL	3.8	1,000	0.0038	114	0.027	EHD (2013)
Danafloxacin		–	–	–	–	–	0.042	–
Enoxacin		–	–	–	–	–	0.219	–
Enrofloxacin		NOAEL	1.2	1,000	0.0012	36	0.219	EAEM (1998)
Fluconazole		NOAEL	5	1,000	0.005	150	0.75	Pfizer (2016)
Gemfibrozil		NOAEL	200	1,000	0.2	6,000	0.293	Pfizer (2018)
Ibuprofen		NOAEL	1.33×10^{-6}	100	1.33×10^{-4}	400,000,000	< 125	EPHC (2008)
Ketoprofen		NOAEL	2	1,000	0.002	60	0.561	EMEA (1995)
Loratadine		MDTD	167	1,000	0.167	5.01×10^{-3}	0.055	Sweetman (2009)
Mebendazol		NOAEL	125	100	1.25	37,500	185	EAEM (2001)

(*continued*)

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Table 2 | continued

Parameter	Class	Dose Descriptor	(mg/kg)	UF	TDI	GV (μg/L)	MAX (μg/L)	Reference
Norfloxacin		MDTD	13,300	1,000	13.3	3.99×10^{-5}	0.21	EPHC (2008)
Paracetamol		NOAEL	0.05	100	0.0005	1.50×10^{-1}	< 40	EPHC (2008)
Prednisone		MDTD	42	1,000	0.042	1.26×10^{-3}	6.32	Sweetman (2009)
Propylparaben	PCP	NOAEL	5500	100	55	1.65×10^{-6}	0.13	Toxnet (2019a, 2019d)
Methylparaben		NOAEL	11	100	0.11	3,300	< 0.003	Toxnet (2019b)
Triclosan		NOAEL	5,700	100	57	1.71×10^{-6}	< 0.08	Toxnet (2019c)
Berylium	Metal	NOAEL	0.1	1,000	0.0001	3	0.28	WHO (2009a)
Cobalt		NOAEL	0.54	1,000	0.00054	16	56.2	EPA (2008)
Tin		NOAEL	2	100	0.02	600	1.26	Fawell *et al.* (2004)
Vanadium		NOAEL	4.1	1,000	0.0041	123	2.53	ATSDR (2020)
Benzoylecgonine	Illicit drug	–	–	–	–	6,810	0.022	Mendoza et al. (2014)
Cocaine		–	–	–	–	2.28	0.652	Mendoza et al. (2014)
Phenolphithalein		NOAEL	6.48	100	0.0648	1.94×10^{-3}	< 0.009	ECHA (1979)
Caffeine		NOAEL	151	100	1.51	4.53×10^{-4}	2.76	ECHA (1983)

ED, Endocrine Disruptor; TDI, Tolerable Daily Intake; GV, Guideline Value.

2019) release raw sewage into the environment with the risk of contaminating water supply sources.

Drugs for medical purposes are known to improve the quality of life by curing and preventing diseases. However, there are pharmaceutical products that, when diffused through the environment by various routes, can have severe harmful effects on living organisms (Jose *et al.* 2020). A case study in the water supply system of Changzhou in China investigated the seasonal and spatial variations of 43 types of pharmaceutical and personal care products. The total concentrations ranged from 6.37 to 809.28 ng/L. In summer, more parameters at higher concentrations in drinking water in urban areas were detected (Jiang *et al.* 2019). Atenolol, an antihypertensive, is not removed in sewage treatment plants and is relatively persistent in aqueous matrices, and is one of the drugs most frequently detected in the aquatic environment (Godoy *et al.* 2015). In the case of drug residues, it has been observed that only 18–32% of drug residues could be degraded by secondary sewage treatment and removal has been increased to 30–65% by tertiary treatment (Khan *et al.* 2020).

In a review based on studies performed in 11 different countries in Latin America between 1999 and 2019, Brazil had the highest number of investigations (53%), where bisphenol A and estrone were the most common endocrine disruptors reported in effluents from wastewater treatment plants (Peña-Guzmán *et al.* 2019). Bisphenol A is used in the production of polycarbonate resin for the manufacturing of bottles, toys, containers and water pipes. Bisphenol A enters into adipose tissue during fetal development and may affect adult health, through adverse effects on the growth and development of organs and tissues. Exposure to disruptor endocrines can cause immune effects, metabolic effects, reproductive abnormalities, behavioral changes, diabetes, obesity, cardiovascular diseases, neurological disorders, disrupted fetal development and growth, and a wide variety of cancers (Wee & Aris 2017). Agents that mimic the action of estrogens on target cells and are part of the group of endocrine disruptor compounds are termed estrogenic. Exposure to these compounds causes a number of negative effects, including breast cancer, infertility and animal hermaphroditism (Vilela *et al.* 2018). Estrone and 17 α-ethinyl estradiol found in drinking water are estrogenics. The synthetic estrogen is more persistent in the environment than natural estrogens and may be a greater cause for environmental concern; 17 alpha ethinylestradiol is a synthetic compound widely used in the generation of contraceptive pills. It is present in the urine of women taking contraceptives and its presence has been confirmed at increasing concentrations contaminating rivers all

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over the world (Meyer et al. 2019). Pregnant women could be indirectly exposed to drugs and endocrine disruptors in drinking water (even after drinking water treatment (DWT)), as shown in Figure 3.

Organic contaminants in drinking water were evaluated by capturing rainwater from cisterns in 36 polystyrene reservoirs installed in two communities in rural areas of Bahia's semi-arid region. The authors concluded that the organic compounds came from the materials of cisterns exposed to the sun (Moura *et al.* 2018). In this research, the eight unregulated organic parameters in Brazilian drinking water were quantified in São Domingos – BA.

The presence of illicit drugs in drinking water was described for the first time in 2008. These substances enter the water cycle through sewage systems, and cities where wastewater treatment facilities are insufficient could have higher levels of illicit drugs in tap water. Every day new illicit substances, some even active at low concentrations such as fentanyls, are synthesized and put on the market with a total lack of toxicological information and are now detectable in drinking water. In our era of megacities, urban planners must consider these aspects in territorial planning (Davoli *et al.* 2019). Samples from five sites in four cities were analyzed in drinking water in São Paulo's state, and the presence of cocaine (COC) and benzoylecgonine (BE) were detected in all, with BE being 10–652 ng/L and COC 6–22 ng/L (Campestrini & Jardim 2017). Once consumed, COC is excreted mainly in urine, with about 35–55% of the consumed dose being excreted as BE, and only 1–9% as COC (EMCDDA 2008). A study of illicit drugs was also carried out on wastewater from a hospital in Santa Maria – RS (Martins *et al.* 2017). High concentrations and frequency of detection of BE in raw sewage can serve to calculate cocaine consumption by a population in sewage epidemiology applications.. The application of this knowledge about environmental chemistry, using advanced analytical methodologies, can contribute to fields far beyond public health, such as public safety, since the level of drug use can be estimated.

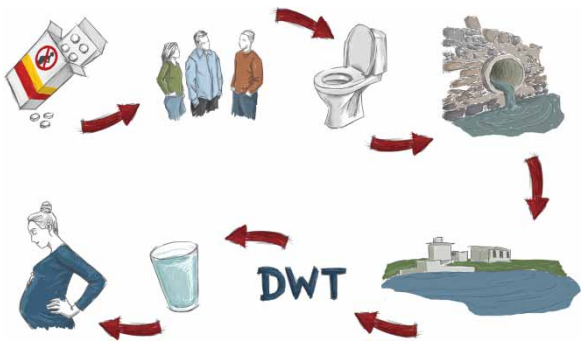

Figure 3 | Indirect exposure of drugs and endocrine disruptors in pregnant women through drinking water.

Propylparaben is a stable, non-volatile compound used as an antimicrobial preservative in foods, drugs and personal care products, methyl and propylparaben are the predominant parabens found in aquatic environments (Soni *et al.* 2001; Haman *et al.* 2015). In research carried out in Rio Grande – RS, the occurrence of parabens was analyzed (including isomers) in drinking water, mineral water and decanter sludge; only methylparaben, one of nine compounds, was detected in QL traces of <0.08 μg/L (Marta-Sanchez *et al.* 2018). Chlorinated parabens are more persistent than natural parabens. Their chlorinated by-products are more stable and persistent than the parent species and further studies are needed to improve knowledge regarding their toxicity (Haman *et al.* 2015).

Anthropic actions contribute to different emerging contaminants, such as estrogens, xenoestrogens and illicit drugs, as pointed out in previous studies (Jardim *et al.* 2012; Machado *et al.* 2016). Emerging pollutants found, to be categorized in terms of health risks, should be evaluated according to toxicological and epidemiological studies available in the literature.

Guideline's proposition for emerging pollutants found in Brazilian drinking water and health risk evaluation

One of the great challenges of chemical contamination is that it manifests health effects after long-term exposure, so that not knowing what contamination an individual is being exposed to is a risk situation, given that actions to reduce contamination are not taken. The first information on health effects considered for guidelines of exposure in chemical contamination is a study of the human population; however, this is somewhat limited due to the ethical issue involving toxicological studies in humans. The second most frequent information source is studies on animals in the laboratory, carried out with a small number of

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experiments and whose administered doses are relatively high. These studies are carried out with high doses generating uncertainties that are extrapolated to humans and for exposures in low doses. No-observed-adverse-effect level (NOAEL) is defined as the highest dose or concentration of a chemical in a single study, found by experiment or observation, that causes no detectable adverse health effect. If a NOAEL is not available, the lowest observed adverse effect level (LOAEL) may be used, which is the lowest observed dose or concentration of a substance at which there is a detectable adverse health effect (WHO 2017).

A drinking water guideline value represents the concentration of a constituent that does not exceed tolerable risk to the health of the consumer over a lifetime. In Table 2, the maximum quantified concentrations of emerging pollutants' results from Table 1 were compared with guideline propositions based on guidelines methodology from the World Health Organization and toxicological research. For all parameters, NOAEL or LOAEL used was the lowest available dose response. Uncertainty factor (UF) is used to extrapolate between species (inter-species differences), inter-individual differences (intra-species differences), and exposure route/duration was utilized as part of the tolerable daily intake (TDI) calculation. The guideline value proposed was calculated by multiplying the TDI by a typical average body weight of 60 kg and divided by a daily water consumption of 2 L. For pesticides, drugs, PCPs and caffeine, drinking water may not be the only exposure source, and an allocation factor (WHO 2017) should be considered. Nevertheless, in the GV calculated in Table 2, allocation factor was not used.

For the illicit drugs CO and BE, the proposed GVs were based on toxicological studies with algae and cladocerans (Mendoza et al. 2014). No LOAEL or NOAEL was found for hexanaldehyde, danafloxacin, enoxacin, androstano and cholesterol, pointing to the need for toxicological studies for these parameters.

Four parameters were quantified in concentrations above the proposed guidelines: propionaldehyde 3.55, acetone 2.5, beryllium 3.51, 17 α-ehinyl estradiol 52,549 times of the GV. Although the sampling strategy was material from a residential water filter instead of water samples, the estimated order of magnitude for 17 α-ehinyl estradiol is worrying, considering that it is carcinogenic for humans (IARC 2012). For the drugs atenolol and paracetamol, the quantification limits are above the GV, and the potability could not be measured.

All other parameters from the classes organic, disruptor endocrine, pesticide, drug (except atenolol and paracetamol), personal care products, illicit drugs, tin, phenolphthalein and caffeine were not quantified in concentrations which individually pose an appreciable human health risk. The drinking water guideline values proposed in this systematic review may alter when new toxicological or exposure information becomes available. They are however considered adequate for the health risk evaluation in the present study, which primarily aimed to assess the risks of emerging pollutants quantified in Brazilian drinking water.

Relevant considerations about sampling strategies and rain water

Research has been focused more generally on development and validation of a new analytical method, and secondarily, on the strategy behind the risk analysis in the sample's representativeness and watershed monitoring schedule. Two studies stand out in the findings (Table 1): one is the evaluation of drinking water samples from 22 Brazilian capitals, describing sampling methodology – collections of 200 mL made every 2 hours (Machado *et al.* 2016). The second is the evaluation of residential filters (Furtado & von Mühlen 2015) with representativeness of up to six months from drinking water samples and making a superficial but innovative estimate of the possible endocrine disruptors' contamination, covering two limitations of environmental chemistry: reaching the limits of detection and quantification in analytical methods (for evaluating an accumulation/concentration point) and sample's representativeness. In this same strategy line, there are studies that evaluate the settler's sludge of water treatment plants, which can represent 1–6 months of water production, making it possible to identify contamination in raw water at a point of accumulation like settler's sludge (Wasserman *et al.* 2018).

Evaluation in rainwater has highlighted that acrolein was found, proving the volatilization of pesticides used in

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agricultural processes and their precipitation through rain, that is, the transport of pesticides can occur in the precipitation stage of the water cycle (Moreira *et al.* 2012). This finding is important, since the criteria used to include or exclude a pesticide parameter from the national potability standard, in the environmental dynamics, mostly consider the risks involved in transporting via soil and water (in the liquid state), disregarding contribution portions that may come by air (drift), or by rainwater. In this sense, in the United States, the Environmental Protection Agency could include restrictions on the timing of atrazine's application due to rain, as a mitigation measure to reduce damage in the impacted watershed (EPA 2006). The question of the authors cited (Moreira *et al.* 2012) remains: what would be the possible acute and chronic effects of the exposure of pesticides to the populations that live and have lived around the territory where the agricultural application is carried out?

CONCLUSIONS

Brazil, in the context of being a mostly agricultural country with some regionalized population concentrations, has springs subject to pesticides and sewage (treated or not) and the consequent chemical contamination of underground, surface and even rainwater sources. In the present systematic review, 77 different chemical contaminants were found in Brazilian drinking water, 22 of which were predicted in the Brazilian health-based target and 54 emerging pollutants where guidelines were proposed. Cadmium, aluminum, iron, nickel, mercury and atrazine were quantified in concentrations above HBT and propionaldehyde, beryllium, acetone and 17 α-ehinyl estradiol above GV, demonstrating that the population was exposed to non-potable water because of chemical contamination. 17 α-ehinyl estradiol is the priority parameter because it is carcinogenic and its concentration was estimated at 52,549 times above the proposed GV. These results can serve for the regulation of emerging pollutants by environmental and public health agencies, in order to subsidize public policies that promote actions to control and reduce these contaminations, and consequently reduce the burden of morbidity in humans linked to environmental factors, according to the 69th World Health Assembly's report.

Health risks could not be assessed for carbofuran, atenolol and paracetamol because the limits of quantification of the analytical methods were below the limit values for drinking water, and hexaldeyde, danafloxacin, enoxacin, androstane and cholesterol because no toxicological studies were found.

The speed of advance in knowledge about contaminants in drinking water is not accomplished by knowledge of risks, nor by measures necessary to reduce them. Some parameters may, perhaps, present risks that go far beyond an individual or a population since they can cause mutations capable of transcending future generations. From the chemical contamination found in drinking water, the questions remain: what are the toxicological risks and epidemiological impacts? How sensitive do analytical methods need to become for water quality screening, at what levels do water suppliers need to take action and how do effective treatment methods need to be designed to remove contaminants sufficiently? What other contaminants may not have been analyzed and may be present in drinking water?

DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

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