



Occurrence and removal of drugs and endocrine disruptors in the Bolonha Water Treatment Plant in Belém/PA (Brazil)

Luiza C. G. M. Teixeira · Juliane Ribeiro das Chaves ·
Neyson Mendonça · Ananda L. Sanson · Mariana C. P. Alves ·
Robson J. C. F. Afonso · Sérgio F. Aquino

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Abstract This study aimed to investigate the occurrence of drugs and endocrine disruptors in water supplies and in water for human consumption. Twelve sampling campaigns were carried out during the rainy and dry season at four sampling points in the Bolonha Complex, in the city of Belém, northern region of Brazil: Bolonha reservoir (catchment) and Water Treatment Plant (WTP) Bolonha (filtered water chamber, treated water tank, and washing water from the filters). The determination of the compounds was performed by solid phase extraction followed by gas and liquid chromatography coupled to mass spectrometry. The results confirmed the anthropic influence that the reservoir and WTP-Bolonha have been suffering, as consequence of the discharge of domestic sewage *in natura*. Among 25 microcontaminants analyzed, 12 were quantified in raw water and 10 in

treated water. The antiallergic Loratadine (LRT) was the contaminant that occurred most frequently in all sample points, having been poorly removed (median 12%) in the conventional treatment used. Losartana (LST), 4-octylphenol (4-OP), and Bisphenol A (BPA) also occurred very frequently in raw water with concentrations ranging from 3.7 to 194 ng L⁻¹. Although such contaminants occurred in treated water in concentrations varying from 4.0 to 135 ng L⁻¹, the estimated margin of exposure ranged from 55 to 3333 times which indicates low risk of human exposure to such contaminants through ingestion of treated water.

Keywords Microcontaminants · Water treatment · Risk analysis · Endocrine disruptors

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L. C. G. M. Teixeira · J. R. das Chaves · N. Mendonça
Postgraduate Program in Civil Engineering (PPGEC),
Universidade Federal Do Pará (UFPA), Belém,
PA 66075-110, Brazil

A. L. Sanson · M. C. P. Alves · R. J. C. F. Afonso ·
S. F. Aquino (✉)
Environmental Engineering Postgraduate Program
(PROAMB), Universidade Federal de Ouro Preto (UFOP),
Campus Morro Do Cruzeiro, Ouro Preto, MG 35400-00,
Brazil
e-mail: sergio@ufop.edu.br

Introduction

The use of drugs, cleaning products, and personal hygiene by society contributes to the occurrence of emerging concern in the environment, particularly in aquatic compartments. Such substances occur at concentrations from micrograms per litre (µg L⁻¹) to nanograms per liter (ng L⁻¹) and are called micro-pollutants (Brandt et al., 2013; Lima et al., 2017); once they reach aquatic ecosystems when they are consumed and excreted, leached from inappropriate disposal of unused drugs, they can contaminate the water supply (Fick et al., 2009). Little is known about the capacity of conventional water treatment systems

to remove such micropollutants on a full scale. The environmental prevalence of such contaminants combined with the finding that conventional treatment systems are inefficient in removing micropollutants from water may lead to the need for refining treatment methods to remove these contaminants of emerging concern, thereby avoiding human exposure and population health risk (Pádua, 2009).

The concern with these organic microcontaminants arises from the increased frequency they have been detected in the environment in several countries (Branchet et al., 2019; Charuau et al., 2019; García-Gil et al., 2018; J. Liu et al., 2018; Rivera-Jaimes et al., 2018), as well as some adverse effects observed in aquatic organisms. Contaminants of emerging concern can be subdivided into several groups, with endocrine disruptors (ED) and drugs being the focus of this work. The EDs affect the endocrine system posing a threat to human and animal health and interacting with a receptor of hormones, thus causing several metabolic alterations in the organism (Bila & Dezotti, 2007). Although such contaminants are usually found in the environment at low concentrations, some of them are toxic or cause adverse effects at concentrations of nanograms per liter (Bila & Dezotti, 2007; Newbold et al., 2008; Quignot et al., 2012a; Quignot et al., 2012b; Uchtmann et al., 2020) The drugs are composed of different chemical classes with different toxicity. Antibiotics, in particular, constitute a class of major concern due to their ability to induce and disseminate antimicrobial resistance in the environment. Studies have been conducted in order to report possible effects of drugs on the environment and on human beings (Bisognin et al., 2018; Montagner et al., 2017), and these impacts have not yet been fully understood (Veras et al., 2019).

Most of the WTPs implanted in the urban areas of Brazil are of the complete cycle type (coagulation, flocculation, sedimentation, filtration, and disinfection). Research studies have reported its low removal efficiency for emerging contaminants, since conventional WTPs were not designed for such purpose. According to Lima et al. (2017), the stages of coagulation, flocculation, and sedimentation have low efficiency (< 50%) in the removal of such contaminants. Better efficiencies are generally achieved for compounds that have a hydrophobic character, as they tend to be adsorbed in suspended solids that are retained in the sedimentation tank sludge and filters.

In relation to the disinfection stage, the removal of such contaminants depends mainly on the redox potential of disinfectant and contact time (Lima et al., 2017; Rigobello et al., 2013) and the contact time often needed for the complete removal of emerging contaminants is reported to be much higher than that usually employed (about 30 min) in a WTP (Lima et al., 2017; Rigobello et al., 2013).

The presence of contaminants of emerging concern in water supply sources causes a preoccupation in society and leads to a debate about the relevance of including drugs and endocrine disruptors in the Brazilian standards of water potability. Considering that the Potable Water Ordinance is based on scientific criteria and that the methodology of quantitative assessment of chemical risk (QACR) used in the process is based on the combination of exposure versus toxicity, it is essential to know the occurrence of drugs and endocrine disruptors in water supplies and in treated water from the 5 regions of the country. In the present study, the north region (represented by the metropolitan region of the city of Belém, State of Pará) was considered, evaluating the occurrence and possible correlations of microcontaminants in the source (Bolonha reservoir) and in water for human consumption (WTP-Bolonha) with the other physicochemical and biological characteristics, as well as the risk assessment of the most frequently detected microcontaminants. Thus, it was possible to establish a hierarchy of the most prevalent and/or toxic compounds that, therefore, should deserve greater attention from the authorities responsible for revising the Brazilian regulations for potability.

Material and methods

Study area and collection points

The study was conducted at the Bolonha Complex, more specifically at the Bolonha Reservoir and the WTP-Bolonha, which is within the boundaries of the Environmental Protection Area of the city of Belém (EPA Belém) at the latitude 1° 25' 14" S and longitude 48° 26' 04" O coordinates (Fig. 1). The Bolonha Reservoir, despite being within this protected area, has suffered the impacts caused by disorderly occupation of the population in its surroundings, and its

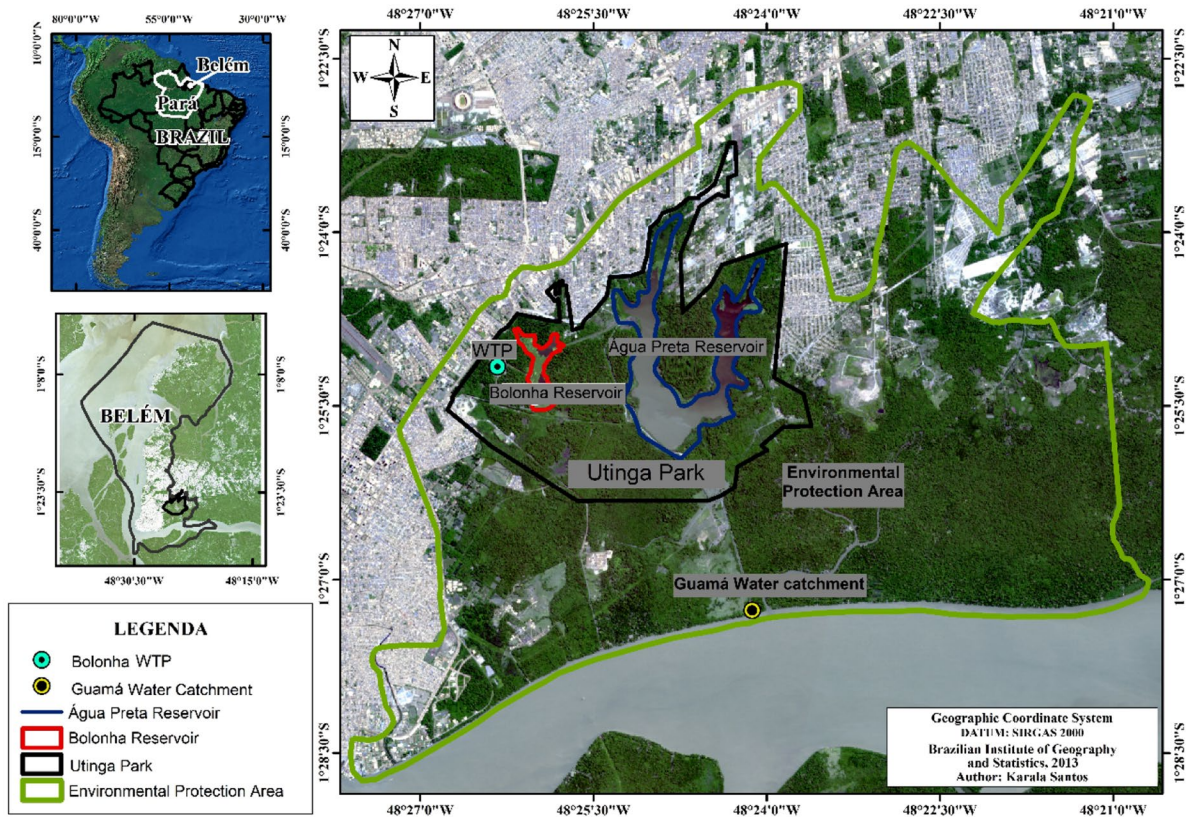


Fig. 1 Study location—Bolonha Reservoir and WTP-Bolonha

eutrophication has become a chronic problem (Araújo Júnior, 2015; Gutierrez et al., 2017).

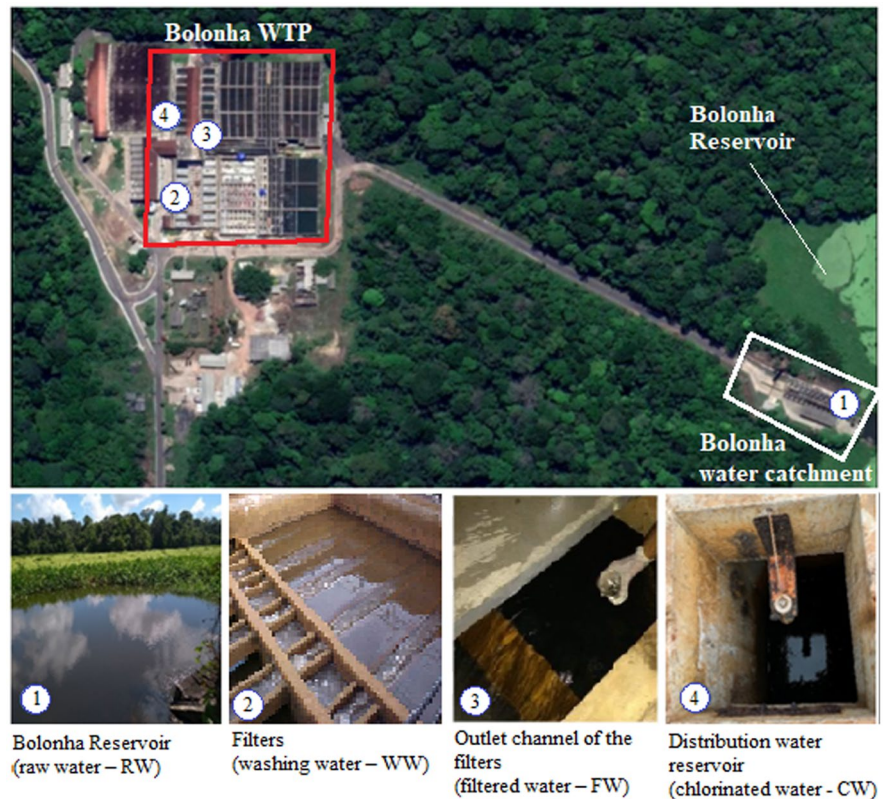
According to the Belém Municipal Plan for Basic Sanitation, Water Supply, and Sanitary Sewage (Belém, 2015), the volume of water available to the city monthly is 6,900,000 m³ per month, of which 70% of this flow is provided by the Bolonha Reservoir and 30% from groundwater sources. The Bolonha reservoir contributes 100% to the feed water of Bolonha Water Treatment Plant (WTP), which has a nominal capacity of 6.4 m³ s⁻¹ and operates with 5 m³ s⁻¹, employing full cycle treatment using aluminum polychloride (PAC) as a primary coagulant (6 to 14 mg L⁻¹), polyacrylamide as a coagulation aid (0.05 to 0.1 mg L⁻¹), and chlorine gas as a disinfectant agent (3 mg L⁻¹) (Belém, 2015).

Samples were collected at four different points. The first point, called raw water (RW), was located in the Bolonha reservoir, at the entrance of the WTP-Bolonha water catchment. The second point, named washing water (WW), was situated in the filters,

and the collection occurred when the washing of one of them was performed. The compounds with higher lipophilicity or less solubility in water can be adsorbed on the organic matter entrapped in the filters of the treatment plant. Thus, evaluating the WW of these filters provides important information, as the disposal of this waste can be a new source of contamination. The third point, named filtered water (FW), was in the outlet channel that collected the effluent from the filters. Finally, the fourth collection point was situated in the distribution water reservoir, after the disinfection stage, designated as chlorinated water (CW) (Fig. 2).

Twelve (12) sampling campaigns were conducted, of which six (6) related to the rainy period (January to March 2018) and another six (6) to the dry period (September to November 2018), a sampling per month. Composite sample was used for determination of the physicochemical variables and microcontaminants in the four collection points using the amber glass bottles (1 L) immersion

Fig. 2 Bolonha Complex location and sampling location: 1—RW (Bolonha reservoir), 2—WW (filter washing waters), 3—FW (Outlet channel of the filters), and 4—CW (Distribution water reservoir)



technique at a depth of 0 to 30 cm from the water (CETESB, 2011). Collections at all points were performed every 0 min in the interval from 07:00 a.m. to 07:00 p.m. by a team of six people.

In order to obtain a composite sample, the water was collected every 30 min in a glass bottle and then 170 mL was measured and poured into an amber glass bottle, totaling about 4 L after 12 h of collection. At the 2nd point (WW), unlike the other ones, the collection was performed with the aid of a 500-mL beaker, because the turbulent flow and difficult access in the filtered water chamber made it impossible to use the amber bottle (1 L). As in the other points, the water was homogenized and passed to a graduated cylinder and then to the amber bottle (4 L). All glassware used in this study was previously decontaminated with Extran solution and acetonitrile before use. The samples collected were kept in icebox and immediately taken to the laboratory where they were kept under refrigeration until processed.

Physicochemical and biological analysis

The analytical procedures used to determine the variables alkalinity, conductivity, apparent color, dissolved oxygen (DO), pH, turbidity, and *Escherichia coli* followed the standardized and validated methodology as described in the Standard Methods for the Examination of Water and Wastewater (APHA/AWWA/WEF, 2017), and the HACH® Spectrophotometer Manual. *E. coli* was determined by enzyme substrate tests Colilert® that use hydrolyzable chromogenic and fluorogenic substrates to simultaneously detect enzymes produced by total coliforms and *E. coli*. The physicochemical analyses were performed at the Multi-user Water Treatment Laboratory (LAMAG) of Federal University of Pará (UFPA), which is under the management of the Water Management and Wastewater Reuse Study Group (GESA). The methods used for analysis of each variable are listed in Table 1, and for all parameters analysis of distilled water was

Table 1 Methods of analysis used for quantification of physicochemical and biological parameters in waters collected at WTP-Bolonha (Belém—PA), Brazil

| Variable (unit) | Method | Equipment |
|--|----------------|--|
| Total alkalinity (mg L ⁻¹) | Titulometric | pH meter PG 1800 Gehaka®, magnetic stirrer and automatic pipette |
| Free residual chlorine (mg L ⁻¹) | Colorimetric | Checker® HC Free Chlorine—HI701 (Hanna®) |
| Electrical conductivity (µS cm ⁻¹) | Potentiometric | Multiparameter Meter HI9829 (Hanna®) |
| Apparent color (UH) | Colorimetric | Policontrol®- Aquacolor Colorimeter |
| DO (mg L ⁻¹) | Potentiometric | Multiparameter Meter HI9829 (Hanna®) |
| pH (–) | Potentiometric | Multiparameter Meter HI9829 (Hanna®) |
| Turbidity (UNT) | Nephelometric | Turbidimeter Ap2000—Policontrol® |
| <i>E-coli</i> (NMP per 100 mL) | Colilert | Cardboard, Quanti-Tray®/2000 Sealer and an oven Q316M2 Quimis® |

carried out as blank to offset any eventual glassware contamination.

Extraction of micropollutants

The analyses of drugs and endocrine disruptors were based on the studies conducted by Corrêa et al. (2021) and Sanson (2012), developed at the Laboratory of Molecular Characterization and Mass Spectrometry (LABMASSAS) of Federal University of Ouro Preto (UFOP). For this purpose, water samples collected were immediately submitted to vacuum filtration processes in fiberglass membranes of different porosities (8 µm, followed by 2 µm and 0.45 µm) for the removal of particulate material. It is important to note that the samples began to be analyzed soon after collection, and for microcontaminants analysis filtration was performed the day after collection.

For the extraction, 1000 mL of sample were used. The pH of the filtered samples was adjusted to 2.0 ± 0.2 with hydrochloric acid (25%), followed by the addition of 500 mg of ethylenediaminetetraacetic acid (EDTA). The samples were kept at rest and then agitated every 20 min to be submitted to solid phase extraction (SPE) after 60 min of EDTA addition (metal chelating agent). Subsequently, samples were subjected to extraction processes by solid phase extraction cartridges filled with the modified divinylbenzene adsorber phase consisting of lipophilic and hydrophilic sites (Strata X®), with a flow rate of 5 to 10 mL·min⁻¹. The extraction procedure was performed using positive nitrogen pressure, according to the methodology of Sanson et al. (2014).

The SPE cartridges containing the compounds of interest were identified and stored in a freezer

(–20 °C) protected from light, to be further sent to the Molecular Characterization and Mass Spectrometry Laboratory (LABMASSAS) of UFOP. In LABMASSAS the SPE cartridges were submitted to elution of the analytes using 9 mL of ethyl acetate in a 12-port manifold (homemade) (Corrêa et al., 2021). Subsequently, the resulting extracts were dried with gaseous nitrogen by means of a concentrating apparatus that kept the extracts at room temperature during the drying process. The flasks with the dried extracts were kept in a freezer until the analysis.

GC–MS analysis

The extracts from the solid-phase extraction were redissolved in 500 µL of HPLC-grade methanol (J.T. Baker), agitated by vortex for approximately 30 s and transferred to two vials containing flow restrictors. The vial (A) contained 100 µL of sample and the vial (Aspike) included 70 µL sample + 30 µL standard solution of 100 µg L⁻¹ methanol. Extracts were then completely dried under nitrogen gas flow and stored in a freezer (–26 °C) until analyzed (Sanson, 2012).

For the analytical curves, stock solutions in methanol HPLC-grade (J.T. Baker) of each analyte (ibuprofen, paracetamol, 4-nonylphenol, 4-octylphenol, bisphenol A, gemfibrozil, estrone, estradiol, ethinylestradiol, and estriol) were prepared at a concentration of 1 g L⁻¹. From these solutions, a 1-mg L⁻¹ working solution in methanol containing all the analytes was prepared, which was also stored in a freezer. Dilutions with methanol were performed for the analytical curves from the working solution on the day of the analysis, in a concentration range of 2.5 to 100 µg L⁻¹. The vials containing the solutions for the

construction of the analytical curve were also submitted to dryness under nitrogen gas flow. All samples were derivatized and then redissolved with 75 μL of N,O-Bis (trimethylsilyl) trifluoroacetamide: trimethylchlorosilane (BSTFA:TMCS, 99:1, GCMS, Sigma Aldrich) and 25 μL of pyridine solution (Merck) containing 200 $\mu\text{g L}^{-1}$ of 4-n-nonylphenol- 2,3,5,6-d4 (CDN Isotopes), used as internal standard (IS). Subsequently, they were maintained at 80 $^{\circ}\text{C}$ for 30 min and then analyzed by gas chromatography coupled to mass spectrometry (GC–MS) (Sanson, 2012).

All analyses were performed in a gas chromatograph coupled to the GCMS-QP2010 Plus (Shimadzu) mass spectrometer at LABMASSAS of the UFOP. Injection of 1 μL of each sample was performed by the automatic injector model AOC-20i (Shimadzu), and the chromatographic column used was the Zebron ZB-5MSi (30 m \times 0.25 mm \times 0.25 μm , Phenomenex). The temperature program consisted of an isotherm at 120 $^{\circ}\text{C}$ for 1 min, followed by a temperature rise up to 227 $^{\circ}\text{C}$ at a rate of 15 $^{\circ}\text{C min}^{-1}$, then increasing to 240 $^{\circ}\text{C}$ at 10 $^{\circ}\text{C min}^{-1}$ until finally reaching 330 $^{\circ}\text{C}$ at 15 $^{\circ}\text{C min}^{-1}$ and remaining at this temperature for 2 min. Samples were injected in the splitless mode for 0.5 min, followed by a 1:20 split ratio, purge flow rate of 5.0 mL min^{-1} , and injector temperature of 280 $^{\circ}\text{C}$. Helium 5.0 was used as carrier gas at a total flow rate of 25.9 mL min^{-1} and a linear velocity of 36.5 cm s^{-1} . For the mass spectrometer temperatures of 280 $^{\circ}\text{C}$ were used at the interface and 250 $^{\circ}\text{C}$ at the ionization source, using 70 eV for electronic ionization (Sanson, 2012).

The mass/charge ratios (m/z) monitored for each derivatized analyte are described in Table 2, as well as their retention times (Sanson, 2012). The response used to construct the analytical curves was the relationship between the analyte area and the internal standard (IS) area (y -axis) and the concentration of the analyte (x -axis). Thus, for the samples, the ratio between the areas of analyte/IS was also used. The matrix effect (ME) was evaluated by Eq. 1, in which A_{spike} is the area of the analyte in the spike vial, A is the area of the analyte in the sample vial, and in the denominator is represented the area of the substance at 30 $\mu\text{g L}^{-1}$ according to the equation of the analytical curve. Therefore, the correction of ME was made punctually in relation to the samples as well as to the analytes. The ME can compromise the quantification of the compounds, increasing or decreasing their signal, normally by blocking the active sites of the free silanol groups at the inlet of the GC system (Bizkarguenaga et al., 2012; H. Liu et al., 2010; Mastovsha et al., 2005). Moreover, the correction was performed regarding the recovery of the analytes in the extraction procedure.

$$ME = \frac{A_{\text{spike}} - 0,7 \times A}{\text{standard area } 30 \mu\text{g/L}} \quad (1)$$

LC–MS/MS analysis

The method for analysis by LC–MS/MS was developed at LABMASSAS, and this data has not yet been

Table 2 Retention times and mass/charge ratios (m/z) of microcontaminants analyzed by GC–MS

| Analyte | Acronym | Retention time (min) | m/z quantification | m/z identification |
|-------------------------|---------|----------------------|----------------------|--------------------------------|
| Ibuprofen | IBU | 7.145 | 160.00 | 263.00; 234.00; 278.00 |
| Paracetamol | PCT | 7.224 | 206.00 | 280.00; 295.00; 116.00 |
| 4-octylphenol | 4OP | 8.460 | 179.00 | 278.00; 180.00; 279.00 |
| 4-n-nonylphenol-d4 (IS) | 4NPd | 9.197 | 183.00 | 281.00; 296.00; 207.00 |
| 4-nonylphenol | 4NP | 9.312 | 179.00 | 292.00; 277.00; 165.00 |
| Gemfibrozil | GEM | 9.418 | 201.00 | 122.00; 194.00; 202.00 |
| Bisphenol-A | BPA | 11.397 | 357.00 | 358.00; 207.00; 359.00; 372.00 |
| Estrone | E1 | 13.896 | 342.00 | 257.00; 218.00; 244.00 |
| Estradiol | E2 | 14.237 | 416.00 | 285.00; 326.00; 417.00; 232.00 |
| Ethinylestradiol | EE2 | 14.832 | 425.00 | 426.00; 440.00; 285.00 |
| Estriol | E3 | 15.413 | 504.00 | 311.00; 345.00; 386.00; 414.00 |

published. The extracts obtained from the SPE were redissolved in 500 μL of HPLC grade methanol (J.T. Baker), agitated in a vortex for approximately 30 s, and transferred (100 μL) to a vial containing a volume restrictor. This extract was then dried under nitrogen gas flow and kept in a freezer ($-26\text{ }^\circ\text{C}$) until analysis.

For the analytical curves, stock solutions in methanol HPLC grade (J.T. Baker) of each of the analytes (metformin, acyclovir, atenolol, caffeine, linezolid, propranolol, diltiazem, promethazine, losartan, bezafibrate, diclofenac, dexamethasone, loratadine, sulfamethoxazole, and naproxene) were prepared in a concentration of 1 g L^{-1} . The working solution containing all the analytes was prepared from these solutions at a concentration of 1 mg L^{-1} in methanol, which was also stored in a freezer. For the analytical curves, dilutions were made with methanol containing 0.1% v/v formic acid (88%, J.T. Baker) from the working solution on the day of analysis, with a concentration range of 2.5 to $50\text{ }\mu\text{g L}^{-1}$. In addition, vials named spike (A_{spike}) were prepared, containing standard solution in methanol with 0.1% v/v formic acid with all the analytes at a concentration of $30\text{ }\mu\text{g L}^{-1}$, and the vial named solvent (A_{sol}) containing methanol with 0.1% v/v formic acid.

On the day of sample analyses, the vials containing the dry extract were redissolved with 100 μL of methanol with 0.1% v/v formic acid. The analyses were performed using the LCMS-8040 (Shimadzu) equipment coupled with the UHPLC system Nexera (Shimadzu) comprising the following modules: CBM-20A controller, 3 LC-30AD pumps, SIL-30AC sampler, CTO-30A column oven, and DGU-20As degasser. A C18 chromatographic column model Kinetex (Phenomenex) $100\text{ mm} \times 2.1\text{ mm} \times 2.6\text{ }\mu\text{m}$ was used. The mobile phase consisted of (A) ultrapure water with 0.1% v/v formic acid and (B) acetonitrile (HPLC grade, J. T. Baker) with 0.1% v/v formic acid, using the following gradient steps of solvents: 5% B from 0 to 1 min, reaching 60% B at 12 min, rising to 95% B at 13 min, and returning to the initial condition at 14 min. This resulted in a total running time of 16 min under a flow rate of 0.250 mL min^{-1} . A third mobile phase (C), acetonitrile solution containing 3.5 mM ammonium hydroxide (28%, Sigma Aldrich), was subsequently added to the column at a flow rate of 0.03 mL min^{-1} .

Each sample was injected twice: (A_{sol}) 10 μL + 5 μL solvent sample and (A_{spike}) 10 μL + 5 μL spike.

This analysis was performed to calculate the punctual matrix effect for each sample and each analyte. The same injection model was performed with standard solutions of the analytical curves, so that the calibration curve was built using the ratio estimated by Eq. 2 and the analyte concentration.

$$\text{ratio} = \frac{\text{analyte area } (A_{\text{sol}})}{\text{analyte area } (A_{\text{spike}}) - \text{analyte area } (A_{\text{sol}})} \quad (2)$$

The general conditions employed in the method used for the mass spectrometer are presented in Table 3, whereas the precursor ions, products monitored in Multiple Reaction Monitoring (MRM) mode, and the retention times used for each analyte are described in Table 4. After the LC-MS/MS analyses, data were treated considering the recovery percentage of each analyte. The matrix effect was corrected using the ratio as a response; i.e., the correction of the effect was punctual in relation to the sample and the analyte.

Risk analysis

Risk analysis was performed by calculating the margin of exposure (MOE) of compounds with the highest frequency of occurrence. The MOE was estimated by the ratio between the guide value (calculated from epidemiological and/or toxicological information) and the concentration of the contaminant in the distributed water (Eq. 3). The MOE represents whether the occurrence of the compound in question is lower or higher than its guide value, being interpreted as follows: (i) $\text{MOE} \leq 1$ for compounds in treated water in concentrations higher than or equal to the guide values and therefore represent health risks,

Table 3 Conditions established in the method for the analysis of pharmaceuticals by liquid chromatography coupled to mass spectrometry (LC-MS/MS)

| Parameter | Condition used |
|-------------------------------------|---------------------------|
| Collision cell gas (CID)—argon | 230 kPa |
| Interface temperature | 350 $^\circ\text{C}$ |
| Temperature of desorption line (DL) | 200 $^\circ\text{C}$ |
| Nebulizer gas flow (nitrogen) | 1.50 L min^{-1} |
| Heating block temperature | 400 $^\circ\text{C}$ |
| Drying gas flow (nitrogen) | 15.00 L min^{-1} |

Table 4 Mass/charge ratio (m/z) of precursor and products monitored in LC/MS in Multiple Reaction Monitoring (MRM) mode

| Analyte | Acronym | Retention time (min) | Precursor (m/z) | Products (m/z) |
|------------------|---------|----------------------|---------------------|-----------------------------------|
| Metformin | MET | 1.009 | 130.10 | 59.95 and 60.10 |
| Acyclovir | ACV | 1.065 | 226.00 | 151.95 and 185.10 |
| Atenolol | ATN | 2.812 | 267.05 | 144.95; 190.05 and 56.00 |
| Caffeine | CAF | 4.161 | 195.00 | 138.10 and 42.00 |
| Linezolid | LNZ | 6.494 | 338.20 | 296.00 and 235.00 |
| Propranolol | PNL | 6.627 | 260.25 | 116.10; 56.00; 74.15 and 183.05 |
| Diltiazem | DTZ | 6.646 | 414.95 | 177.95; 150.00; 109.10 and 201.00 |
| Promethazine | PRO | 6.661 | 285.05 | 86.00; 71.10; 197.85 and 239.90 |
| Losartan | LST | 6.762 | 423.10 | 207.10; 405.15 and 180.00 |
| Bezafibrate | BEZ | 6.764 | 362.00 | 138.95; 316.05 and 276.05 |
| Diclofenac | DCF | 6.785 | 295.90 | 214.95; 249.90 and 213.95 |
| Dexamethasone | DXM | 6.783 | 393.10 | 373.15; 355.10 and 149.00 |
| Loratadine | LRT | 6.782 | 383.05 | 336.95; 266.95 and 259.05 |
| Sulfamethoxazole | SMX | 6.500 | 253.95 | 155.95; 108.00 and 92.10 |
| Naproxen | NPX | 6.621 | 231.00 | 185.10; 170.35 and 77.35 |

(ii) $1 < \text{MOE} < 10$ for compounds found in treated water in concentrations lower than the guide values, but that are in the same order of magnitude as the concentrations which would pose health risks, and (iii) $\text{MOE} \geq 10$: compounds that are found in treated water at concentrations lower than the guide values in more than one order of magnitude (EPHC NHMRC NRMCC, 2008; USEPA, 2016).

$$\text{Margin of exposure (MOE)} = \frac{\text{VG}(\text{ngL} - 1)}{\text{OC}(\text{ngL} - 1)} \quad (3)$$

where MOE is the margin of exposure, VG is the guide value (calculated by Eq. 4 using the lowest tolerable daily intake value reported in the literature), and OC is the occurrence of the compound in treated water (95th percentile of the occurrence in treated water).

$$\text{Guide value } (\mu\text{gL} - 1) = \frac{\text{TDI } (\mu\text{g kg} - 1 \text{ day} - 1) \times \text{BW}(\text{kg}) \times \text{AF}}{V \text{ (L/day)}} \quad (4)$$

where TDI is the tolerable daily intake ($\mu\text{g kg}^{-1} \text{ day}^{-1}$), derived from epidemiological or toxicological studies and, in the case of drugs, the TDI can be estimated by the therapeutic doses reported by manufacturers or pharmacopoeias considering

an uncertainty factor, as presented in Eq. 5; BW means body weight (60 kg for the Brazilian population); AF means allocation factor (proportion of TDI attributed to water intake, which varies according to the contaminant), and V is the daily average water consumption (2 L day^{-1} for the Brazilian population). Different values for AF were adopted depending on the authorized use of the medicine (e.g., for humans only or also for veterinary application) according to the Australian Guide for Water Reuse for Human Supply approach (EPHC NHMRC NRMCC, 2008).

$$\text{TDI } (\mu\text{gkg} - 1 \text{ day} - 1) = \text{MDTD}/(\text{UF} \times \text{BW}) \quad (5)$$

where MDTD means the minimum daily therapeutic dose (mg day^{-1}) and UF is the uncertainty factor, which was typically 1000 to take into account intra (10) and

interspecies (10) variations, and the fact that the MDTD is not a level without effects (10), that is, the approach is similar to the application of LOAEL (lowest adverse effect level) instead of NOAEL (no observed adverse effect level) (EPHC NHMRC NRMCC, 2008).

Results and discussion

Occurrence and removal of microcontaminants in WTP-Bolonha

The average monthly rainfall in the collection periods was 505 mm during the rainy period (January to March 2018) and 180 mm during the dry period (September to November 2018); thus, indicating that in the dry period, there was nearly three times less rainfall (Agência Nacional de Águas, 2020). Table 5 shows the values obtained for the physicochemical and biological variables monitored in the reservoir (RW) that supplies the WTP-Bolonha (Belém/PA).

See also the Supplementary Table 1A–C for data regarding the characterization of WW, FW, and CW.

It was observed an increase in the median concentration of the parameters apparent color, turbidity, and electrical conductivity in the rainy period of 112%, 85%, and 82% in relation to the dry period, which can be explained by the increase in surface runoff, with consequent carrying of solids, caused by the intense rainfall typical of the region. The increased contribution of biodegradable solids (suspended and dissolved) may explain the reduction in the content of dissolved oxygen in the rainy season, since the system under study is inserted in an area that suffers from a disorderly population increase, with inadequate

Table 5 Descriptive statistics of the physicochemical and biological variables determined in the water from the reservoir (RW) that supplies WTP-Bolonha (Belém-PA)

| Variables | Alk (mg L ⁻¹) | DO (mg L ⁻¹) | pH (-) | Cond. (µS cm ⁻¹) | Color A. (uH) | Turb. (NTU) | <i>E. coli</i> (NMP per 100 mL) |
|-------------------|---------------------------|--------------------------|--------|------------------------------|---------------|-------------|---------------------------------|
| Rainy period 2018 | | | | | | | |
| <i>N</i> | 6 | 6 | 6 | 6 | 5 | 6 | 6 |
| Minimum | 10.2 | 3.3 | 5.6 | 58.0 | 56.0 | 7.5 | 146 |
| Mean | 11.5 | 4.3 | 5.9 | 85.3 | 84.6 | 17.0 | 288 |
| Median | 11.5 | 4.3 | 5.8 | 84.0 | 85.0 | 16.9 | 272 |
| Maximum | 12.5 | 4.9 | 6.3 | 112.0 | 108.0 | 23.7 | 502 |
| SD | 0.8 | 0.6 | 0.3 | 23.3 | 20.4 | 5.9 | 149 |
| CV (%) | 6.5 | 15.1 | 4.5 | 27.4 | 24.1 | 34.5 | 52 |
| Dry period 2018 | | | | | | | |
| <i>N</i> | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Minimum | 8.8 | 5.8 | 6.0 | 40.0 | 26.9 | 4.8 | 38 |
| Mean | 12.4 | 6.0 | 6.3 | 49.6 | 41.8 | 9.3 | 386 |
| Median | 13.2 | 6.0 | 6.2 | 46.1 | 40.1 | 9.1 | 320 |
| Maximum | 13.9 | 6.4 | 6.5 | 68.8 | 56.7 | 13.5 | 932 |
| SD | 2.0 | 0.2 | 0.2 | 10.5 | 13.3 | 3.7 | 380 |
| CV (%) | 16.3 | 3.2 | 3.4 | 21.1 | 31.7 | 39.2 | 98 |
| Annual 2018 | | | | | | | |
| <i>N</i> | 12 | 12 | 12 | 12 | 11 | 12 | 12 |
| Minimum | 8.8 | 3.3 | 5.6 | 40.0 | 26.9 | 4.8 | 38 |
| Mean | 11.9 | 5.1 | 6.1 | 67.5 | 61.2 | 13.2 | 337 |
| Median | 11.7 | 5.4 | 6.0 | 61.5 | 56.0 | 13.2 | 272 |
| Maximum | 13.9 | 6.4 | 6.5 | 112.0 | 108.0 | 23.7 | 932 |
| SD | 1.5 | 1.0 | 0.3 | 25.4 | 27.5 | 6.1 | 280 |
| CV (%) | 12.7 | 20.2 | 5.2 | 37.7 | 44.9 | 46.5 | 83 |
| CONAMA Standards | - | >5 | 6–9 | - | - | 100 | 1000 |

Water quality fixed for different uses according to Brazilian legislation on water resources (CONAMA, 2005). The values shown here refer to the limits for Class 2 Water Bodies, intended for public supply after conventional water treatment

Alk. total alkalinity, *DO* dissolved oxygen, *Cond.* electrical conductivity, *Color A.* apparent color, *Turb.* turbidity, *SD* standard deviation, *CV* coefficient of variation

solid waste collection services and without sewage treatment.

The raw data on the occurrence of drugs and endocrine disruptors in raw water (RW), shown in Table 6, indicated that 12 out of 25 compounds monitored were not detected in any of the 12 raw water samples analyzed. On the other hand, 4-octylphenol (4OP), bisphenol A (BPA), and losartan (LST) compounds were present in concentrations above the quantification limits (lowest concentration of a substance that can be correctly ascertained) of the analytical method in all analyzed RW samples, and loratadine (LRT) was quantified in RW in 11 of the 12 analyzed samples. The supplementary material (Table 2A–C) presents the concentration of the target compounds in the WW, FW, and CW samples.

The 4OP is a by-product of the degradation of alkylphenol ethoxylated surfactants, of wide domestic use; the BPA is a chemical compound used in the manufacture of plastics and resins that coat

packaging, which can leach from them (Wee & Aris, 2017); the LST and LRT are drugs used for the treatment of hypertension and allergies, respectively (“ChemIDplus” n.d.; NATIONAL CANCER INSTITUTE, 2020). The presence of such contaminants at high frequency in the Bolonha reservoir has confirmed its history of contamination evidenced by recurrent eutrophication events.

In turn, the GEM drug (gemfibrozil, an antilipemic) was quantified in 4 RW samples, all collected during the dry period, while E1 (estrogen, estrogenic hormone), EE2 (ethinylestradiol, synthetic estrogen), and BZF (bezafibrate, hypolipidemic drug) were detected in only 2 RW samples. On the other hand, the compounds ACV (acyclovir), NPX (naproxene), IBU (ibuprofen), PCT (paracetamol), and 4NP (4-nonylphenol) were detected in only 1 of the RW samples collected over the 12 sampling campaigns.

The lower occurrence of these compounds is expected in RW samples, as they have value for the

Table 6 Concentration (ng L⁻¹) of drugs and endocrine disruptors in raw water (RW) of WTP-Bolonha (Belém-PA) considering the dry and rainy periods

| Analyte | Rainy period | | | | | | Dry period | | | | | |
|---------|--------------|-------|-------|-------|-------|--------|------------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 1 | 2 | 3 | 4 | 5 | 6 |
| IBU | n.d | n.d | n.d | n.d | 9.1 | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| PCT | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | 3.7 | n.d |
| 4OP | 2.6 | 9.2 | 3.5 | 7.4 | 12.2 | 33.4 | 3.9 | 5.6 | n.d | 3.4 | 3.9 | 2.2 |
| CAF | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| 4NF | n.d | n.d | n.d | n.d | n.d | 42.9 | n.d | n.d | n.d | n.d | n.d | n.d |
| GEM | n.d | n.d | n.d | n.d | n.d | n.d | 18.0 | 11.4 | n.d | n.d | 23.5 | 13.1 |
| NPX | n.d | n.d | n.d | n.d | n.d | n.d | 351.8 | n.d | n.d | n.d | n.d | n.d |
| BPA | 153 | n.d | 67.9 | 30.2 | 129.3 | 27.7 | 145.7 | 110.6 | 44.0 | 107.2 | 155.2 | 45.3 |
| DCF | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| E1 | n.d | n.d | n.d | n.d | n.d | 42.6 | n.d | 15.3 | n.d | n.d | n.d | n.d |
| E2 | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| EE2 | n.d | n.d | n.d | n.d | n.d | n.d | n.d | 78.7 | n.d | n.d | 113.9 | n.d |
| E3 | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| MET | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| ACV | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | 31.5 | n.d | n.d |
| LNZ | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| PNL | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| DTZ | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| PRO | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| LST | 494 | 143.7 | 210.6 | 171.3 | 177.8 | 578.8 | 233.0 | 86.9 | 139.7 | 132.5 | 239.9 | 112.4 |
| BEZ | n.d | n.d | 1365 | n.d | 269.6 | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| DXM | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |
| LRT | 22.8 | n.d | 45.0 | 20.0 | 24.0 | 37.0.9 | 21.6 | 15.7 | 17.3 | 18.4 | 31.1 | 18.2 |
| SMX | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d | n.d |

n.d not detected

organic carbon–water (K_{oc}) partition above 300, indicating high adsorption in sediments and suspended solids and, consequently, reduced availability in the water column (“Soil Adsorption Coefficient ($K_d/K_f/K_{oc}/K_{foc}$)” 2016). Except for ACV and PCT, these compounds have low K_{oc} values (10 and 21, respectively), indicating low adsorption to sediments and suspended solids. However, the ACV has high biodegradability, as demonstrated by Prasse et al. (2011), who found a biodegradation half-life value of 5.3 h. The carboxy-ACV by-product is found with greater frequency and concentration in samples of surface and groundwater compared to ACV (Prasse et al., 2011). On the other hand, PCT is eliminated preferentially as a glucuronide conjugate and a sulfate conjugate, with less than 5% being excreted in the form of free PCT (“Acetaminophen” n.d.).

The concentration values observed in RW were higher in the rainy season for LST and 4OP compounds, while these were higher in the dry period for BPA and similar between the dry and rainy periods for LRT. While the rainy period implies a greater dilution of the drugs brought into the water body via sewage discharges, it also increases the amount of pollutants present in the soil and carried by surface runoff.

Regarding the filtered water (FW) and chlorinated water (CW) from WTP-Bolonha, the same compounds (4OP, BPA, LST, and LRT) were highlighted (data not shown) due to their high frequency of occurrence, but without significant differences in concentration between the dry and rainy periods. The presence of 4OP, BPA, LST, and LRT compounds was also higher in the filter washing water (FWW). In this case, there was a different frequency of occurrence between the dry and rainy periods, with the highest concentrations observed in the rainy period, except for BPA, which showed higher absolute values in the dry period.

The endocrine disruptor 4OP and the drugs LST and LRT showed high octanol/water partition coefficients (K_{ow}), with log K_{ow} values estimated at 4.01, 5.2, and 5.76 respectively (PubChem, 2020), thus indicating a high sorption tendency in hydrophobic materials. The higher turbidity and apparent color of the raw water in the rainy season potentially leads to a higher input of solids (not retained in the sedimentation tanks) into the sand filters, which could justify the higher concentration of 4OP, LST, and LRT

compounds in the filter wash water if the retained solids would actually contain such microcontaminants. The desorption of such hydrophobic compounds from the solids retained in the filters may occur by displacement of the chemical equilibrium when “washing” the solids containing microcontaminants with an aqueous solution (washing water) that contains a lower concentration of these compounds, as the filters receive the water after the settler and work in 24-h cycles. At the end of each cycle, washing is performed and samples are collected. In addition, the settlers operated above the designed flowrate so that part of the unretained sludge was carried to the filters. Since some of these compounds have a high affinity to sludge, their concentration on the WW may be affected by these factors.

Table 7 presents the descriptive statistics of the 4 microcontaminants which occurred most frequently in the samples collected at WTP-Bolonha. As there was a relatively large variation in the concentration of each contaminant over the 12 sampling campaigns, the standard deviation was high and the mean was considerably affected by the extreme values. The analysis of the median concentration values showed that there was no significant difference when comparing RW and FW, with the exception of BPA and LST compounds during the rainy season, indicating that the clarification step (coagulation \geq flocculation \geq decantation \geq filtration) had little effect on the removal of the most prevalent contaminants in RW. The clarification step was responsible for removing up to 15% of BPA, LST, and LRT in the dry season, whereas for the rainy season, the clarification contributed to the removal (in median terms) of 50% of LST present in RW. The concentration of BPA in the FW seems to be affected by the increase in water flow during the rainy season. This is because it results in a greater supply of solids from the decanter, due to the overload of the system, and a drag of the BPA adsorbed onto the filter particles. The increase in the concentration of BPA in the treated water also occurs occasionally, as reported by Dupuis et al. (2012).

However, concentrations of BPA and LST were significantly lower in chlorinated water (CW), therefore suggesting that the disinfection step was responsible for the median removal of 54% (rainy season) to 64% (dry season) of BPA and 55% (rainy season) to 90% (dry season) of LST. The highest removal efficiencies in the dry period coincided with the highest

Table 7 Descriptive statistics for compounds quantified with high frequency at the 4 collection points of WTP-Bolonha (Belém-PA)

| Analyte | Unit | Raw water | Filtered water | Chlorinated water | Washing water |
|--------------|--------------------|----------------|----------------|-------------------|----------------|
| Dry period | | | | | |
| 4OP | ng L ⁻¹ | 3.2 ± 1.9* | 4.2 ± 0.6* | 4.2 ± 1.4* | 5.8 ± 1.8* |
| | | 3.7** | 4.0** | 4.3** | 5.8** |
| BPA | ng L ⁻¹ | 101.3 ± 47.8* | 125.5 ± 84.9* | 35.0 ± 10.4* | 221.0 ± 166.8* |
| | | 108.9** | 107.3** | 39.0** | 197.2** |
| LST | ng L ⁻¹ | 157.4 ± 64.0* | 133.4 ± 51.0* | 16.2 ± 13.8* | 0.2 ± 0.0* |
| | | 136.1** | 135.2** | 13.8** | 0.2** |
| LRT | ng L ⁻¹ | 20.4 ± 5.6* | 17.3 ± 1.0* | 14.4 ± 6.9* | 17.2 ± 3.5* |
| | | 18.3** | 16.9** | 16.2** | 16.7** |
| Rainy period | | | | | |
| 4OP | ng L ⁻¹ | 11.4 ± 11.4* | 10.9 ± 5.3* | 13.8 ± 13.5* | 9.0 ± 8.5* |
| | | 8.3** | 10.3** | 9.8** | 7.4** |
| BPA | ng L ⁻¹ | 68.0 ± 61.1* | 145.1 ± 182.0* | 42.0 ± 32.5* | 151.6 ± 141.7* |
| | | 49.1** | 84.2** | 38.3** | 97.6** |
| LST | ng L ⁻¹ | 296.0 ± 189.3* | 99.0 ± 67.8** | 99.4 ± 157.3* | 0.8 ± 1.6* |
| | | 194.2** | 96.2* | 43.3** | 0.2** |
| LRT | ng L ⁻¹ | 25.1 ± 15.3* | 23.2 ± 11.5* | 19.2 ± 3.0* | 27.4 ± 18.1* |
| | | 23.4** | 19.9** | 18.9** | 26.3** |

*Mean and standard deviation

**Median

median concentrations of BPA and LST observed in filtered water and may indicate that the oxidation rate is dependent on the concentration of the microcontaminant, as found in first order kinetic models (Levenspiel, 2000).

From Table 7 it can be seen that the global removal, expressed as medians, of the most prevalent microcontaminants in WTP-Bolonha was from -16% (dry) to -18% (rainy) for 4OP (the median concentration in chlorinated water was higher than in raw water, which may have occurred due to the chemical oxidation of ethoxylated alkylphenols in the chlorination step), from 22% (rainy) to 64% (dry) for BPA, from 78% (rainy) to 90% (dry) for LST, and from 11.5% (dry) to 19% (rainy) for LRT. Although there was a high removal of LST in both sampling periods, it was noticed that the water distributed to the population contained this antihypertensive drug in median concentrations varying from 13.8 to 43.3 ng L⁻¹. Subsequently, a human health risk analysis will be performed on the presence of the 4 microcontaminants detected most frequently in the water treated and distributed by WTP-Bolonha.

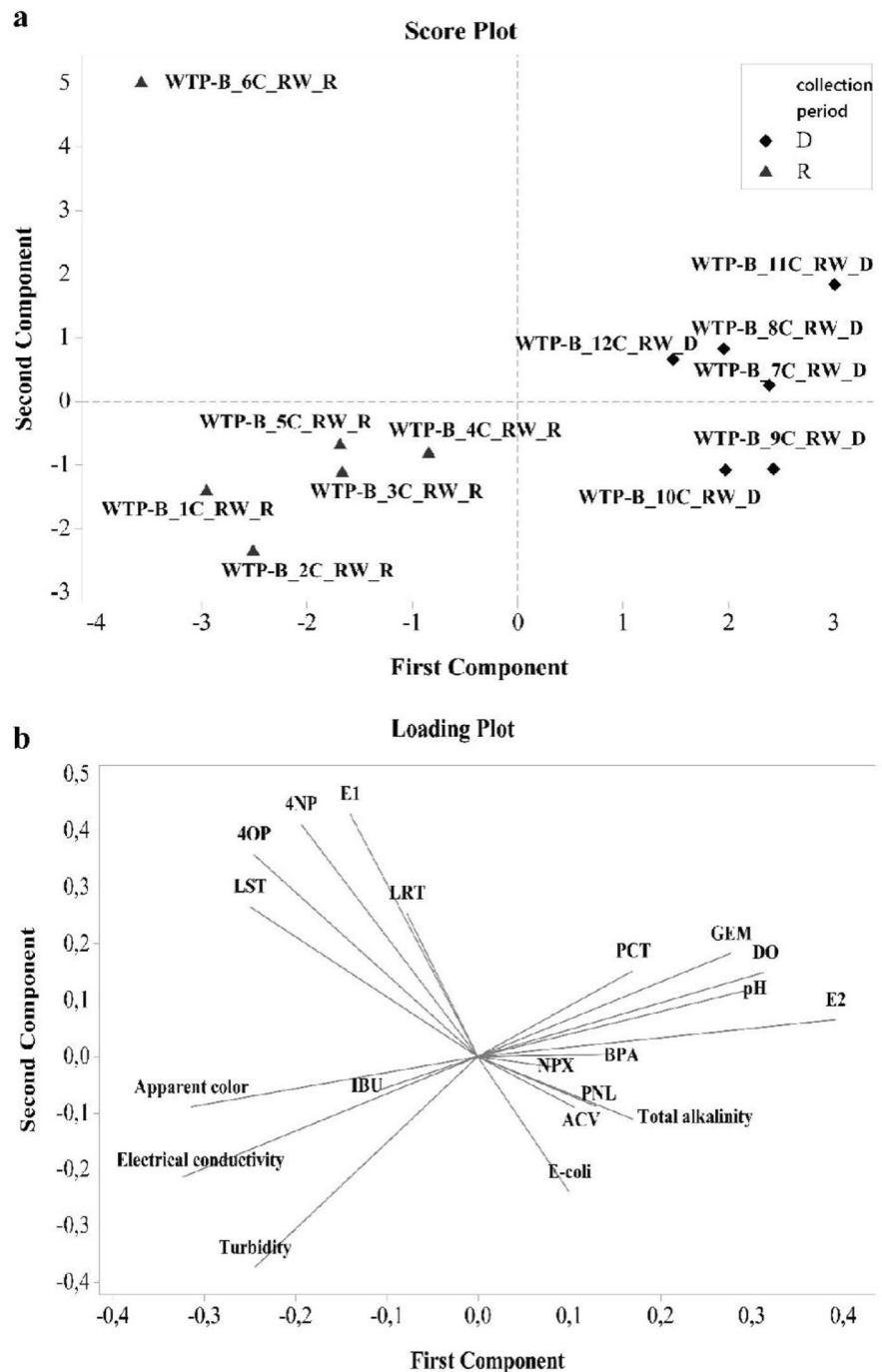
Correlations between raw water characterization parameters

Figure 3 shows the principal component analysis (PCA) graphs obtained from the multivariate

statistical treatment of the occurrence data of microcontaminants in the raw water of WTP-Bolonha. The PCA was performed to allow visualization of the sample groupings and the relationship with each of the analyzed variables, both in relation to microcontaminants, as well as physical-chemical and biological analyzes. Calderón-Preciado et al. (2011), Calderón-Preciado et al. (2013), Chamorro et al. (2013), and Peré-Trepát et al. (2004) also performed the PCA to interpret data on the occurrence of microcontaminants in waters. Figure 3a shows that samples from the dry and rainy periods are grouped separately, since in quadrants 1 and 4 there are samples from the rainy period, with positive weight in PC1, and in quadrants 2 and 3 there are samples from the dry period, with negative weight. The WTP-B_6C_RW_R sample (raw water sample collected in the sixth campaign, during the rainy season) in the 1st quadrant was highlighted in the rainy season. Although the weight chart indicates that its distribution is due to five variables, the ones with greater weight are 4OP, 4NF, and E1, which occurred in high concentrations. In turn, the other samples in the rainy period were grouped according to the highest weight of the parameters' apparent color, conductivity, and turbidity.

Two groups can be observed in the samples collected in the dry period, one in the 2nd and the other in the 3rd quadrant. The samples of campaigns 7, 8,

Fig. 3 Analysis of principal components (PCA) of microcontaminant concentrations and indicator parameters of raw water quality that supplies the WTP-Bolonha: **a** score plot; **b** loading plot



11, and 12 were grouped due to the weight of 5 variables, among them GEM which occurred in relatively high concentrations (11.4 to 23.5 ng L⁻¹). In the samples of the sampling campaigns 9 and 10 (3rd quadrant), the highest concentrations of *E. coli* (932 and 659 NMP per 100 mL, respectively) were observed,

thereby contributing to the grouping of these two samples belonging to the dry period.

Figure 3b shows that LRT, LST, 4OP, 4NP, and E1 microcontaminants appeared grouped in the first quadrant due to the higher frequency and/or concentration they were found in raw water. Furthermore, it

can be noticed that the endocrine disruptor BPA did not follow the tendency of the other 3 microcontaminants which occurred at high frequencies in WTP-Bolonha and that water quality indicator parameters (e.g., turbidity, color, *E.coli*) did not group or accompanied the tendency of the microcontaminants monitored in this study. This shows the difficulty in using usual parameters of characterization as indicators of the presence of drugs and endocrine disruptors in contaminated waters.

Table 8 shows the result of the correlation matrix of the microcontaminants monitored at the different sampling points of WTP-Bolonha. Concerning the characteristics of RW with respect to the presence of microcontaminants, it was found that three main components with variances equal to the eigenvalues greater than 1.0 accounted for about 91% of total variability. This suggests that these three main components adequately explain the variation in the data, whose presence was due to 4OP, BPA, LST, BZF, and LRT. It is possible to verify that PC1 with 42.2% (Fig. 4a) has large positive factor loads for LRT (0.570), LST (0.524), and BZF (0.281), while 4OP and BPA, respectively, have negative factor loads of -0.505 and -0.259 (Table 8). This resulted in the final partition of the formation of two distinct groupings for raw water, as can be seen in Fig. 4b, with greater affinity between 4OP and LST and for BZF and LRT.

Risk analysis

Considering the four contaminants which occurred most frequently in the chlorinated water (distributed drinking water) of WTP-Bolonha, a risk analysis was performed by means of the MOE calculation.

According to the information reported in the literature, Brandt et al. (2019) have compiled TDI values for several drugs and endocrine disruptors; for the compounds of interest in this study the lowest TDI values were as follows (at $\mu\text{g kg}^{-1} \text{day}^{-1}$): LRT—0.17; LST—0.42; BPA—4, and 4OP—15. Using such values in Eq. 3 and considering FA values equal to 1 for LRT and LST (EPHC NHMRC NRMCMC, 2008), 0.6 for BPA (EFSA, 2015), and 0.2 for 4OP (USEPA, 2016), guide values (GV) for these microcontaminants were estimated at $5.1 \mu\text{g L}^{-1}$ ($5,100 \text{ ng L}^{-1}$) for LRT, $12.6 \mu\text{g L}^{-1}$ ($12,600 \text{ ng L}^{-1}$) for LST, $72 \mu\text{g L}^{-1}$ ($72,000 \text{ ng L}^{-1}$) for BPA, and $90 \mu\text{g L}^{-1}$ ($90,000 \text{ ng L}^{-1}$) for 4OP.

Using the calculated GV and considering the 95th percentile values of LRT, LST, BPA, and 4OP in the chlorinated water of ETA-Bolonha, estimated at 22.7 ng L^{-1} , 230.8 ng L^{-1} , 74.5 ng L^{-1} , and 27.0 ng L^{-1} , respectively, Eq. 4 provided the following MOE values for the compounds: 224.7 for LRT, 54.6 for LST, 966.4 for BPA, and 3333.3 for 4OP. These results indicated that the concentration of drugs and endocrine disruptors present in the treated water of WTP-Bolonha was 50 to 3300 times lower than that which would cause some adverse effect. This approach used the 95th percentile of monitoring data (OC) and uncertainty factors (UF) of at least 1000; 10 for differences in response among humans, including sensitive individuals (intra-species variation); 10 for protection of sensitive subgroups, including children and infants; and 10 for the fact that the lowest daily therapeutic dose is not an effect-free level (EPHC NHMRC NRMCMC, 2008). However, there is limited literature on the synergistic effects of these compounds for both humans and biota (D Calderón-Preciado et al., 2011; Fent et al., 2006; McEneff et al., 2014).

Table 8 Correlation matrix for raw water quality evaluation regarding the presence of microcontaminants in WTP-Bolonha

| ID-AM | Autoanalysis (eigenvalues and eigenvectors) of the correlation matrix | | | | | |
|----------------|---|---------------|--------|--------|--------|--------|
| Raw Water (RW) | Eigenvalue | 2.1099 | 1.4016 | 1.0238 | 0.2947 | 0.1699 |
| | Proportion | 0.422 | 0.280 | 0.205 | 0.059 | 0.034 |
| | Accumulated | 0.422 | 0.702 | 0.907 | 0.966 | 1.000 |
| ID-AM | Variable | CP1 | CP2 | CP3 | CP4 | CP5 |
| Raw Water (RW) | 4OP | -0.505 | 0.454 | 0.148 | 0.709 | 0.122 |
| | BPA | -0.259 | 0.010 | -0.895 | 0.347 | 0.103 |
| | LST | 0.524 | 0.355 | -0.375 | -0.433 | -0.522 |
| | BZF | 0.281 | -0.733 | -0.009 | 0.358 | -0.506 |
| | LRT | 0.570 | -0.362 | -0.189 | -0.249 | 0.668 |

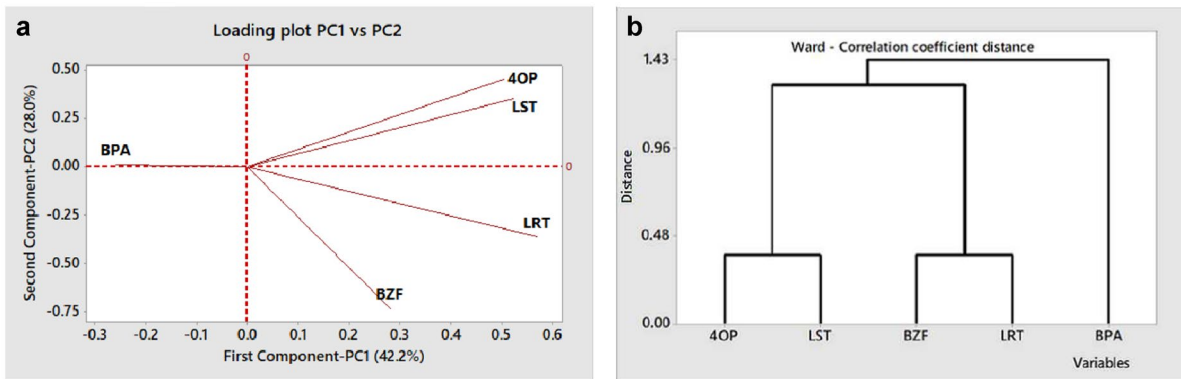


Fig. 4 PCA and hierarchy analysis with data of occurrence of drugs and endocrine disruptors in raw water that supplies WTP-Bolonha

Conclusions

The monitoring of 25 microcontaminants classified as drugs and/or endocrine disruptors in a water supply source in Belém (State of Pará-PA, Brazil) indicated that 12 of these were not detected in any raw water samples during the 12 sampling campaigns conducted. However, the endocrine disruptors bisphenol A and 4-octylphenol and the drugs loratadine and losartan were detected in practically all samples analyzed. In addition, differences were observed between the median concentrations of losartan, 4-octylphenol, and bisphenol-A compounds found in the dry and rainy periods. The conventional treatment used in WTP-Bolonha was efficient in the removal of losartan, moderately efficient in removing bisphenol-A and poorly efficient or inefficient in the removal of loratadine and 4-octylphenol, with the chlorination step being decisive in the removal of bisphenol-A and losartan. The multivariate analysis of the data indicated no significant correlation between the presence of microcontaminants and the usual raw water quality indicators. The risk analysis demonstrated that the concentration of contaminants frequently quantified in chlorinated water and distributed to the population was 55 to 3333 times lower than estimated limit values that may cause chronic adverse effects to human health.

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Author contribution Luiza C. G. M. Teixeira: Formal analysis, Investigation, Writing—Original Draft; Juliane Ribeiro das Chaves: Formal analysis, Investigation, Writing—Original Draft; Neyson Mendonça: Writing—Review & Editing; Ananda L. Sanson: Methodology, Validation, Review & Editing; Mariana C. P. Alves: Methodology, Validation, Formal analysis, Review & Editing; Robson J. C. F. Afonso: Review and Editing, Supervision; Sérgio F. Aquino: Review and Editing, Supervision, Project administration, Funding acquisition.

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Declarations

Conflict of interest The authors declare no competing interests.

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