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Occurrence of drugs and endocrine disruptors in the filters washing water from a water treatment plant in Belém (PA), Brazil

Ocorrência de fármacos e desreguladores endócrinos na água de retrolavagem proveniente da filtração de uma Estação de Tratamento de Água em Belém (PA), Brasil

Clara Cardoso Ferreira[1], *Luiza Carla Girard Mendes Teixeira*[1], *Sérgio Francisco de Aquino*[2]

ABSTRACT

The present work aimed to investigate the occurrence of 24 drugs and endocrine disruptors in the filters washing water from the Bolonha Water Treatment Plant in Belém, State of Pará, Brazil, since these residues are often released into water courses. The correlation of these microcontaminants with physicochemical and biological characteristics investigated in the studied matrix was also evaluated. For the research, six sampling campaigns were carried out during the rainy season and six in the dry season. The compounds determination was performed by solid phase extraction and chromatography coupled to mass spectrometry, gas chromatography for Ibuprofen, Paracetamol, 4-Nonylphenol, 4-Octylphenol, Bisphenol A, Gemfibrozil, Estrone, Estradiol, Ethinylestradiol, and Estriol, and in liquid phase for the other compounds. The compounds detected at higher concentrations than the others were Losartan (5.5 to 738.7 ng/L) and Bisphenol A (20.9 to 518.9 ng/L), also with the highest frequency. Multivariate analyzes showed that drugs and endocrine disruptors were more positively related to each other and to turbidity during the rainy season, with emphasis on 4-Octylphenol, Bisphenol A, Losartan and Loratadine, results that strengthen the hypothesis of precipitation's influence on the variables studied.

Keywords: microcontaminants; sludge; seasonality.

RESUMO

O presente trabalho teve como objetivo investigar a ocorrência de 24 fármacos e desreguladores endócrinos na água de lavagem dos filtros da estação de tratamento de água (ETA) Bolonha, Belém, Pará, Brasil, uma vez que esses resíduos muitas vezes são lançados em cursos d´água. Buscou-se avaliar também a correlação desses microcontaminantes com características físico-químicas e biológicas investigadas na matriz estudada. Para a pesquisa foram realizadas seis campanhas amostrais durante o período chuvoso e seis campanhas amostrais no período seco. A determinação dos compostos foi feita por extração em fase sólida e cromatografia acoplada à espectrometria de massas, cromatografia em fase gasosa para Ibuprofeno, Paracetamol, 4-Nonilfenol, 4-Cctilfenol, Bisfenol A, Genfibrozila, Estrona, Estradiol, Etinilestradiol e Estriol e em fase líquida para os demais compostos. Os compostos Losartan (5,5 a 738,7 ng/L) e Bisfenol A (20,9 a 518,9 ng/L) foram detectados com concentrações mais elevadas que os demais, sendo também os compostos com maior frequência de ocorrência. As análises multivariadas mostraram que os fármacos e desreguladores endócrinos estiveram mais relacionados positivamente entre si e com a turbidez durante o período chuvoso, com destaque ao 4-Octilfenol, Bisfenol A, Losartan e Loratadina, resultados que fortalecem a hipótese de influência da precipitação nas variáveis estudadas.

Palavras-chave: microcontaminantes; lodos; sazonalidade.

[1]Universidade Federal do Pará – Belém (PA), Brazil.

[2]Universidade Federal de Ouro Preto – Ouro Preto (MG), Brazil.

Correspondence address: Clara Cardoso Ferreira – Travessa de Breves, Passagem da Luz, 39 – Cidade Velha – CEP: 66020-350 – Belém (PA), Brazil. E-mail: clara_cardoso@outlook.com.br

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Introduction

The microcontaminants' presence in water causes concern in the scientific community since they can adversely affect the aquatic ecosystem and human health, being detected in various environmental matrices such as surface, treated, groundwater, and raw and treated sewage (Lima et al., 2017; Montagner et al., 2017; Floripes et al., 2018; Bisognin et al., 2018). Among these microcontaminants, drugs and endocrine disruptors (ED) stand out. The first group is found in the formulation of a series of drugs, such as anti-inflammatories, lipid regulators, antibiotics, contraceptives, natural (17-B estradiol) and synthetic (ethinyl estradiol) hormones, and others. The second consists of several types, such as pesticides (insecticides, herbicides, and fungicides), plasticizers (bisphenol-A and phthalates), alkylphenols (nonylphenol – surfactant metabolites), and others (Lima et al., 2017). Microcontaminants can reach the environment through various routes, however, the main ones come from anthropic activities such as the release of sanitary effluents (treated or not), industrial and hospital effluents, sludge from wastewater treatment plants (WWTP), and water treatment plants (WTP), landfills and surface runoff, mainly from water resources (Bu et al., 2016; Souza, 2019). Published studies by Bila and Dezotti (2003), Sodré et al. (2007), Montagner and Jardim (2011), Américo-Pinheiro et al. (2017), Escher et al. (2019), and Teixeira et al. (2021) show the presence of several microcontaminants in raw and treated Brazilian surface waters, as well as a varied concentration of these compounds. There is also an increasing trend in the number of drugs detected in surface waters in several countries such as Spain (Mastroianni et al., 2016), Iraq (Al-Khazrajy and Boxall, 2016), Tanzania (Hossein et al., 2018), and Korea (Choi et al., 2008), among others.

The WTP residues release (mainly from decanters and filters washing water) in springs may change the physicochemical water properties, since they can present significant amounts of metals, turbidity, chemical oxygen demand (COD) (Assis, 2014; Viana et al., 2014), and others, such as drugs and ED. Some of these substances can adhere to the sludge, which evidences the importance of developing studies to investigate their presence in WTP residues (Demoliner et al., 2010; Pereira et al., 2016; Lima et al., 2017). This fact becomes more relevant because WTP sludge is often discarded directly into the environment and into springs that are used for public supply (Demoliner et al., 2010; Pereira et al., 2016). Besides, studies show that the most used processes in WTPs in Brazil (coagulation, flocculation, sedimentation, filtration, and disinfection) have low efficiency in removing microcontaminants in drinking water (Huerta-Fontela et al., 2011; Rigobello et al., 2013; Lima et al., 2017).

Although filters washing water (FWW) is classified by NBR 10.004 (ABNT, 2004) as solid waste, in this study, it was compared with effluent, especially because its disposal is often made in water bodies without any type of treatment (without water reduction and, consequently, no increase in solids content) and due to its liquid characteristic (solids content < 5%). In addition, this same comparison was previously carried out in other studies (Silveira et al., 2013; Camargo et al., 2014).

In this way, this work objective was to investigate the drugs and ED occurrence in the FWW of Bolonha WTP, located in the city of Belém (PA), Brazil, in order to contribute to the adequate residue management in the country and subsidize government actions. As far as the authors are aware, this is the first work published in a journal on this topic in Brazil.

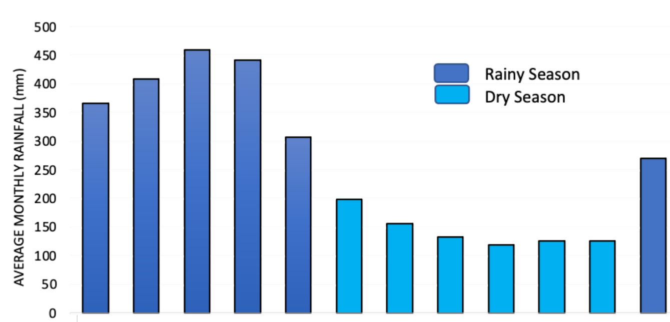
Methodology

Study area and sample collection points

The research was conducted at Bolonha WTP, Belém (PA), Brazil, with a nominal capacity of 6.4 m^3/s, consisting of two 6-inch Parshall flume to promote rapid mix, 12 mechanized flocculators (turbine-type) equipped with three chambers in series, six manual cleaning decanters and six high-rate decanters, 16 granular media filters (sand and anthracite), and chlorine gas for disinfection. The coagulant used was poly-aluminum chloride (PAC), with a dosage of 6 to 14 mg/L.

The WTP is located in Utinga State Park and within the Belém Environmental Protection Area limits, which, despite the area being a Full Protection Conservation Unit (Pará, 1993), is influenced by the nearby population. In order to carry out the collections, the normal rainfall in the period from 1989 to 2018 was taken into account (Figure 1). Thus, it was found that the city has two well-defined periods during the year, the rainy period considering December, January, February, March, April, and May, and the dry period (less rainy) that extends through the months of June, July, August, September, October, and November. The experimental development took place from September to November (09/04/2018, 09/24/2018, 10/05/2018, 10/23/2018, 11/08/2018, and 11/26/2018), contemplating the dry period, and from January to March (01/08/2019, 01/22/2019, 02/06/2019, 02/22/2019, 03/07/2019, and 03/21/2019), during the rainy season, making a total of 12 sampling campaigns.

The FWW collection was carried out using a beaker, because the flow was turbulent and the filtered water chamber was difficult to access. The sampling was of composite type and the collection occurred every 30 minutes or whenever a filter was washed, in a 500 mL beaker, in the washing water channel that gathers all the filter discharges.



Source: Hidroweb (ANA, 2021).

Figure 1 – Climatological Normal of the Belém city in Pará, Brazil (1989 to 2018).

This point was selected once the sampling could be performed safely for the collector and with the aim of having various filter samples throughout the day and the contents of the discharge channel. Next, the water was homogenized and passed into a test tube where 170 mL was measured, and then into an amber flask (4 L), totaling about 4 L after 12 hours.

Physicochemical and biological analysis

The variables were total alkalinity (2320), electrical conductivity (2510 B), apparent color (2120 B), total iron (3030), hydrogen ion concentration - pH (4500H^+ B), turbidity (2130), and *Escherichia coli* (9223 B) as described in the Standard Methods for the Examination of Water and Wastewater (APHA; AWWA; WEF, 2017) and carried out at the Multiuser Laboratory of Water Treatability (LAMAG) at the Universidade Federal do Pará.

Microcontaminants extraction

The drugs and ED monitored in this study were selected based on the international literature and feasibility determinations. In this way, the following were monitored: ibuprofen (IBU), paracetamol (PCT) 4-octylphenol (4OP), caffeine (CAF), 4-nonylphenol (4NP), gemfibrozil (GEM), naproxen (NPX), bisphenol A (BPA), diclofenac (DCF), estrone (E1), estriol (E3), ethinyl estradiol (EE2), estradiol (E2), metformin (MET), acyclovir (ACV), linezolid (LNZ), propranolol (PNL), diltiazem (DTZ), promethazine (PTZ), losartan (LST), bezafibrate (BZF), dexamethasone (DXM), loratadine (LRT), and sulfamethoxazole (SMX). Such microcontaminants were extracted from the liquid phase and concentrated using solid phase cartridges (SPE - solid phase extraction) of the OASIS-HLB type, following the methodology developed by Sanson (2012). The collected samples were immediately subjected to vacuum filtration on fiberglass membranes at different porosities (8 μm, followed by 2 μm and 0.45 μm) to remove particulate material. The cartridge used in the solid phase was Strata-X (Phenomenex®) 500 mg/ 6 mL, which aimed to activate the cartridge polymeric phase binding sites making them available for the analytes contained. The phase started with 5 mL of ethyl acetate (an eluting solvent used to remove possible interference), followed by 5 mL of methanol, and 5 mL of ultrapure water. After cleaning, the extraction apparatus was placed in an amber bottle containing 1 L of sample already prepared in the filtration and pH adjustment step. Then, a N_2(g) pressure was applied, and a small amount of the sample was propelled into the upper part of the cartridge. It passed through the cartridge with a flow of approximately 5 mL/min (≅ 100 drops/ min). Thus, by controlling the N_2(g) pressure flow, dripping was maintained. After passing the entire volume, the third phase began, where the cartridges were dried with the aid of N_2(g) pressure for 10 minutes.

Microcontaminants analysis

The microcontaminants analysis was performed using the techniques LC-MS/MS (liquid chromatography coupled to sequential mass spectrometry) for the compounds MET, ACV, CAF, LNZ, PNL, DTZ, PTZ, LST, BZF, DCF, DXM, LRT, SMX, and NPX, and GC-MS (gas chromatography coupled to mass spectrometry) for the IBU, PCT, 4NP, 4OP, BPA, GEM, E1, E3, EE2, and E2 (Sanson, 2012; Sanson et al., 2014). The methods were chosen to minimize interference from the matrix effect and increase sensitivity on the analyte detection in question.

In the LC-MS/MS analysis, the extracts were resuspended in 500 μL of high-performance liquid chromatography (HPLC) grade methanol (JTBaker), vortexed for 30 seconds and 100 μL transferred to a vial containing a volume restrictor. These extracts were completely dried with nitrogen gas and kept in a freezer (-26°C) until analysis. For the analytical curves, stock solutions in HPLC grade methanol (JTBaker) were prepared, at a concentration of 1 g/L, of each analyte under study. From these solutions, a working solution was prepared at a concentration of 1 mg/L in methanol containing all the analytes, which was stored in a freezer. Dilutions with methanol containing 0.1% v/v of formic acid (88%; JTBaker) were also performed from the working solution on the analysis day, with a concentration range of 2.5 to 50 μg/L, for the analytical curves. The vials containing the solutions were called spike, with the standard in methanol with 0.1% v/v of formic acid with all analytes at a concentration of 30 μg/L, and the solvent vial containing methanol with 0.1% v/v of formic acid. The vials containing the dry extract were suspended with 100 μL of methanol containing 0.1% v/v formic acid. The analyzes were carried out on the LCMS-8040 (Shimadzu), coupled to the UHPLC Nexera model (Shimadzu) with the following modules: CBM-20ª controller, 3 LC-30AD pumps, SIL-30AC sampler, CTO-30ª column oven, and DGU-20ªs degasser.

The chromatographic column used was C18 Kinetex model (Phenomenex) with 100 mm × 2.1 mm × 2.6 μm. The mobile phase consisted of (A) ultrapure water with 0.1% v/v formic acid and (B) acetonitrile (HPLC grade; JTBaker) with 0.1% v/v formic acid. The following gradients were performed under constant flow of 0.250 mL/min: 5% B from 0 to 1 min; 60% B at 12 min; 95% B at 13 min; returning to the initial condition at 14 min; and 16 min total running time. A third mobile phase of acetonitrile with 3.5 mM ammonium hydroxide (28%; Sigma Aldrich), with a flow rate of 0.03 mL/min was added post column.

For the GC-MS analysis, as well as the LC-MS/MS analysis, the extracts were resuspended, vortexed for 30 seconds and the volume generated with the resuspension was transferred to two vias containing a volume restrictor: A: 100 μL of sample; and, Aspike: 70 μL of sample + 30 μL of 100 μg/L standard solution in methanol.

Subsequently, the extract was completely dried under nitrogen gas flow and stored in a freezer (-26°C) until analysis. For the analytical curves, stock solutions in methanol HPLC grade (JTBaker) of the compounds studied (IBU, PCT, 4NP, 4OP, bisphenol BPA, GEM, E1, E2, EE2, and E3) were prepared at the concentration of 1 g/L. From these solutions, a working solution was made containing the analyte, with a concentration of 1 mg/L in methanol, stored in a freezer. Dilutions with methanol were performed from the working solution on the analysis day, with a concentration ranging from 2.5 to 100 μg/L. The vials of the analytical curve points were also subjected to drying under a flow of nitrogen gas (Sanson, 2012).

All samples were derivatized and then resuspended with 75 μL of BSTFA:TMCS (99:1; GCMS, Sigma Aldrich) and 25 μL of solution used as an internal standard. This was done to solubilize the dry extract. The vials were kept at 80°C for 30 minutes and then submitted for GC-MS analysis. The analysis was performed on the GC-2010 gas chromatograph coupled to the GCMS-QP2010 Plus (Shimadzu) mass spectrometer.

The following values were used in the microcontaminants analysis by gas chromatography and spectrometry processes: injection of 1 μL of the samples, performed by the AOC-20i (Shimadzu) automatic injector model, and the chromatographic column used was the Zebron ZB-5MSi (30 m × 0.25 mm × 0.25 μm; Phenomenex). The temperature ramp was 120°C for one minute, increasing to 227°C at a rate of 15°C/min, then increasing to 240°C at a rate of 10°C/min, reaching the end at 330°C at a rate of 15°C/min, and remaining at this temperature for two minutes. The injection mode was spitless for 0.5 minutes followed by a split rate of 1:20, purge flow of 5.0 mL/min, and injector temperature of 280°C.

The carrier gas chosen was helium 5.0 with a total flow of 25.9 mL/min and linear velocity of 36.5 cm/sec. For the mass spectrometer, the temperature used was 280°C at the interface and 250°C at the ionization source, using 70 eV of voltage for electron ionization (Sanson, 2012; Sanson et al., 2014).

The results of drug and ED occurrence were evaluated through principal component analysis (PCA) and hierarchical cluster analysis (HCA). Pearson correlation matrix (PCM) was used for correlation. The analyses were divided by seasons (rainy and dry), using RStudio 4.1.3 and OriginPro 8 softwares.

The descriptive statistics results of the physicochemical and biological variables were compared with the National Environmental Council (CONAMA) n. 40 Resolution (Brazil, 2011), which establishes effluent discharge standards, and with CONAMA n. 57 Resolution (Brazil, 2005). However, there were no parameters established in the first one, since the variables not included must comply with the quality standards of the class in which the receiving body is classified.

Environmental risk

The environmental risk of drugs and ED frequently detected in the FWW was assessed by calculating the risk quotient (RQ), obtained by dividing the maximum expected pollutant concentration (MEC) in the water body by the concentration at which no adverse effect is predicted (PNEC) on aquatic organisms. PNEC values were obtained from the literature (USEPA, 2010; Baran et al., 2023). The MEC were used in the FWW of Bolonha WTP, considering that there would be no dilution during disposal into the environment.

Results and Discussion

Table 1 presents the descriptive statistics results of the physicochemical and biological variables monitored in the FWW. It is possible to infer that the highest turbidity means, apparent color, *Escherichia coli*, total iron, and electrical conductivity occurred in the months with the highest rainfalls since, at this time, there is an increase in solids in raw water. Due to CONAMA n. 430 Resolution (Brazil, 2011), parameters are not established for all physicochemical and biological characteristics surveyed, only for pH and total iron and, according to Art. 5, § 2º from the same resolution, the parameters not included must comply with the quality standards of class in which the receiving body is classified. The other characteristics were compared with CONAMA n. 357 Resolution (Brazil, 2005) and with values found by other authors.

Among all the characteristics, turbidity was the only outside the standards for class 2 (Guamá River) of CONAMA n. 357 Resolution (Brazil, 2005) in all periods, especially in the rainy season. The pH and total iron were within the effluent discharge standards in both periods, according to CONAMA n. 430 Resolution (Brazil, 2011). On the other hand, *Escherichia coli* was above (1,102 MPN/100 mL) the recommended by CONAMA n. 357 Resolution (Brazil, 2005) during the rainy season. This may be due to the increase in surface runoff and, consequently, to the domestic sewage which, at this time of the year, reaches the water source since the surrounding area is devoid of sewage treatment and also by the disorderly occupation (Araújo Júnior, 2015; Gutierrez et al., 2017). Belém municipality has one of the lowest coverages of sewage collection and treatment in the country, with only 17.12% of the population served with sewage collection, while only 3.63% of sewage is treated (ABES, 2021; Instituto Trata Brasil, 2023).

Table 2 presents data on the occurrence of drugs and ED in the FWW, their detection frequency in this matrix, the values of detection limits and analytical method for quantification used. Data indicated that of the 24 microcontaminants studied, 10 were not detected in the FWW. Also, the compounds DCF, E3, LNZ, PNL, DTZ, DXM, and SMX were not detected in raw water arriving at Bolonha WTP, neither in the same dry season (2018) nor in the rainy (2019) (Teixeira et al., 2021). The acidity constant (pK_a) basic character of the analytes E3, PNL, DTZ, and DXM, drugs low sorption potential LNZ, PN, DTZ, DXM, and SMX, and the extraction of compounds in acidic pH = 2 are factors that can explain its non-detection in the FWW. Although PCT, EE2, and BZF indicate high adsorption in sediments and suspended solids – high pK_a and octanol/water partition coefficient (log Kow) values – they were not detected in FWW. Possibly they were retained in the steps prior to filtration since they were detected in low occurrence in raw water (1 sample for PCT 3.7 ng/L; 2 samples for EE2 78.7 ng/L and 113.9 ng/L; and 2 samples for BZF 269.9 and 1,364.9 ng/L) (Teixeira et al., 2021), or on the suspended solids filtered from the sample. Among the compounds, CAF had the highest concentration (1,090.2 ng/L), but it was found in only one sample (rainy season) representing 8% of the 12 campaigns. On the other hand, the compounds LST and BPA were present in 100% of the

Table 1 – Physicochemical and biological variables descriptive statistics of filters washing water of the studied periods.

Rainy Season							
Variables	**N**	**Minimum**	**Average**	**Median**	**Maximum**	**SD**	**CV (%)**
Alkalinity (mg/L)	6	6.9	**7.3**	7.5	7.6	0.3	4.1
Conductivity (µS/cm)	6	57	**62.5**	60	74	6.7	10.7
Apparent color (uH)	6	355	**579.2**	462	976	276	47.7
Total iron (mg/L)	6	4.2	**4.9**	5	5.3	0.4	8.2
pH	6	5.4	**5.8**	5.8	6.3	0.4	6.9
Turbidity (NTU)	6	205	**354**	356.5	465	88.7	25.1
Escherichia coli (MPN/100mL)	6	328	**1,102**	1,011	2,419	743	67
Dry Season							
Alkalinity (mg/L)	6	7.5	**12.7**	11.3	20	5	39.4
Conductivity (µS/cm)	6	41.9	**50.8**	50	66.9	8.8	17.3
Apparent color (uH)	6	97.6	**408.3**	239	956	349.3	85.5
Total iron (mg/L)	6	0	**0.2**	0.08	0.6	0.3	150
pH	6	6	**6.2**	6.2	6.5	0.2	3.2
Turbidity (NTU)	6	60.5	**218.5**	207	429	137.2	62.8
Escherichia coli (MPN/100mL)	6	71	**453**	147	1,553	595	131
Annual Season 2018/2019							
Alkalinity (mg/L)	12	6.9	**10**	7.6	20	4.4	44
Conductivity (µS/cm)	12	42	**57**	57.5	74	10	17.5
Apparent color (uH)	12	98	**494**	362.5	976	313	63.4
Total iron (mg/L)	12	0	**2.6**	2.4	5.3	2.5	96.2
pH	12	5.4	**6**	6.1	6.5	0.4	6.7
Turbidity (NTU)	12	60.5	**286.3**	316.5	465	130.9	45.7
Escherichia coli (MPN/100mL)	12	71	**778**	616	2,419	726	93

N: number of samples; SD: standard deviation; CV: coefficient of variation; NTU: nephelometric turbidity units; MPN: most probable number.

samples collected, in both seasons, in concentrations much higher than the analytical method quantification limit, being also detected in all raw water samples with values of 86.9 at 578 ng/L (Teixeira et al., 2021). This can be explained because LST is a drug widely used in the hypertension treatment and BPA is a chemical substance used in plastics, resins, water supply pipes, among other manufactures.

Other contaminants with a high occurrence frequency on FWW were 4OP (92%) and LRT (92%). The LRT constancy may be associated with its sale without a medical prescription and its high consumption by the population since this medicine is indicated for allergy treatment, and 4OP is widely used as an additive in plastics, detergents, paints, and herbicides (Arruda et al., 2021). Diniz et al. (2020), in a study on the occurrence of 16 drugs in water samples from the Extremoz Water Treatment Plant in Natal (RN), and on the removal evaluation of these compounds, found that the drug LRT continued to show high concentrations after filtration, which is mainly justified for its high consumption. The higher occurrence of these four compounds (BPA, LST, 4OP, and LRT) may be associated with their use and/or physicochemical characteristics. The 4OP is a hydrophobic compound (Chemidplus, 2022; Drugbank, 2022; PubChem, 2022), which has a high tendency to adsorb on organic matter of low polarity, used as an additive in plastics, raw materials to obtain surfactants (alkylphenols and ethoxylates) (Yao et al., 2017); BPA, which is also quite hydrophobic (Chemidplus, 2022; Drugbank, 2022; PubChem, 2022), is used as an industrial raw material and is present in plastics and resins manufacture that cover packaging; and LST and LRT are drugs used in the hypertension and allergy treatment, respectively, which also have a hydrophobic character (log Kow ≥ 4) and a tendency to become trapped in flakes containing low polarity organic material (Teixeira et al., 2021). The LRT highest concentrations occur in the rainy seasons (Amazonian winter), which can be explained mainly by the increase in air relative humidity, providing greater fungi and other microorganisms proliferation (Valença et al., 2006).

The CAF presence in only one sample may be associated with its easy degradation under natural conditions (exposure to solar radiation), its high solubility (13.5 g/L), and its low Kow (Ide et al., 2013).

Table 2 – Variation in concentration, occurrence frequency and limit of detection and quantification of the compounds studied in the filters washing water in the 12 campaigns.

Compound	Concentration Range (ng/L)	DL (ng/L)	QL (ng/L)	Occurrence Frequency (%)
Ibuprofen (IBU)	8.2 – 233.8	0.3	0.9	25
Paracetamol (PCT)	< DL	0.2	0.7	0
4-Octylphenol (4OP)	3.4 – 24.6	0.2	0.7	92
Caffeine (CAF)	1,090.2	162.1	540.2	8
4-Nonylphenol (4NP)	7.2	0.1	0.3	8
Gemfibrozil (GEM)	7.0 – 80.6	0.3	1.1	50
Naproxen (NPX)	157.6 – 703.2	37.5	125	33
Bisphenol A (BPA)	20.9 – 518.9	0.05	0.1	100
Diclofenac (DCF)	< DL	118.7	395.7	0
Estrone (E1)	8.2	0.1	0.2	8
Estradiol (E2)	5.6	0.3	0.8	8
Ethinylestradiol (EE2)	< DL	0.4	1.3	0
Estriol (E3)	< DL	0.1	0.3	0
Metformin (MET)	22.1	1.4	4.6	8
Acyclovir (ACV)	49.4	0.9	3.2	8
Linezolid (LNZ)	< DL	1.7	5.8	0
Propranolol (PNL)	< DL	8.3	27.7	0
Diltiazem (DTZ)	< DL	1.2	4.1	0
Promethazine (PTZ)	4.0	0.3	1.0	8
Losartan (LST)	5.5 – 738.7	1.0	3.3	100
Bezafibrate (BZF)	< DL	71.7	239.1	0
Dexamethasone (DXM)	< DL	2.9	9.5	0
Loratadine (LRT)	13.5 – 51.3	1.9	6.3	92
Sulfamethoxazole (SMX)	< DL	2.0	6.8	0

DL: detection limit; QL: quantification limit.

Furthermore, this compound consistently showed concentrations below the detection and quantification limits in the 12 samples taken in the study by Teixeira et al. (2021) and in the 15 samples from the Bega et al. (2021) survey. In the study by Teixeira et al. (2021), carried out in the same period and place as the present study, the compounds 4NP, E1, and ACV were detected in low occurrence in the raw water, while E2, PTZ, and MET were not detected, possibly being linked to its greater propensity for degradation (Radjenović et al., 2009; Luo et al., 2011; Dias et al., 2018) and/or its lower availability on the investigated matrix.

LRT was detected in FWW with an average concentration of 32.7 standard deviation (SD) ± 14.2 ng/L in the rainy season, and 17.2 ± 3.5 ng/L in the dry. The LST averaged 329.7 ± 320.9 ng/L and 99.6 ± 75.8 ng/L, respectively, with the highest concentrations obtained during the rainy season, with a maximum of 738.7 ng/L. The 4OP was detected at low concentrations, with an average of 10.8 ± 8.2 ng/L in the rainy season, and 5.8 ± 1.8 ng/L in the dry, while BPA averaged 151.6 ± 141.7 ng/L and 221 ± 166.8 ng/L, respectively. Unlike the other compounds, the highest BPA concentrations occurred in the dry period at 518.9 ng/L. According to Teixeira et al. (2021), the BPA concentration in the water can be affected by the increase in rainfall (rainy season) due to higher solids input from the decanter, which overloads the system and causes BPA adsorbed drag on the filter particles. In the study by Arruda et al. (2021), in the sludge sedimentation pond supernatant of a WTP located in the Goiânia (GO) municipality, the authors found, among the investigated 24 contaminants, that the compounds with the highest occurrence frequencies were also 4OP, BPA, LST, and LRT (7, 11, 11 and 8 samples, respectively), with maximum concentrations higher than those observed in this study for 4OP (242.91 ng/L), BPA (1,276.98 ng/L), and LRT (23.67 ng/L).

Despite the difference in concentrations between the seasons (rainy and dry) for 4OP and BPA, the Student *t*-test and Mann-Whitney U test did not show a significant difference, with p-values (p) of

0.18153 and 0.29795, respectively. As for the LST and LRT compounds, the Student *t*-test showed a significant difference between the dry ($p = 0.03824$) and rainy ($p = 0.02784$) seasons. The concentration difference between the periods for LST and LRT can be explained by their high sorption potential (log Kow equal to 4.01 and 5.02, respectively) in hydrophobic materials. Besides, the rainy season increases solids entry into the filters due to surface runoff (Teixeira et al., 2021).

Table 3 presents descriptive statistics for the most frequently detected microcontaminants in the FWW. The difference in concentration between the dry and rainy seasons may be related to the high log Kow estimated values: LST at 4.01, LRT at 5.20, and 4OP at 4.22 (Chemidplus, 2022; Drugbank, 2022; PubChem, 2022), indicating their hydrophobic character, which means that they have a greater tendency to adsorb on suspended solids (sedimentation process remnants). In addition, in WTPs that use a complete cycle treatment, as in the Bolonha WTP case, the best removal efficiencies (clarification processes) are obtained for microcontaminants that present high Kow values (hydrophobic character) and, therefore, have greater removal capacity (Huerta-Fontela et al., 2011; Dias, 2014; Lima et al., 2017), being able to confirm the higher recurrence and concentration of 4OP, BPA, LST, and LRT in the FWW.

The greater presence and recurrence of these compounds in the FWW can also be influenced by the water treatment processes (Chaves, 2020) since the LRT was removed by 22% after filtration. In the study by Lima et al. (2017), the removal of 4OP and BPA in Brazilian WTPs that use the complete water purification cycle process was less than 50%. Diniz et al. (2020) determined the occurrence of 16 drugs in water samples from the Extremoz WTP in Natal (RN) and found that the LRT continued to show high concentrations after filtration, which is justified mainly by its high consumption. Thus, as shown in the research, most microcontaminant occurrences and concentrations verified in this study were removed significantly at the filtration stage, therefore having a higher probability of being detected in the residues from this treatment stage.

Table 4 and Figure 2 show the PCA and HCA results for the rainy and dry seasons. The PCA for the rainy season showed that the three principal components (PC1, PC2, and PC) described 81.17% of the total data variance. PC1 described 35.90%, and the variables LRT (0.820), BPA (0.816), pH (0.713), 4OP (0.658), LST (0.473), and turbidity (0.514) had high positive factor loadings. Electrical conductivity showed disagreement with the other variables, indicating a negative correlation (-0.566). Despite the highest average (62.5 ± 6.7 µS/cm) at this time of year, this variable did not follow the microcontaminants trend (negative correlations) monitored in the study, which may demonstrate the difficulty in using this water quality parameter as an indicator of the contaminants poorly soluble presence or incompletely ionized. The first group formed in the HCA, comprised of LST, BPA, CAF, PTZ, GEM, and LRT, was turbidity and total alkalinity composed, with strong to moderate correlations observed between them. These compounds, except for CAF, had similar characteristics mainly due to their high Kow. Despite having a low log Kow (-0.07), CAF was strongly correlated with most compounds and moderately correlated with turbidity. Its concentration was the highest among all compounds (1,090.2 ng/L) and the correlation may be related to physicochemical characteristics, especially with BPA and PTZ for their similar pK_a values (14.00, 10.20, and 9.81, respectively). This is because the highest concentrations of this variable and all the compounds, except BPA, occurred during the greatest precipitation and runoff season. Thus, it is possible to verify that a potential increase in solids on the filters can change the drugs and ED concentration (Camargo, 2011; Oliveira et al., 2012; Teixeira et al., 2021) due to the desorption process caused by equilibrium displacement in the washing process with water that contains a lower concentration of such contaminants.

Table 3 – Most frequent compounds descriptive statistics in filters washing water in the rainy and dry seasons of the studied period.

Rainy Season								
Drugs and ED (ng/L)	**N**	**Minimum**	**Average**	**Median**	**Maximum**	**SD**	**CV**	**Fq (%)**
4-Octylphenol (4OP)	5	4.0	10.8	9.6	24.6	8.2	76.2	83
Bisphenol A (BPA)	6	52.4	**151.6**	97.6	431.4	141.7	93.4	100
Losartan (LST)	6	36.3	**329.7**	195.8	738.7	320.9	97.3	100
Loratadine (LRT)	5	18.0	**32.7**	32.4	51.3	14.2	43.3	83
Dry Season								
Drugs and ED (ng/L)	**N**	**Minimum**	**Average**	**Median**	**Maximum**	**SD**	**CV**	**Fq (%)**
4-Octylphenol (4OP)	6	3.4	5.8	5.8	8.0	1.8	31.1	100
Bisphenol A (BPA)	6	20.9	**221.0**	197.2	518.9	166.8	75.5	100
Losartan (LST)	6	5.5	**99.6**	80.8	208.9	75.8	76.2	100
Loratadine (LRT)	6	13.5	**17.2**	16.65	23.4	3.5	20.4	100

N: sample numbers where microcontaminants were detected; SD: standard deviation; CV: coefficient of variation; Fq: frequency.

Table 4 – Principal component analysis for the variables investigated in the rainy and dry seasons.

Eigenvectors and Eigenvalues of the Correlation Matrix						
Rainy	Eigenvalue	6.463	5.173	2.975	2.193	1.196
	Proportion	35.90	28.74	16.53	12.18	6.65
	Accumulated	35.90	64.64	81.17	93.35	100.00
Season	**Variables**	**PC1**	**PC2**	**PC3**	**PC4**	**PC5**
Rainy	Alkalinity	0.455	-0.137	0.717	-	-
	Conductivity	-0.566	0.026	0.106	-	-
	Apparent color	0.455	-0.131	-0.798	-	-
	Total iron	0.174	0.127	-0.842	-	-
	pH	0.731	0.349	-0.528	-	-
	Turbidity	0.514	-0.492	0.578	-	-
	Escherichia coli	0.250	0.918	0.057	-	-
	Ibuprofen (IBU)	0.558	0.798	0.203	-	-
	4-Octylphenol (4OP)	0.658	0.628	0.032	-	-
	Caffeine (CAF)	0.688	-0.709	-0.120	-	-
	4-Nonylphenol (4NP)	0.565	0.796	0.179	-	-
	Gemfibrozil (GEM)	0.962	-0.136	0.049	-	-
	Naproxen (NPX)	-0.198	-0.032	0.539	-	-
	Bisphenol A (BPA)	0.816	-0.552	0.009	-	-
	Estradiol (E2)	0.549	0.793	0.198	-	-
	Promethazine (PTZ)	0.688	-0.709	-0.120	-	-
	Losartan (LST)	0.473	-0.533	0.190	-	-
	Loratadine (LRT)	0.820	-0.070	0.125	-	-
Eigenvectors and Eigenvalues of the Correlation Matrix						
Dry	Eigenvalue	5.797	4.318	3.29	2.436	1.157
	Proportion	34.10	25.4	19.35	14.33	6.80
	Accumulated	34.10	59.5	78.85	93.2	100.00
Season	**Variables**	**PC1**	**PC2**	**PC3**	**PC4**	**PC5**
Dry	Alkalinity	0.116	0.229	-0.589	0.759	-
	Conductivity	0.980	0.148	0.113	0.076	-
	Apparent color	-0.257	-0.591	-0.681	0.093	-
	Total iron	-0.497	0.823	0.202	0.149	-
	pH	0.655	-0.500	0.477	0.304	-
	Turbidity	-0.445	-0.596	0.129	0.639	-
	Escherichia coli	-0.181	0.977	-0.061	0.085	-
	Ibuprofen (IBU)	-0.030	0.885	-0.433	0.047	-
	4-Octylphenol (4OP)	0.842	-0.311	-0.075	-0.012	-
	Gemfibrozil (GEM)	0.834	0.027	0.384	-0.160	-
	Naproxen (NPX)	-0.106	-0.181	-0.139	0.967	-
	Bisphenol A (BPA)	0.859	0.131	0.384	0.265	-
	Estriol (E1)	-0.516	0.184	0.800	0.098	-
	Metformin (MET)	-0.362	-0.357	-0.490	-0.479	-
	Acyclovir (ACV)	-0.516	0.184	0.800	0.098	-
	Losartan (LST)	0.509	0.707	-0.329	0.153	-
	Loratadine (LRT)	0.880	0.182	-0.207	-0.106	-

PC: principal component.

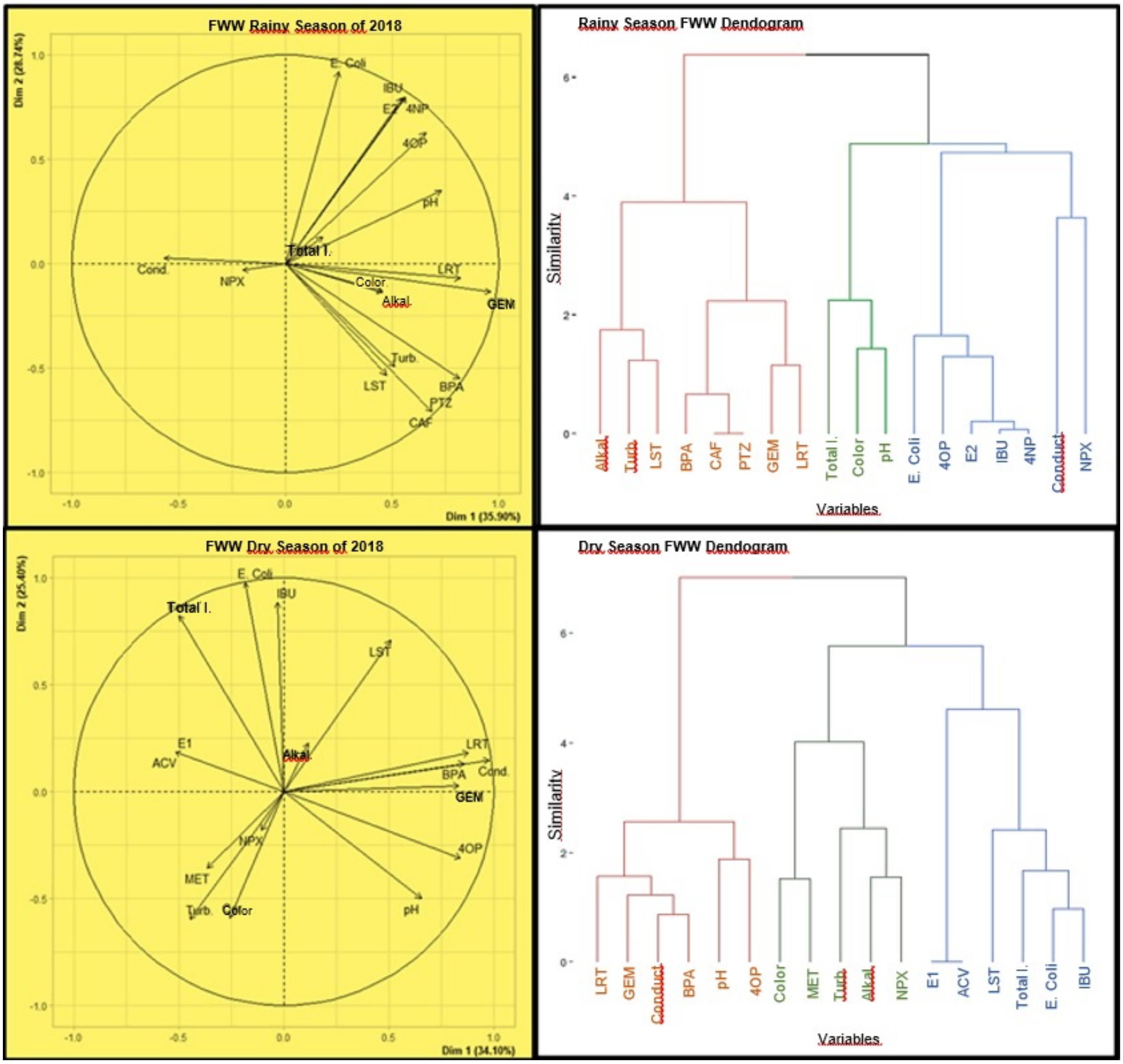


Figure 2 – Principal component analysis graphs and hierarchical clustering analysis dendrogram of the variables investigated in the filters washing water during rainy and dry season.

The second group was formed only by physicochemical water characteristics, such as pH, total iron, and apparent color. These characteristics indicated a direct relationship along PC1 and a closer approximation, less related to microcontaminants in the 2019 rainy season. The third group gathered 4OP, 4NP, E2, IBU, NPX, *Escherichia coli*, and electrical conductivity. The IBU, 4OP, 4NP, and E2 were strongly correlated with each other and in a direct relationship along PC1. Their characteristics were also similar, especially due to the high Kow, indicating the potential for sorption in hydrophobic materials. The compounds showed weak and negative correlations with conductivity, as well as an indirect relationship with PC1, reaffirming the difficulty in using this parameter as an indicator of microcontaminants presence in FWW. The highest concentrations occurred in the rainy season, strengthening the precipitation influence hypothesis and the increase in the surface runoff of domestic sewage on raw water and consequently in the FWW.

Based on the PCA results obtained for the dry season, it was noted that only with the PC4 it was obtained more than 80% of the total data variance. PC1 represented 34.10% of variance and a contrast was observed between electrical conductivity (0.980), LRT (0.880), BPA (0.859), 4OP (0.842), GEM (0.834), pH (0.655), and LST (0.509), and between E1 (-0.516) and ACV (-0.516). According to the ACP, it was observed that most of the compounds were moderately and negatively related to the FWW physicochemical and biological variable characteristics in the dry period.

By the HCA, it was verified three distinct groups of variables between drugs and ED (Figure 2). The first group was composed of LRT, GEM, BPA, 4OP, electrical conductivity and pH. Drugs and ED had similar characteristics, especially in relation to their Kow. In addition, the compounds were directly and strongly correlated with pH and electrical conductivity. The second group was formed by apparent color, turbidity, total alkalinity, MET, and NPX. It is noteworthy that turbidity, total alkalinity, and apparent color were less related to microcontaminants in the dry season than in the rainy.

Lastly, the third group was composed of E1, ACV, LST, IBU, total iron, and *Escherichia coli*. The smaller influence of E1, ACV, and IBU in the FWW in the dry period and its poor correlation with the other compounds were highlighted, probably because E1, ACV, and IBU presented low concentrations and were detected in only one sample.

Comparing the seasons, different correlations were verified, in which drugs and ED were more positively related to the variables during the rainy season. Electrical conductivity was the water quality characteristic least related to microcontaminants during the rainy season. In the dry season, however, it was more strongly correlated with the compounds, particularly 4OP, GEM, BPA, and LRT. The lowest electrical conductivity values occurred during the dry period, with an average of 50,8 ± 8,8 μS/cm, suggesting that the correlation is strengthened with the lowest concentration of this variable in the FWW. In the dry season, turbidity, total alkalinity, and apparent color were the physicochemical characteristics less related to contaminants. This can be explained by its decrease during this time of year, with a reduction in contaminant concentrations, except BPA. The lowest microcontaminant concentrations in the dry period occurred together with the lowest turbidity values, which may indicate their decrease with the turbidity reduction in the FWW. It is worth noting that the compounds that were most strongly correlated with each other and with the FWW variables, in both periods, were 4OP, BPA, LST, and LRT. They also had the highest occurrence during the 12 sampling campaigns.

The environmental risk assessment carried out for the drugs 4OP and BPA was considered an extremely conservative scenario from an environmental point of view since the MEC of such drugs observed in the FWW were used as environmental concentrations. In such a scenario, using the PNEC values for BPA (1,500 ng/L; USEPA, 2010) and 4OP (330 ng/L; inhibition of development in fish *Oryzias latipes* [Ministério do Meio Ambiental do Governo do Japão, 2009]), it was observed that the impact on the aquatic environment would be very small since the calculated RQ would be less than a unity, 0.07 and 0.02 for 4OP and 0.29 and 0.35 for BPA, in the rainy and dry season, respectively. Unfortunately, no PNEC values were found for LRT and LST to enable environmental risk assessment for these compounds.

Conclusions

The results obtained showed that the most frequently quantified compounds in the FWW of Bolonha WTP were 4OP (3.4 to 34.6 ng/L), BPA (20.9 to 518.9 ng/L), LST (5.5 to 738.7 ng/L), and LRT (13.5 to 51.3 ng/L). The highest concentrations, except for BPA, occurred during the rainy season and the risk assessment carried out for BPA and 4OP indicated that, even at the maximum concentrations observed, the environmental impact on the water body was small for the species evaluated based on available toxicological information.

Regarding the FWW physicochemical and biological characteristics, these compounds were more related to turbidity in the rainy season, while in the dry season they were more linked to electrical conductivity.

From the data multivariate analysis, it was verified that the LST, BPA, LRT, and 4OP were more strongly correlated with each other and with the investigated variables in a positive way during the rainy season. The strong correlation between these compounds can be explained by their characteristic similarity, especially the high Kow.

Contribution of authors:

FERREIRA, C. C.: investigation; writing – original draft; formal analysis. TEIXEIRA, L. C. G. M.: formal analysis; supervision; validation; writing – review & editing. AQUINO, S. F.: conceptualization; formal analysis; supervision; validation; writing – review & editing; project administration.

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