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Presence Of Non-Steroidal Anti-Inflammatories In Brazilian Semiarid Waters

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Abstract Non-steroidal anti-inflammatory drugs (NSAIDs) act as antipyretics, analgesics and anti-inflammatories. Among them, diclofenac and ibuprofen are the most consumed drugs worldwide. During the COVID-19 pandemic, some NSAIDs, such as dipyrone and paracetamol, have been used to alleviate the symptoms of the disease, causing an increase in the concentrations of these drugs in water. However, due to the low concentration of these compounds in drinking water and groundwater, few studies have been carried out on the subject, especially in Brazil. Thus, this study aimed to evaluate the contamination of the surface water, groundwater, and water treated with diclofenac, dipyrone, ibuprofen, and paracetamol at 3 cities (Orocó, Santa Maria da Boa Vista and Petrolândia) in the Brazilian semiarid region, in addition to analyzing the removal of these drugs by conventional water treatment (coagulation, flocculation, sedimentation, filtration and disinfection) in stations to each city. All drugs analyzed were detected in surface and treated waters. In groundwater, only dipyrone was not found. Dipyrone was seen in surface water with a maximum concentration of 1858.02 μg.L^{-1}, followed by ibuprofen (785.28 μg.L^{-1}), diclofenac (759.06 μg.L^{-1}) and paracetamol (533.64 μg.L^{-1}). The high concentrations derive from the increased consumption of these substances during the COVID-19 pandemic. During the conventional water treatment, the maximum removal of diclofenac, dipyrone, ibuprofen and paracetamol was 22.42%; 3.00%; 32.74%; and 1.58%, respectively, which confirms the inefficiency of this treatment in removing drugs. The variation in removal rate of the analyzed drugs is due to the difference in the hydrophobicity of the compounds.

Keywords Diclofenac · Emerging pollutants · Ibuprofen · Pharmaceuticals · Pharmaceutical compounds · Water contamination · Water treatment

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1 Introduction

The high rate of urbanization added to the intense industrial activities has been the main responsible for environmental contamination, above all, for the pollution of water matrices. In addition, in recent decades, society has been recognized for its high consumption of pharmaceutical products (Gebhardt & Schröder, 2007). Nonetheless, several emerging micropollutants have only recently been detected in different environments as potential pollutants, bringing significant concerns to the scientific community (Montagner et al., 2017).

Emerging micropollutants involve a range of compounds, such as steroid hormones, personal care products, industrial chemicals, pharmaceutically active residues, and other toxic substances (Bhatt et al., 2022). Although they are present in trace concentrations (ng.L^{-1} or µg.L^{-1}) in aquatic matrices (Alder et al., 2010), they can cause disturbance to the ecological system. In addition, they affect human health, causing problems in some organs, such as liver and kidneys, and increasing the risk of cancers (Kumar et al., 2020).

Drugs are biologically active chemical substances synthesized to produce a physiological effect at small concentrations in humans, animals or plants (Lima et al., 2017). Their residues originate from leftover medicines, expired pharmaceutical products, or part of the medicines not metabolized by the human, animal or plant. These residues tend to reach the aquatic environment through point or diffuse sources, with domestic and industrial effluents being the primary sources of contamination of water sources by these compounds (Li, 2014). Point pollutions are those where dumping occurs in a discrete spatial location, and include municipal, industrial and hospital liquid waste, as well as leachate from landfills. At the same time, diffuse pollutions occur on a large geographic scale and are exemplified by agricultural runoff, rainwater and leaks in water distribution networks (Nawaz & Sengupta, 2019).

The most common drugs in nature are non-steroidal anti-inflammatory drugs, antibiotics, beta-blockers, blood lipid-lowering agents, antihistamines, antidepressants, hormones, and antiepileptics (Khetan & Collins, 2007). However, non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most consumed worldwide among the therapeutic classes of drugs (Izadi et al., 2020). Furthermore, these drugs in the aquatic environment are also quite common (Bisognin et al., 2018). The use of NSAIDs results in analgesic, anti-inflammatory and antipyretic effects (Day & Graham, 2013). Diclofenac (DCF), ibuprofen (IBP) and naproxen are the most frequently used worldwide (Martinez-Sena et al., 2016).

During the COVID-19 pandemic, the consumption of some drugs, especially NSAIDs, has increased due to their use in the treatment or reduction of the symptoms of the disease. Paracetamol (PCM) and dipyrone (DIP), for example, are recommended as analgesics or to control fever (Carlotti et al., 2020; Januário et al., 2022), in addition to being low-cost and sold without a prescription in several, which leads to an increase in the concentration of these compounds in the water.

Knowledge about the damage drugs in water can bring to the environment and humans is still scarce. However, some studies have already correlated these drugs present in water with dysfunctions in animals and humans. Among animals, drug residues in water are able to affect the swimming activity of freshwater fish *Lota lota* (Sundin et al., 2019), alter the migratory behavior of sea trout (*Salmo trutta*) (Mccallum et al., 2019), reduce the reproductive capacity of wild carp (*Cyprinus carpio*) (Petrovic et al., 2002), among others.

The presence of DCF in water can bring effects such as the induction of oxidative stress in the fish *Danio rerio* (Bio & Nunes, 2020), changes in the defense system of the crustacean *Daphnia magna* (Nkoom et al., 2019), and changes in the biochemical parameters of the macrophyte *Lemna minor* (Alkimin et al., 2019). Among the few studies that have evaluated the toxic effects of DIP in water, Pamplona et al. (2011) show damage to the DNA of the fish *Rhamdia quelen*. The ecotoxicological effects of IBP in water may present behavioral and phenotypic changes in the fish *Clarias gariepinus* (Ogueji et al., 2018) and damage to the reproduction of the fish *Oryzias latipes* and the crustaceans *Daphnia magna* and *Moina macrocopa* (Han et al., 2010). PCM is another drug widely studied as an environmental contaminant in water resources. Barbosa et al. (2020) detected neurotoxicity in the annelids *Hediste diversicolor* exposed to the drug in water. Genotoxic effects were also observed in the fish *Cyprinus carpio* (Sharma et al., 2019), as well as changes in the biochemical processes of the macrophyte *Lemna minor* (Kummerová et al., 2016).

According to Januário et al. (2022), about 33% of drugs are excreted after oral use, and conventional water treatment methods are not sufficient for the effective removal of these compounds. Water treatment plants (WTPs) remove particulate matter and microorganisms. Therefore, it is common to apply the stages of coagulation, flocculation, sedimentation or flotation, filtration, and disinfection to achieve this objective (Lima et al., 2014). However, due to the low concentration of drugs in drinking water, few studies have been carried out on the presence of pharmaceutical compounds in treated water and the behavior of these pollutants during conventional water treatment (Boleda et al., 2011). In Latin America, in a vast study carried out by Souza et al. (2022), it was found that studies on emerging pollutants in aquatic matrices are concentrated in surface water (38%) and wastewater (19%), therefore, studies that analyze the presence of drugs in groundwater and treated water are not very expressive. on the mainland.

In Brazil, 433 points have already reported the presence of Pharmaceuticals and Personal Care Products (PPCPs) in the literature, with 311 occurrences in surface waters (Marson et al., 2022). In the country, several NSAIDs are sold without a medical prescription. A large part of the population does not have access to the sanitary sewage system, which facilitates the arrival of drugs in the country's aquatic matrices. In the Lower Middle region of the São Francisco River, more than half of the population does not have access to sewage collection. It has intense agricultural activities (CBHSF, 2016), with an intense use of pharmaceutical products.

The Brazilian legislation that determines the parameters of water potability is established in Ordinance No. 888/2021 of the Ministry of Health, and provides the physicochemical and biological characteristics of water acceptable for human consumption, as well as the maximum concentrations of compounds that may present a risk to health (Brazil, 2021). Nevertheless, there is no mention of the maximum limits permitted for medicines in water intended for human consumption in the country's legislation.

Thus, this study aimed to evaluate the presence and concentration of the NSAIDs DCF, DIP, IBP and PCM in a section of the São Francisco River sub-area, in the Brazilian semiarid region, in addition to verifying the efficiency of the conventional water treatment in the removal of these compounds. In this sense, the study covers the knowledge on drug concentrations in the country's water matrices, generating a database for these compounds to be regulated in the future.

2 Methodology

2.1 Characterization of the Study Area

The São Francisco river basin has a drainage area of 639,219 km^2, which is equivalent to 7.5% of the total area of Brazil, and with an average flow of 2850 $m^3.s^{-1}$. Its main river – São Francisco River – has its source in Serra da Canastra, state of Minas Gerais, passes through Goiás, Federal District, Bahia, Pernambuco, and flows into the Atlantic Ocean, on the border between the states of Alagoas and Sergipe. In addition, 505 Brazilian municipalities are in the São Francisco river basin region, making it essential for the country due to its extension and water volume, especially for the semiarid region (CBHSF, 2020).

Among the municipalities bathed by the São Francisco River, three were evaluated for contamination and drug removal in the semiarid region of the state of Pernambuco: Orocó, Santa Maria da Boa Vista and Petrolândia, all located in the Sub-medium region of the São Francisco River. In Fig. 1, the cities studied and the collection points are presented. The municipality of Orocó has 554.76 km^2 of land area and 13,180 inhabitants; Santa Maria da Boa Vista has 3000.774 km^2 of land area and 39,435 inhabitants; and Petrolândia has 1,056,592 km^2 and 32,492 inhabitants (IBGE, 2010). In this region, the average monthly rainfall varies between 8.5 mm and 133.8 mm in September and March, respectively, with the rainy season between January and June and the dry season between July and December (APAC, 2022).

In the Sub-medium region of the São Francisco River, about 40% of the population works with agriculture, livestock, forestry and aquaculture; and agricultural establishments occupy 72.8% of the land. In addition, only 45.2% of the households in this region have access to the sewage system (CBHSF, 2016).

The three selected municipalities have a Water Treatment Plants (WTP) that uses the conventional methodology for water treatment (coagulation, flocculation, decantation, filtration and disinfection). Initially, five study points were used to collect the surface and treated water: two collection points located in the city of Orocó (P1 and P2) and three in the municipality of Santa Maria da Boa Vista (P3, P4 and P5). The collections at these points occurred between February and May 2021, totaling six campaigns. Subsequently, three more points were used to collect

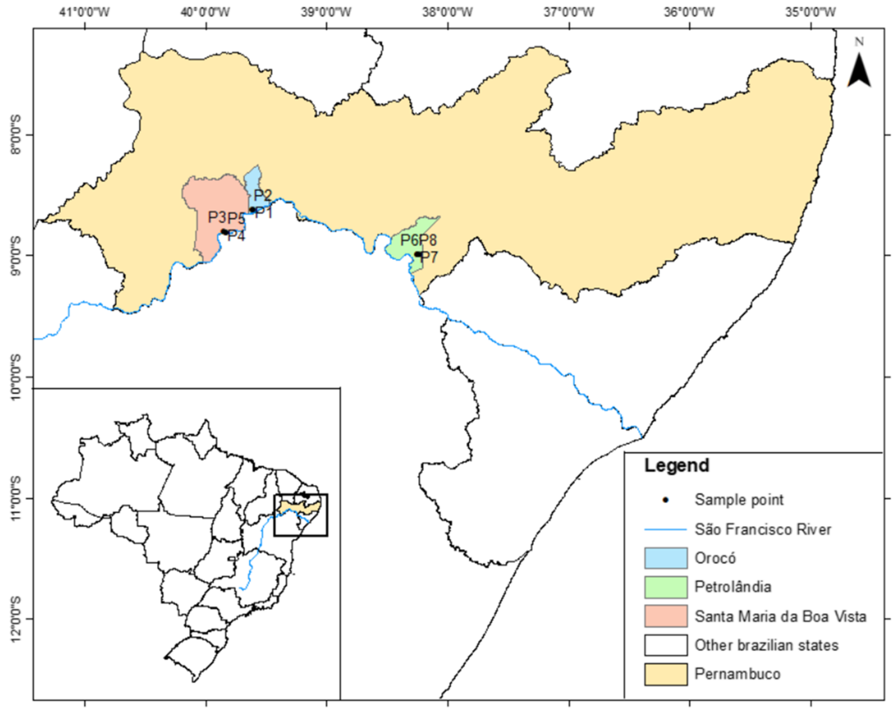

Fig. 1 Location of the collection points along the São Francisco River

surface, underground and treated water in the city of Petrolândia (P6, P7 and P8) in June 2021, with two campaigns. Table 1 presents the characteristics of each of the collection points.

2.2 Sample Collection and Drug Concentration Analysis

Samples for drug analysis were collected and stored in adequately washed 100 mL amber bottles. Then, in a cooler with ice, all flasks were taken to the Laboratory of Molecular Biology and Environmental Technology (LABIOTA), where the extraction of the analytes was performed. After extraction, the samples were taken to the Laboratory of Environmental Engineering and Quality (LEAQ), both from the Federal University of Pernambuco (UFPE), in amber vials and under refrigeration, where all pharmacological analyses were performed.

For all collection points (P1 to P8), the concentrations of four NSAIDs were evaluated: DCF, DIP, IBP and PCM. Solid-phase extraction (SFS) was used for sample preparation employing Strata-X cartridges (Phenomenex). For this step, cartridge conditioning was carried out with a mixture of acetic acid 0.1% and acetonitrile 65:35, then ultrapure water was percolated, the sample to be analyzed and finally, again the mixture of solvents used in conditioning. This procedure was carried out with the aid of a peristaltic pump, allowing the analytes contained in the sample to be in the appropriate solvent for the chromatographic analysis.

Table 1 Characteristics of the collection points in the three selected municipalities

Sample point	Geographic coordinates	Type of water	Country
P1	8°37′25.23″S and 39°35′54.30″W	Surface raw water	Orocó
P2	8°37′2.77″S and 39°36′13.77″W	Potable water	
P3	8°48′1.55″S and 39°50′34.74″W	Surface raw water	Santa Maria da Boa Vista
P4	8°48′34.92″S and 39°49′33.00″W	Surface raw water	
P5	8°48′33.08″S and 39°49′31.04″W	Potable water	
P6	8°59′10.30″S and 38°14′46.57″W	Surface raw water	Petrolândia
P7	8°59′6.08″S and 38°13′51.62″W	Potable water	
P8	8°59′12.73″S and 38°14′42.50″W	Groundwater	

Table 2 Limit of detection (LD), limit of quantification (LQ), and coefficient of variance (CV) used in pharmaceutical compounds detection method

Fármaco	LD (mg.L^{-1})	LQ (mg.L^{-1})	CV (%)
Diclofenaco	0.19	0.74	2.89
Dipirona	0.24	0.72	2.19
Paracetamol	0.36	1.12	4.08
Ibuprofeno	5.33	16.15	1.56

The identification and quantification of all compounds was carried out via high performance liquid chromatography (Shimadzu), using a C18 column, operating in reverse mode (mobile phase—acidified water with acetic acid 0.1% and acetonitrile 65:35). The methodology used was previously validated by Napoleão et al. (2018) for DCF, DIP and PCM. For IBP, the methodology validated by Monteiro et al. (2018) was used. For the validation of the chromatographic method under study, the following validation parameters were analyzed and determined: limit of detection (LD), limit of quantification (LQ), and precision. Precision analysis was performed based on the coefficient of variance (CV) (Table 2).

3 Results and Discussion

3.1 Concentration of the Pharmaceutical Compounds in Water

The minimum and maximum concentrations of DCF, DIP, IBP and PCM are shown in Table 3, while the means are shown in Fig. 2. In the three cities evaluated, DCF was detected in approximately 76% of the samples analyzed. At points P3, P7 and P8, this compound was detected in 100% of the samples, with the highest concentration of 759.06 µg.L^{-1} at point P3. Peña-Guzmán et al. (2019) presented data on emerging pollutants in Latin America. The authors observed high maximum values for drinking water for the compound of DCF (150 µg.L^{-1}), IBP (625 µg.

Table 3 Minimum and maximum concentrations of the pharmaceutical compounds

		P1	P2	P3	P4	P5	P6	P7	P8
Diclofenac (µg.L^{-1})	Min	ND	ND	614.10	ND	ND	ND	612.60	607.92
	Max	616.26	645.66	759.06	673.50	610.80	607.26	612.84	609.12
Dipyrone (µg.L^{-1})	Min	ND	ND	ND	ND	ND	ND	ND	ND
	Max	1675.50	1717.08	1858.02	1502.34	1573.32	1526.94	1481.10	ND
Ibuprofen (µg.L^{-1})	Min	88.02	ND	ND	ND	ND	ND	88.62	91.62
	Max	359.82	114.18	785.28	188.46	219.12	116.40	117.12	117.12
Paracetamol (µg.L^{-1})	Min	ND	ND	387.66	ND	ND	ND	371.52	ND
	Max	400.50	381.90	533.64	481.14	395.76	361.02	371.52	373.08

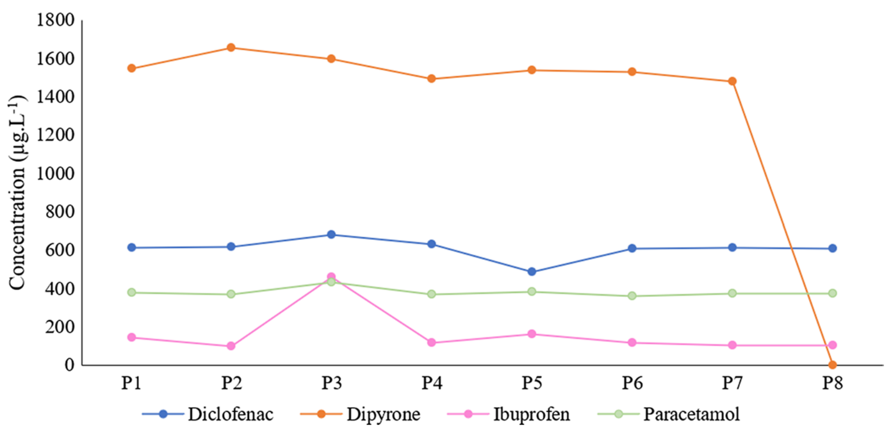

Fig. 2 Mean concentrations of the pharmaceutical compounds in the studied points

L^{-1}) and PCM (200 μg.L^{-1}), values that correspond to those obtained in this study.

Except for DIP, point P3 had the highest mean concentration of all evaluated drugs (Fig. 2). This phenomenon was expected, since this point proved to be eutrophic, with macrophytes on the surface. Thus, this stretch of the river possibly receives domestic and industrial effluents, which is attributed as the leading cause of the concentration of drugs in surface waters (Américo-Pinheiro et al., 2017).

The DCF concentrations in the São Francisco River are above those determined in the world literature (Martinez-Sena et al., 2016; Schmidt et al., 2018; Sibeko et al., 2019; Sousa et al., 2017). Similar values have been found by Carvalho Filho (2019) and Santos (2020), who have evaluated the rivers Ipojuca and Capibaribe, which are also part of the semiarid region of Pernambuco. Also in northeastern Brazil, Chaves et al. (2020) found concentrations of up to 463 ng.L^{-1} of DCF in Anil and Bacanga rivers. Furthermore, according to Sathishkumar et al. (2020), rivers that pass through urban areas tend to have higher concentrations of pharmaceutical compounds.

According to Pemberthy et al. (2020), the concentration of water pharmaceuticals and personal care products varies seasonally. The authors analyzed three drugs (triclosan, DCF and IBP) in the waters of the Gulf of Urabá, Colombia. They found that DCF doubled in rainy seasons, which can be explained by the reduction in the rate of degradation of these products due to the decrease in sunlight in those times. Since this project was conducted in the rainy season, the high levels of DCF in the water may be related to the rainy season and, consequently, to the reduction in the rate of drug degradation.

In another study carried out in Brazil, Santos et al., (2020) also found a trend towards increased concentration of drugs in surface water during the rainy season, which can be explained by the increased consumption of these drugs at this time of year, and differences in temperature and rainfall. In a study in India, Singh and Suthar (2021) found higher concentrations of NSAIDs in winter due to the lower rate of biodegradation of drugs, which is related to lower temperatures and inadequate sunlight.

Diclofenac strongly absorbs sunlight, which causes direct photodegradation of the drug (Kanakaraju et al., 2014; Mohapatra et al., 2023; Packer et al., 2003). Therefore, the high rates of this compound during the period of analysis are justifiable by the reduction in the incidence of sunlight during the rainy season.

On the other hand, in a study carried out by Souza (2016) on the São Francisco River, an increase in the concentration of pollutants was observed during the rainy season due to the transport of contaminants from the soil to the river, resulting from the planting of fruits that occur at that time in the region. Thus, in addition to reducing the photodegradation of drugs, drugs may also be being carried into the river, which causes high concentrations of drugs in the water. In Brazil, there is no separate drainage system and a low percentage of sanitary sewage, it happens that in the rainy season, the concentration of sewage ends up being carried to the water courses in greater quantities.

As expected, DIP was not detected in most samples (55%), since the drug is hardly found in water due to its activation format. According to Gómez et al. (2008), after the ingestion of DIP, this compound is hydrolyzed into 4-methylaminoantipyrine (4-MAA), which is subsequently metabolized to 4-aminoantipyrine (4-AA), acetylaminoantipyrine (4-AAA) and 4-formylaminoantipyrine (4 -FAA). Thus, in general, what is found in water are the metabolites of this pharmaceutical compound. Nevertheless, DIP was found in part of the surface and treated water samples, being the drug with the highest mean concentration among the four compounds analyzed. In surface water, the concentration of DIP varied between ND (not detected) and 1858.02 μg.L^{-1}, while in drinking water, the concentration was between ND and 1717.08 μg.L^{-1}.

It is an analgesic and antipyretic readily available in Brazil because it does not require a medical prescription. The high concentrations obtained for DIP may be associated with the increased use of this drug during the COVID-19 pandemic, consequently increasing the concentration of this compound in the environment. The trend of using DIP as one of the most common drugs during the pandemic has been reported worldwide (Elbarbary et al., 2020; Rinott et al., 2020).

In addition to surface water contamination, anthropogenic activities, such as improper disposal of domestic and industrial effluents and the use of fertilizers, have caused the dispersion of pollutants into groundwater (Houria et al., 2020). The underground water of the Sub-medium São Francisco is characterized by quality problems, and 5% of it is not potable and around 70% is considered unfit for human consumption, in addition to Petrolândia lithology being predominantly sandy (CPRM, 2022), which causes greater vulnerability to the aquifer. Thus, effluents tend to reach this source more efficiently due to the lack of a sanitary sewage network. At point P8, only DIP was not detected in any campaign (Table 3), which already characterizes the pollution of this water source by pharmaceutical compounds. However, different results have been found by Teijon et al. (2010), Cabeza et al. (2012) and Huntscha et al. (2012), who have detected DIP metabolites in groundwater. Thus, DIP has not been found in groundwater, but there is a possibility that metabolites of this drug are present in this aquatic matrix.

IBP was detected in about 67% of the samples, with mean concentrations ranging between 97.61 and 458.70 μg.L^{-1}. Among the compounds evaluated, it was the one with the lowest concentrations in water. Photolytic processes are an essential mechanism of IBP removal in surface waters that receive solar irradiation (Packer et al., 2003) and, added to biodegradation (Richardson & Bowron 1985), they can explain the lower frequency of detection among the studied drugs. This same result has been obtained by Pemberthy et al. (2020), who evaluated triclosan, IBP and DCF in the Gulf of Urabá, Colombia; and Kramer et al. (2015), who analyzed IBP, DCF and PCM in the Alto Iguaçu watershed, located in the Metropolitan Region of Curitiba, Brazil.

In a study carried out in drinking water in the region of Campinas, Brazil, Maldaner and Jardim (2012) observed maximum concentrations of 635 μg.L^{-1} for the IBP. Reis et al., (2019a, 2019b) evaluated surface waters in the state of São Paulo, and detected concentrations of IBP until 0.33 μg.L^{-1}, while in the state of Pernambuco, Santos (2020) found variations between 724 and 1626 μg.L^{-1} in the Capibaribe River, and between 818 and 2318 μg.L^{-1} in the Ipojuca River, also located in the Brazilian semiarid region.

Lower detection levels of IBP in Brazilian waters are expected because this drug has low consumption by the country's population compared to other drugs (Kramer et al., 2015). Jakimska et al. (2014) evaluated the presence of IBP and five of its transformated products in treated water by WTP, and in the surface water of the Randunia River, Poland, and treated in addition to five of its processing products. IBP was not detected in the samples evaluated, but the products from its transformation were found in almost all of them. According to the authors, this result demonstrates that natural processes occur in the water which decrease or remove IBP, such as the hydrolysis and biodegradation of the drug. Thus, the low consumption of this compound in Brazil and the natural processes in the aquatic environment explain the lower concentration of this drug in water.

PCM was detected in about 81% of the samples, with a mean concentration between 361.02 and 433.85 μg.L^{-1}. In Brazilian surface waters, Américo et al. (2012) determined values between 130 and 1877 μg.L^{-1} in Córrego da Onça, located in Mato Grosso do Sul; Campanha et al. (2014) determined concentrations of up to 30.42 μg.L^{-1} of the drug in the Monjolinho River, state of São Paulo; and Veras et al. (2019) found a concentration of PCM ranging between 3 and 42 μg.L^{-1} in the Beberibe River, in Pernambuco.

Kasprzyk-Hordern et al. (2009) evaluated the surface water of two rivers in the UK: Taff and Ely. The minimum and maximum concentrations found were 0.185 and 1.534 μg.L^{-1} in the Taff River and $<$1.5 and 716 ng.L^{-1} in the Ely River. Rivera-Jaimes et al. (2018) verified the contamination of surface waters in Cuernavaca, Mexico, by pharmaceuticals. Of the 32 compounds analyzed, PCM was among the most abundant, with concentrations varying between 0.354 and 4.460 μg.L^{-1}. Finally, Zheng et al. (2020) analyzed 52 drugs at various points in Qingdao, China. Among them, PCM had the highest concentration in water, reaching up to 4,400 μg.L^{-1}, but with a mean of 0.152 μg.L^{-1}.

The high concentrations of this drug in Brazilian waters may be related to the typical consumption in the country and the possibility of sale without a prescription (Campanha et al., 2014). In addition, like DIP, this drug has an analgesic and antipyretic effect, with increased consumption due to the COVID-19 pandemic (Galani et al., 2021), causing an increase in the concentration of this compound in water resources. Elbarbary et al. (2020) evaluated patients worldwide, including Brazilians, who had the virus. 81% of the respondents used PCM to eliminate the disease symptoms, while 4% used IBP and 1% used DIP. In a study performed in Israel, among

403 patients positive for COVID-19, PCM was used by 32% of them during the treatment of the disease, being the most commonly used antipyretic, followed by IBP (22%) and DIP (3.7%) (Rinott et al., 2020). Grosse et al. (2020) evaluated 14 Austrian patients who had COVID-19. Among them, 12 used PCM during their illness. Due excessive use of analgesics, during the pandemic in Greece, PCM consumption increased from 76.044 g.L^{-1} in 2019 to 226.449 g.L^{-1} in 2020 (Galani et al., 2021).

3.2 Removal of Pharmaceutical Compounds in Water Treatment Plants

Table 4 shows the mean removal of DCF, DIP, IBP and PCM in the three WTPs evaluated. As shown in Fig. 3, the WTP of the municipality Santa Maria da Boa Vista (P5) showed a mean DCF removal of 22.42% by the conventional water treatment. The others showed a slight increase in the concentration of this compound. Likewise, only one WTP (Petrolândia—P7) showed DIP removal during water treatment. There was a removal of 3.00% for this WTP, while the others showed an increase in the mean concentration of this compound in the water. Low levels of drug removal during water treatment have also been reported by Rigobello et al. (2013) and Tröger et al. (2018).

According to Lima et al. (2017), the conventional water treatment removes, on average, less than 50% of the microcontaminants present in surface water. Since this technology has not been designed to attenuate micropollutants, this result was already expected, reinforcing the idea that studies on water treatment techniques that efficiently remove these compounds are necessary. In a study developed by Rigobello et al. (2020), it was found that diclofenac was removed by 97% by conventional water treatment. However, the study determined a drug removal of 35% and 97%,

Table 4 Mean drug removal by the conventional water treatment method

Pharmaceutical	Country	Water type	Sample point	Mean concentration (μg.L^{-1})	Mean removal (%)
Diclofenac	Orocó	Superficial	P1	611.89	-0.77
		Potable	P2	616.62	
	Santa Maria da Boa Vista	Superficial	P4	629.28	22.42
		Potable	P5	488.18	
	Petrolândia	Superficial	P6	607.26	-0.90
		Potable	P7	612.72	
Dipyrone	Orocó	Superficial	P1	1546.01	-7.02
		Potable	P2	1654.50	
	Santa Maria da Boa Vista	Superficial	P4	1494.26	-3.02
		Potable	P5	1539.36	
	Petrolândia	Superficial	P6	1526.94	3.00
		Potable	P7	1481.10	
Ibuprofen	Orocó	Superficial	P1	145.11	32.74
		Potable	P2	97.61	
	Santa Maria da Boa Vista	Superficial	P4	115.64	-38.48
		Potable	P5	160.13	
	Petrolândia	Superficial	P6	116.40	11.62
		Potable	P7	102.87	
Paracetamol	Orocó	Superficial	P1	377.38	1.58
		Potable	P2	371.40	
	Santa Maria da Boa Vista	Superficial	P4	368.36	-4.26
		Potable	P5	384.06	
	Petrolândia	Superficial	P6	361.02	-2.91
		Potable	P7	371.52	

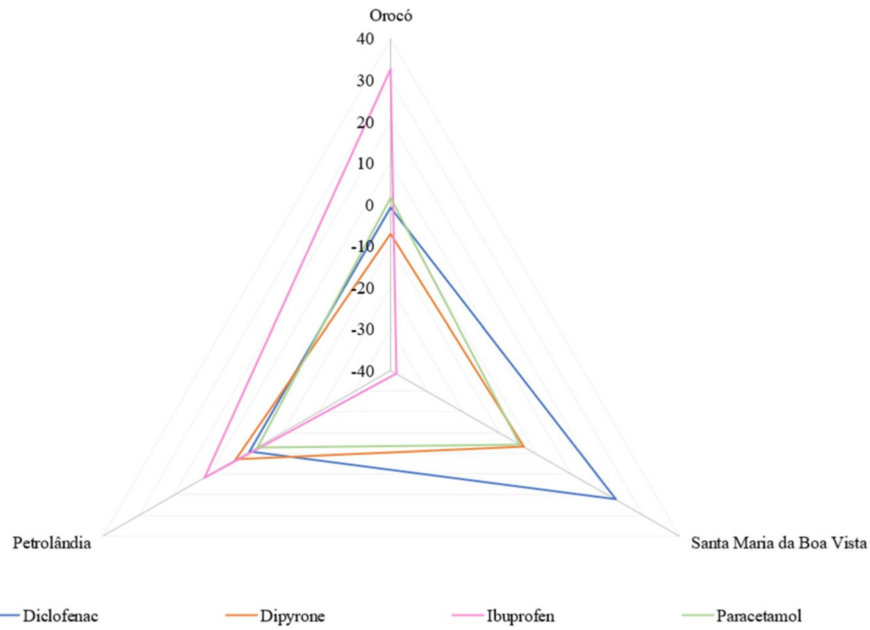

Fig. 3 Mean removal of the pharmaceuticals in percentage per city using the conventional water treatment method

respectively, 30 min and 24 h after the application of chlorine in the water. In this study, the water was collected immediately after the end of the treatment, that is, right after the disinfection step. Therefore, the possibility of chlorination could not cause a significant reduction of diclofenac, thus showing that the conventional treatment is not efficient. However, it may be effective longer after chlorination.

To help understanding the differences in efficiency of each investigated drug, we can observe their hydrophobicity values, as shown in Table 5. According to the classification given by Rogers (1996), for display with logKow lower than 2.5, one can consider low hydrophobicity; between 2.5 and 4.0, preserved hydrophobicity; and logKow greater than 4.0, high hydrophobicity. Studies report that more hydrophobic compounds tend to have greater removals during treatment because they have greater adsorption capacity (Masud et al., 2020; Reis et al., 2019a, 2019b; Stackelberg et al., 2007; Thuy et al., 2008). Thus, as diclofenac and ibuprofen have, respectively, high and protected hydrophobicity, while dipyrone and paracetamol have low hydrophobicity, greater removals are expected for diclofenac and ibuprofen during water treatment."

Table 5 Hydrophobicity values for the investigated drugs

Drugs	Formula	$logK_{ow}$
Diclofenac	$C_{14}H_{11}Cl_2NO_2$	4.51[a]
Dipyrone	$C_{13}H_{16}N_3NaO_4S$	-4.76[b]
Ibuprofen	$C_{13}H_{18}O_2$	3.97[a]
Paracetamol	$C_8H_9NO_2$	0.46[a]

[a]PubChem (2023)

[b]Santos (2015)

The addition of drugs in the treated water has been reported by other authors (Dias, 2014; Ghiselli, 2006; Tröger et al., 2018) and may mean the formation of some precursors of the micropollutants, which was not observed in the surface water sample and might result from an error in the reading equipment (Tröger et al., 2018). In addition, since the raw and treated water samples were collected simultaneously, the retention time of the WTPs was not considered. Thus, drug concentrations in raw water could be different from the characteristics of the water treated at the WTP.

Kasprzyk-Hordern et al. (2009) evaluated the concentration of drugs in surface waters and tributaries and effluents from Sewage Treatment Plants (WWTPs) in the United Kingdom, and also identified an increase in the concentration of some compounds in raw and treated sewage. According to the authors, several processes can cause this increase in concentration, including the hydrolysis of conjugates of pharmaceutical products.

Only in Santa Maria da Boa Vista WTP (P5) there was an increase in the mean concentration of IBP in the water, which can be explained by the lack of consideration of the WTP detention time. In the other WTPs, 32.74% and 11.62% of removal of this drug were observed, respectively, in Orocó and Petrolândia. Regarding PCM removal, except for Orocó (P2), which showed the removal of 1.58% of the drug in the water, there was a slight increase of PCM in the other locations analyzed, comparing the surface and treated waters. These results corroborate the data found for DCF and DIP and demonstrate that the conventional treatment does not efficiently remove pharmaceutical compounds from the water.

4 Conclusion

Based on the investigations conducted during the project, it was found that all drugs analyzed (DCF, DIP, IBP and PCM) were detected in the surface waters of the São Francisco River with concentration varying between not detected (ND) and 759.06 $\mu g.L^{-1}$, ND and 1858.02 $\mu g. L^{-1}$, ND and 785.28 $\mu g.L^{-1}$, and ND and 533.64 $\mu g.L^{-1}$, respectively. The high concentrations of pharmaceutical compounds found in the São Francisco River, especially DIP and PCM, may be associated with increased consumption of these substances during the COVID-19 pandemic to ease the symptoms felt due to the disease. In addition, the investigated drugs can be purchased without a medical prescription in Brazil, which facilitates the use of drugs and, consequently, the insertion of compounds into water bodies.

Among the evaluated drugs, only DIP was not detected in the underground water of Petrolândia (P8), demonstrating that pharmaceutical compounds contaminate this water source in the analyzed site. However, due to its activation format, DIP is rapidly metabolized and, in general, its metabolites are found in water. Thus, DIP has not been found in groundwater, but there is a possibility that metabolites of this drug are present in this aquatic matrix.

The maximum removal of DCF, DIP, IBP and PCM was 22.42%; 3.00%; 32.74%; and 1.58%, respectively, during the conventional water treatment, which confirms the inefficiency of this treatment in removing drugs. The variation in the removal rate of the analyzed drugs is due to the difference in hydrophobicity of the compounds (Kow).

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Declarations

Competing Interests The authors have no relevant financial or non-financial interests to disclose.

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