ISSN 2347-6893

Identification and quantification of ibuprofen in conventional wastewater treatment plants in Rio de Janeiro, Brazil,and their discharge to the aquatic environment

Aldo Pacheco Ferreira

Oswaldo Cruz Foundation, Sergio Arouca National School of Public Health, Center for the Study of Worker's Health and Human Ecology, Rio de Janeiro, Brazil

aldopachecoferreira@gmail.com

ABSTRACT

Pharmaceuticals are continually being introduced into the influent of wastewater treatment plants (WWTPs). The occurrence and fate of trace-level contamination of pharmaceuticals in the aquatic environment has been recognized as one of the emerging issues in environmental chemistry. The effluents of wastewater treatment plants, usually directly emitted to the environment, often contain the anti-inflammatory drug ibuprofen. Studies on the occurrence of pharmaceuticals show that the widely used pharmaceutical ibuprofen is present in relevant concentrations in the environment indicate toxic effects on biota and the lack of profile in sewage removal provided by the city. For this purpose, a survey on the presence of ibuprofen in urban wastewater of Rio de Janeiro was carried out. It were evaluated ibuprofen concentration in the affluent and effluent from WWTP Penha and Ilha do Governador, Rio de Janeiro, Brazil. Samples were collected along the line of treatment of each WWTP, and for clean up the samples was solid phase extraction (SPE), analysed by high performance liquid chromatography (HPLC), assisted by diode array detector (DAD) techniques. The removal efficiency of ibuprofen in the wastewater treatment plants was roughly evaluated. Ibuprofen was detected in all samples analysed, which confirms the low removal efficiency of conventional treatment systems, aerobes and anaerobes.

Indexing terms/Keywords

Ibuprofen residues; sanitation; sewage treatment; solid phase extraction; high performance liquid chromatography

Academic Discipline And Sub-Disciplines

Natural Sciences; Limnology

SUBJECT CLASSIFICATION

Sanitation

TYPE (METHOD/APPROACH)

Wastewater treatment plants

ISSN 2347-6893

INTRODUCTION

The constant exponential growth in human population has created a corresponding intensification in the demand for the earth's limited supply of freshwater (1). Consequently, protecting the integrity of our water resources has become in the most essential environmental issues to be done. Numerous recent pollution problems are a result of the incessant release of chemical substances into the environment (2-4). Their presence is one of the central emerging issues to public and environmental health concern (2,5).

Although the occurrence of pharmaceuticals in the environment are nowadays considered emerging pollutants, as being biologically active molecules they are considered potentially hazardous for aquatic organisms and health of the ecosystem, since they are continuously entering the aquatic environment via sewage systems, and can be found in a number of water bodies (6,7). The occurrence of organic micropollutants such as pharmaceuticals, synthetic hormones, and personal care products has the increasing attention of drinking water companies and water resource institutions (8-10). Furthermore, the development of analytical techniques to measure these compounds at low concentrations has accelerated this awareness(11-12). Thus, pharmaceuticals are becoming ubiquitous aqueous pollutants and as a result, they are detected in remote aquatic environments (13). Even if the effects of pharmaceuticals on living organisms are useful, designed to be biologically active, but some of them are not readily biodegraded (14-16). In the last years, technologies for the removal and recovery of pharmaceuticals residues from wastewater effluents have been developed and implemented into the water cycle infrastructure. As these technologies are designed to deal with bulk load emissions, many organic micropollutants are not removed during the passage through these systems (17).

Sewage and sewage treatment plants are believed to be the main source of human pharmaceutical contamination (16), in the sense that WWTP's compromise the point of release into receiving waters (3,9,18). Thousands of tons of pharmaceuticals are used every year, in both human and veterinary medicine, and are released to the environment through metabolic excretion and improper disposal techniques (9,10). Human-use pharmaceuticals enter sewage effluents via urine and faeces and by improper disposal. These compounds are not completely degraded at the wastewater treatment plants, and many of them are discharged into the environment through many sources and pathways (16). Despite this general finding, the question arises what risks these traces of pharmaceuticals pose for aquatic ecosystems. Figure 1 presents a schematic picture showing the sources and pathways of pharmaceuticals into various water bodies.

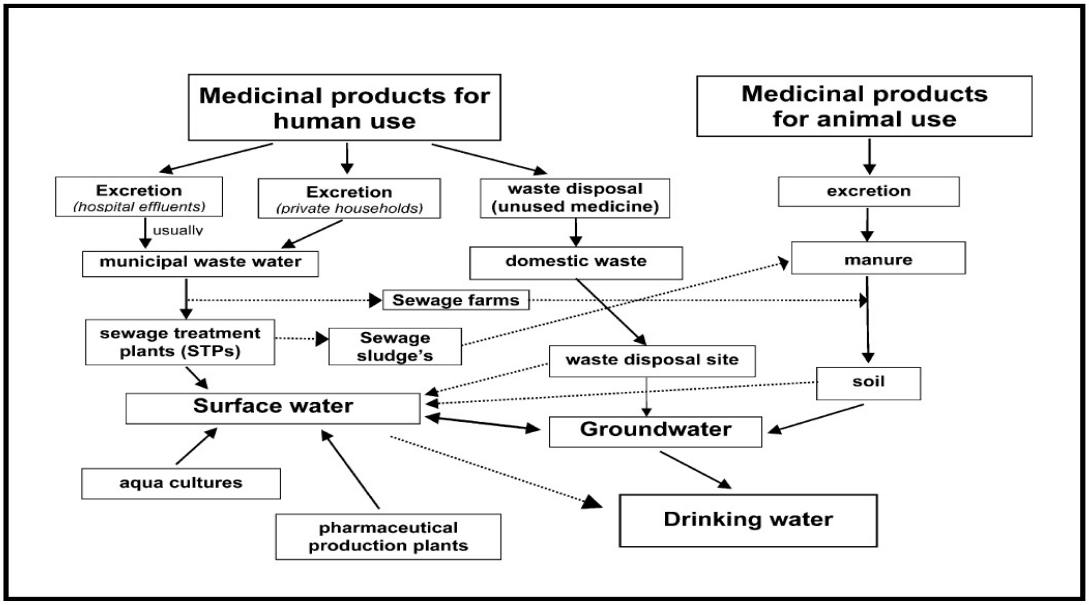


Figure 1: Sources and pathways for the occurrence of pharmaceutical residues in the aquatic environment. Modified from Heberer (11).

Ibuprofen (2-(4-isobutylphenyl) propionic acid) (Figure 2) is available without prescription and is the third most utilized drug in the world (19). It is produced globally at several kilotons per year and is also one of the core medicines listed in Essential Drugs List of World Health Organization, and therefore produced in large amounts worldwide (20,21). Ibuprofen has been placed on this list due to its wide use as an analgesic, antipyretic and anti-inflammatory. It is one of the core medicines included It is available in a number of formulations with the generic names e.g. Advil, Alivium, Brufen, and Nurofen (21). As with many pharmaceutical drugs, ibuprofen is specifically designed to be biologically active for use in human and veterinary medicine, hinting at the broadness of the cyclooxygenase target across species (21,22). Over 70% ofibuprofen is metabolized and excreted in urine. Hydroxylated and carboxylated compounds are the predominant metabolized forms (23).

ISSN 2347-6893

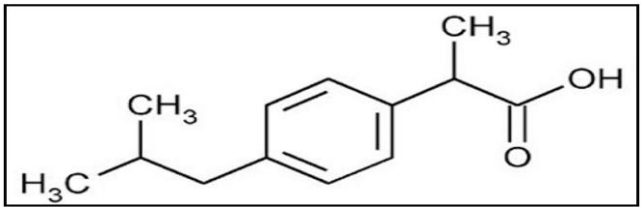


Figure 2: The structure and main properties of Ibuprofen (a-Methyl-4-[isobutyl] phenyl acetic acid)

With growing interest on environmental issues, several intriguing questions related to the removal performance in the WWTPs Penha and Ilha do Governador, to assess the ibuprofen removal efficiency in the processes. This study addresses the basic concepts, sources, mode of action, levels, analytical measurement, bioavailability, and biological role in the environment. An attempt has been made to answer the queries presented by the environmentalists working on various aspects of pharmaceuticals pollution in the environment.

MATERIALS AND METHODS

Process characteristic in WWTPs: Activated sludge

Sewage treatment plants can be equipped with primary, secondary and tertiary treatment steps (24). Primary treatment, often called physical treatment, involves the removal of big objects, floating solids and suspended solids (both fine and coarse) from raw sewage. This step often removes grease as well. Secondary treatment involves biological processes and results in decanted effluents and separated sludge containing microbial mass together with pollutants. The tertiary process removes pollutants not adequately removed by the secondary treatment, particularly nitrogen and phosphorus, often accomplished by some means of chemical treatment, sand filters, or other methods (25). During the tertiary treatment, microorganisms such as pathogens and viruses should also be removed by disinfection (26). Penha and Ilha do Governador WWTPs are submitted to the following operational parameters: pH, total suspended solids, fixed suspended solids, volatile suspended solids, chemical oxygen demand, biochemical oxygen demand, total Kjeldahl nitrogen, ammonia nitrogen, nitrate, nitrite and phosphorus.

According to Ferreira et al. (27), the activated sludge process make use of biological sludge full of microorganisms often combined with bubbling air or oxygen to reduce the organic content from the sewage. Under ideal conditions, a nitrification process takes place in which ammonia is converted to nitrite and nitrate and ultimately to nitrogen gas. This usually takes place in the aeration tank. The microorganisms grow and reproduce by using the organic material as food, and at the same time, they are mixed with air, which results in their aggregation. These biological solids or sludges are more readily sedimented in the secondary clarifiers where they are separated from the treated wastewater. Some fraction of the sludge is returned to the head of the aeration system (40 to 60% of the wastewater flow) while the rest goes to waste. This wasted activated sludge is removed from the treatment process to keep the ratio of biomass to food supplied (sewage or wastewater) in balance (28).

Penha WWTP

Penha WWTP operates with biofilters and activated sludge, treating a flow of around 1,600 L^{s-1}. The pre-treatment starts by medium and fine screening, with removal of solids, followed by removal of sands, oils, and grease. Greases are incinerated. The primary treatment consists of an accelerated lamellar settling in four tanks, with optional physical and chemical treatment, and of three tanks of equalization/homogenization. The secondary biological treatment is performed by means of a continuous-flow activated sludge system with conventional aeration in six aerated tanks by surface aeration, followed by a secondary lamellar settling, in 12 settlers of rectangular plant, with biological sludge recirculation.

Ilha do Governador WWTP

Ilha do Governador WWTP operates with activated sludge, treating a flow of around 525 L^{s-1}. The treatment process works with the steps: the elevated influent pass through a screening formed by grids – a coarse and a medium, responsible for removing coarse solids, followed by the removal of oils, greases and sands, in two grit chambers/degreasers. The resulting by-products of this pre-treatment are later deposited in controlled landfill. The influent is then fed to a homogenization tank e with 4,000 m^3 working volume, whose function is to regularize peaks of pollutant load.

The subsequent primary treatment consists of a preliminary step of physical and chemical treatment, with application of aluminium sulphate, hydrated lime and a polyelectrolyte on two lines of coagulation/flocculation tanks, with primary settling in two tanks of circular plant with bottom and surface scraper. The primary effluent is then fed to the secondary treatment, which is performed by means of activated sludge system, in six aeration tanks provided of two surface aerators each and sludge recirculation tank. The next step is the secondary settling in two settlers of circular plant, with bottom and surface scraper.

Sampling

Samplings were carried out along the line of treatment in Penha and Ilha do Governador WWTPs. The sites sampled were: (1) influent, (2) post preliminary treatment, (3) post-primary treatment and (4) final effluent. Samples were taken in triplicate and stored in amber vials of 250 ml. During the 12 h scheduled for sample collection, which occurred between 8 and 20 h, it was gathered eight samples per site during the collection period. The collections in the WWTPs were performed in February-March 2013, and the results express the consolidated obtained from each analysed site.

Reagents

Ibuprofen, triethylamine, toluene, clofibric acid, mefenamic acid and 2,3,4,5,6-pentafluorobenzyl bromide were all purchased from Sigma-Aldrich (Rio de Janeiro, Brazil). Stock solutions of all compounds were prepared by dissolving the compounds in methanol, and the solutions were stored in glass-stoppered bottles at 4°C prior to use. Working aqueous standard solution was prepared daily. Ultrapure water was provided by a Milli-Q system (Millipore, Rio de Janeiro, Brazil).

Filtration and solid-phase extraction (SPE)

The reasons for needing SPE are many. SPE can be used when wanting to remove interfering compounds from samples, to get higher concentrations of e.g. organic pollutants (pre-concentration), to fraction different groups of compounds in a sample, to store analytes that are unstable in liquids and to derivative reactions between reactive groups of analytes. The SPE process includes five steps: First, the sorbent is activated by letting it pass through a solvent the function of which is to condition the solids surface. Then the solvent is removed by liquid with similar composition as the sample matrix. The third step is the application of sample, or the sorption or retention step. Here the sorbent will retain the analytes. After this, the interfering compounds that were retained are removed with a sorbent that does not remove the analytes. The last step is the elution step where the analytes are eluted from the adsorbent using a solvent (29).

With a Millipore hazardous waste filtration system 250 ml portions of each sample was filtered (0.45 µm). The pH was adjusted to 2 with HCl. Subsequent extraction of solid matter retained by the 0.45 µm filter with diethyl ether did not show any presence of analytes of interest. Extraction was performed by percolation through an ENVI-18 reverse phase packed tube at a flow rate of approximately 3ml/min by applying a low vacuum. The solid phase was previously conditioned by flushing with 3 ml acetone, followed by 3 ml methanol and 3 ml of water adjusted to pH <2. At the end of percolation, Erlenmeyer flasks were washed with 3 x 15 ml of acidified water, which are also passed through the cartridge. After drying the solid phase for 1 h under vacuum, the analytes were eluted with 6 ml of methanol. The methanol extract was evaporated until dryness under a gentle stream of nitrogen (30-32).

Derivatization and clean-up

Derivatization was performed at 90°C for 1 h using 400 ml of 2,3,4,5,6-pentafluorobenzyl bromide (2% in toluene) and 4 ml of triethylamine. The derivatized extract was passed through a SiOH cartridge conditioned with toluene. The analytes were eluted with 15 ml of toluene. The eluate volume was reduced under a gentle stream of nitrogen between 100 and 1500 ml; to be inside the range of concentration tested in the calibration curve (33). If higher/smaller concentration was found, the samples were diluted/concentrated and analysed a second time.

Instrumentation

The HPLC analysis was carried out in a Varian system (HPLC-DAD) with a Varian 920-LC model liquid chromatograph equipped with a 900-LC model autosampler, gradient pump, 330 model DAD, and the Galaxie software for data acquisition and processing. The analyses were carried out in the gradient mode using a Pursuit C_{18} (microsorb-MV100-5, 250 x 4.6 mm). The injection volume of samples was 50 µl.

Method validation

The limit of detection (LOD) and limit of quantification (LOQ) of the chromatographic analysis were estimated as 3 and 10 times the baseline noise, respectively. The overall method detection limit (MDL) was then determined by division of the LOD with E_e for each specific matrix.

Reproducibility, determination of recoveries and detection limits

To determine the initial concentration and to quantify the reproducibility of the whole method, an unspiked sample was analysed four times. To determine the recoveries, samples of wastewater were spiked with the pharmaceutical substance at four concentrations: 50%, 100%, 150% and 200% of the initial concentration or about 5, 10, 15 and 20 times the limit of detection for compounds not found in the wastewater tested (clofibric acid). Samples were taken through the analytical procedure. The experimental quantities expressed as a function of the theoretical quantities enabled to determine a regression line. The recovery rate was then derived from the slope. Deviation standards of slopes were calculated with the method of least squares. Recoveries after filtration, SPE, derivatization and clean-up generally exceeded 70%. Seeing that relative standard deviations on the reproducibility and standard deviation on recoveries varied from 2% to 16%, the precision is sufficient.

Limits of detection (signal/noise ratio of 3) and limits of quantification (s/n ratio of 10) of the entire analytical procedure were calculated with a spiked sample and were corrected for recovery. Limits of detection and quantification were in a range, which allows the detection and the quantification of diclofenac in wastewaters.

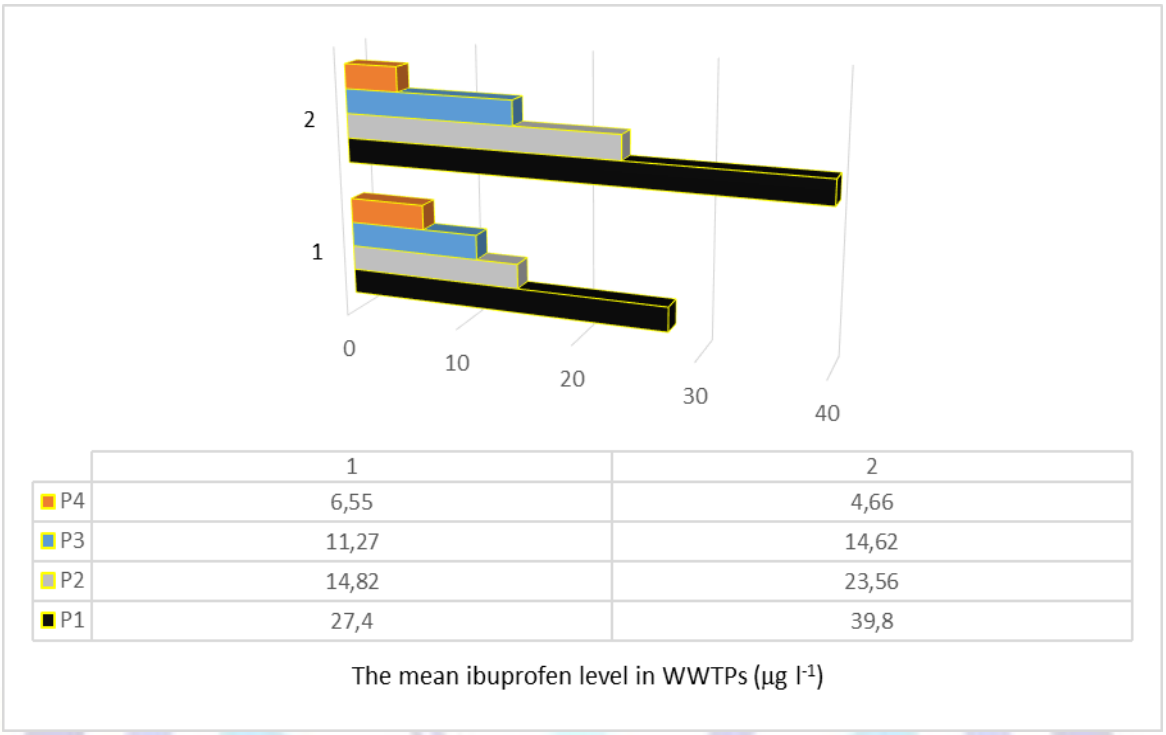
ISSN 2347-6893

Statistical analysis

Statistical analysis were run using the software Origin 8.0 (OriginLab Corporation).

RESULTS

The determination of ibuprofen levels in wastewater samples showed extremely complex, due to interferences that are not eliminated in clean-up process and which absorb UV radiation, which causes severe signals appear at retention times similar to those of the species of interest. However, ibuprofen was detected in the influent and effluent of sewage treatment plants monitored, which confirms the low capacity removal submitted by conventional activated sludge techniques. Ibuprofen has been found in the sewers of all WWTPs evaluated, and occurrence pattern was of the same order of magnitude for all samples (Figure 3).



	1	2
P4	6,55	4,66
P3	11,27	14,62
P2	14,82	23,56
P1	27,4	39,8

The mean ibuprofen level in WWTPs (µg l^{-1})

Figure 3: The mean ibuprofen concentration (µg l^{-1}) at sites of samples collection (P1, P2, P3, P4) in Penha (1) and Ilha do Governador (2) WWTPs

In most analysed samples from WWTP Ilha do Governador were observed the ibuprofen loads increased in the effluent in relation to the influent. According some literature data this fact is due to ibuprofen is conjugated but also metabolised to hydroxyl-ibuprofen (2-(4-(3-hydroxy-2-methylpropyl) phenyl) propanoic acid) and carboxy-ibuprofen (2-[4-(1-hydroxy-1-oxopropan-2-yl) phenyl] propanoic acid). These metabolites have been detected both in WWTP effluents. Since commercial standards were not available, the identification of these compounds must be considered as tentative but the MS-spectrum obtained was in good agreement with previously published spectra (34).

Pharmaceuticals are continually being introduced into the influent of WWTPs. Developing a better understanding of pharmaceutical removal mechanisms within the different treatment processes is vital in preventing downstream contamination of our water resources. Contradictory to the results obtained for ibuprofen research at WWTP Penha and Ilha do Governador, some studies demonstrate a high removal of ibuprofen with biological treatment. Smook et al. (22) in their study with ibuprofen monitoring throughout the City of Guelph municipal WWTP found greater than 95% of ibuprofen was removed in the aeration tank, with aerobic biodegradation being the dominant mechanism. One possible explanation for the different efficiencies found for this drug are the conditions on which the cause sewage treatment, as well as the WWTP design (35), since the removal of ibuprofen is higher anoxic conditions, acid pH and high solar radiation (36). In turn, the reduction ibuprofen photolytic degradation will also depend on some additional parameters, such as eutrophic conditions, degree of particulate material and still depth of the watercourse (11).

The results obtained from the effluents collected along the line of treatment in Penha and Ilha do Governador WWTPs are presented in Tables 1 and 2.

ISSN 2347-6893

Table 1. Ibuprofen concentration (µg l^{-1}) in effluent samples in WWTP Penha

Penha WWTP								
Sites	Statistical analyses							
	X	Sd(yEr±)	Se(yEr±)	Min	Q_1	Median	Q_3	Max
1	27.4	3.89	1.37	21.33	24.37	28.12	29.88	33.13
2	14.82	3.54	1.25	10.21	11.33	15.68	17.56	19.18
3	11.27	3.58	1.26	7.19	8.02	10.81	14.59	16.13
4	6.55	0.69	0.24	5.72	6.06	6.29	7.16	7.63

X-arithmetic mean; Sd- standard deviation; Se- standard error; Q_1 – Percentile 25; Q_3 – Percentile 95, Max – Maximum; Min – Minimum

Table 2. Ibuprofen concentration (µg l^{-1}) in effluent samples in Ilha do Governador WWTP

Ilha do Governador WWTP								
Sites	Statistical analyses							
	X	Sd(yEr±)	Se(yEr±)	Min	Q_1	Median	Q_3	Max
1	39.88	2.75	0.97	37.38	38.56	38.81	40.37	46.17
2	23.56	3.83	1.35	18.19	20.9	22.85	26.74	29.31
3	14.62	2.35	0.83	11.31	13.14	14.67	15.61	18.8
4	4.66	1.98	0.70	1.8	3.3	4.2	6.6	7.28

X-arithmetic mean; Sd- standard deviation; Se- standard error; Q_1 – Percentile 25; Q_3 – Percentile 95. Max – Maximum; Min – Minimum

DISCUSSION

Pharmaceuticals and personal care products have been detected in natural waters throughout the world and are widely recognized as emerging environmental contaminants (37-39). These products find their way into the environment through application, subsequent wastewater introduction, and incomplete removal. Concern regarding their presence in the environment stems not from concentration; most of these compounds are present at low levels, but from chronic exposure to low doses and unknown toxicological impacts of unidentified derivatives.

The presence of drugs in WWTP influent is expected, since these compounds are not completely absorbed by the human body and thus are eliminated through excretion. However in this study for this xenobiotic high concentration in raw sewage, which can be explained by the indiscriminate use by this population, were registered. Even though ibuprofen is one of the most studied pharmaceutical in the aquatic environment, there is still a lack of information about its fate and the generation of different transformation products along WWTPs. Ibuprofen biotransformation products can be generated by human metabolism or by microorganisms present in WWTPs and in natural waters, soils, and sediments, which increase the probability to find them in environment.

In principle, biological techniques can be more robust and cost-effective for the removal of micropollutants, but many micropollutants are not sufficiently removed in the currently operated high organic loaded biological water treatment systems that focus on chemical oxygen demand and nutrient removal (24). In the literature, various removal rates are described for the biological removal of ibuprofen; for example, ibuprofen showed a removal up to 80 % (40). In general, ibuprofen reported removal rates are among the highest ones of all pharmaceuticals, as ibuprofen is known for its easy biodegradability, and removal rates of over 95% are often mentioned in lab-scale and wastewater treatment plants (39). Interestingly, in many cases pharmaceutical loads increased during the wastewater treatment, resulting in a removal efficiency above 100%, due to fluctuating sorption and desorption of the pharmaceuticals to organic matter. Lately, also constructed wetlands were found to effectively remove pharmaceuticals, with ibuprofen removal following predominantly microbial aerobic degradation (41).

The observed concentrations in the effluent were also high, which implies a reduced efficiency on WWTPs in removing it and how current systems of sewage treatment can not totally eliminate this pollutant. Some improvements or modifications should be studied for a complete removal of this compound in order to mitigate risks to public health (27). The continuous increase in the presence of this drug substance in the drinking water supply is one of the world's problems compromising the quality of water intended for human consumption and the inherent losses on aquatic environments impacted by this compound.

Due to this continuous and increasing consumption and their incomplete elimination in WWTPs, pharmaceuticals in general can be detected in rivers, lakes, and coastal waters (42,43). The removal efficiency of WWTPs varies depending on the pharmaceutical, and the treatment applied (44). In general, the WWTP systems are characterised by a high degree of dilution. Dilution is one of the reasons why pharmaceutical compounds are not sufficiently removed. When discharged to surface water they may form a threat to aquatic life and in the worst case may re-enter the water cycle. Source control, i.e. sanitation approaches based on separation at source are based on separation and separation of wastewater streams of different origin. Specific treatments, targeting different flows, may enable elimination of pharmaceuticals and minimisation of the emission of human pharmaceuticals to the environment. However, there are no regulations dealing with the actual levels of pharmaceuticals in various environmental compartments, e.g. minimum removal rates in WWTPs or maximum drug concentration in surface water. In the European Union there are only a scarce guidelines recommending more environmental risk assessment when predicted environmental pharmaceutical concentrations are equal to or higher than 10 ng l (45).

In recent years, a number of new technologies have been developed in order to guard against contamination of aquatic environments by xenobiotic compounds. Although this study holds up in a timely reviewed for the presence and concentration of diclofenac in various stages of sewage treatment, it serves as a guide for future studies to consider a more detailed temporal analysis of WWTP, the compounds and the physical, chemical and biological parameters that act to sewage disposal the drug in the effluent.

Although various single-concentration measurements of pharmaceuticals are available in the literature, detailed information on the variation over time of the concentration and the load in wastewater effluents and rivers and on the fate of these compounds in the aquatic environment are lacking. Tixier et al. (42) measured the concentrations of six pharmaceuticals in the effluents of three WWTPs (Switzerland) over a time period of three months. In WWTP effluents, the concentrations reached 1.3 µg/L for ibuprofen. Costi et al. (12) detected ibuprofen in wastewater from three WWTPs in the south of Spain. The concentration of ibuprofen ranged between 2.0 and 7.4 µg/L in influents and 0.4 and 1.4 µg/L in effluents, respectively. Determination of selected pharmaceuticals with emphasis on ibuprofen and its metabolites were determined in different sewage samples (sewage treatment plants, hospital effluents) from Tromsø/Norway. Ibuprofen and its major metabolites hydroxy- and carboxy-ibuprofen were present in all sewage samples. Concentrations were in the range of 0.1–20 µg/L for ibuprofen+metabolites) (34). All these findings are important data for a risk assessment of these compounds in surface waters.

CONCLUSION

This study demonstrates the need for sensitive and reliable analytical methods for investigating the occurrence and fate of pharmaceuticals in wastewater treatment systems. The ibuprofen levels were relatively high in the effluents, and thus, the risk for surface water contamination was important. This requires a good and extended knowledge about sources, occurrence, fate, toxicity etc. Apart from regulating the waste disposal from the pharmaceutical industry, a deeper understanding of the fate and removal of human drugs and their degradation products in WWTPs is essential. This would help reduce or minimise the introduction of pharmaceuticals into the environment and thereby protect our water bodies. The disposal of unused medication via the toilet seems to be of minor importance but many of the pharmaceuticals applied in human medical care are not completely eliminated in the human body. Frequently they are excreted only slightly transformed or even unchanged mostly conjugated to polar molecules. These conjugates can without difficulty be cleaved during sewage treatment and will then be released into the aquatic environment mostly by effluents from WWTPs. To address the problem of unwanted occurrence of pharmaceuticals in the environment, a more integrated approach is needed to evaluate the real risks of pharmaceuticals and to regulate them.

REFERENCES

[1] Ellis, E.C., Kaplan, J.O., Fuller, D.Q, Vavrus, S., Goldewijk, K.K., and Verburgf, P.H. 2013. Used planet: A global history. Proc Natl Acad Sci U S A. 110(20), 7978-7985.

[2] Aga, D.S. 2008. Fate of pharmaceuticals in the environment and in water treatment systems. CRC Press. Boca Raton.

[3] Al Aukidy, M., Verlicchi, P., Jelic, A., Petrovic, M., and Barcelò D.. 2012. Monitoring release of pharmaceutical compounds: occurrence and environmental risk assessment of two WWTP effluents and their receiving rivers in the Po Valley. Italy. Sci. Total Environ. 438, 15-25.

[4] Fent, K., Weston, A.A., and Caminada, D. 2006. Ecotoxicology of human pharmaceuticals. Aquat. Toxicol. 76, 122-159.

[5] Neto, M.L.F., and Ferreira, A.P., 2007. Perspectivas da sustentabilidade ambiental diante da contaminação química da água: desafios normativos. Interfacehs 2(4), 1-15.

[6] Baumgarten, S., Schroder, H.F., Charwath, C., Lange, M., Beier, S., and Pinnekamp, J. 2007. Evaluation of advanced treatment technologies for the elimination of pharmaceutical compounds. Water Sci. Technol. 56(5), 1-8.

[7] Bell, K.Y., Wells, M.J.M., Traexler, K.A., Pellegrin, M.L., Morse, A., and Bandy, J. 2011. Emerging Pollutants. Water Environ. Res. 83(10), 1906-1984.

[8] Bendz, D., Paxeus, N.A., Ginn, T.R., and Loge, F.J. 2005. Occurrence and fate of pharmaceutically active compounds in the environment. Case study: Hoje River in Sweden. J. Hazard Mater. 122(3), 195-204.

[9] Kimura, K., Hara, H., and Watanabe, Y. 2007. Elimination of selected acidic pharmaceuticals from municipal wastewater by an activated sludge system and membrane bioreactors. Environ. Sci. Technol. 41(10), 3708-3714.

[10] Yu, Y., Wu, L., and Chang, A.C. 2013. Seasonal variation of endocrine disrupting compounds, pharmaceuticals and personal care products in wastewater treatment plants. Sci Total Environ. 442, 310-316.

[11] Heberer, T. 2002. Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data. Toxicol. Letters 131(1-2), 5-17.

[12] Costi, E.M., Goryacheva, I., Sicilia, M.D., Rubio, S., and Pérez-Bendito, D. 2008. Supramolecular solid-phase extraction of ibuprofen and naproxen from sewage based on the formation of mixed supramolecular aggregates prior to their liquid chromatographic/photometric determination. J Chromatogr A. 1210(1), 1-7.

[13] Félix-Cañedo, T.E., Durán-Álvarez, J.C., and Jiménez-Cisneros, B. 2013. The occurrence and distribution of a group of organic micropollutants in Mexico City's water sources. Sci. Total Environ. 454-455, 109-118.

[14] Sebok, A., Vasanits-Zsigrai, A., Palkó, G., Záray, G., and Molnár-Perl, I. 2008. Identification and quantification of ibuprofen, naproxen, ketoprofen and diclofenac present in wastewaters, as their trimethylsilyl derivatives, by gas chromatography mass spectrometry. Talanta 76(3), 642-650.

[15] Hashim, N.H., and Khan, S.J. 2011. Enantioselective analysis of ibuprofen, ketoprofen and naproxen in wastewater and environmental water samples. J Chromatogr A. 1218(29), 4746-4754.

[16] Ferrando-Climent, L., Collado, N., Buttiglieri, G., Gros, M., Rodriguez-Roda, I., Rodriguez-Mozaz, S., and Barceló, D. 2012. Comprehensive study of ibuprofen and its metabolites in activated sludge batch experiments and aquatic environment. Sci Total Environ. 438, 404-413.

[17] Sagristà, E., Larsson, E., Ezoddin, M., Hidalgo, M., Salvadó, V., and Jönsson, J.A. 2010. Determination of non-steroidal anti-inflammatory drugs in sewage sludge by direct hollow fiber supported liquid membrane extraction and liquid chromatography-mass spectrometry. J Chromatogr A. 1217(40), 6153-6158.

[18] Khalaf, S., Al-Rimawi, F., Khamis, M., Zimmerman, D., Shuali, U., Nir, S., Scrano, L., Bufo, S.A., and Karaman, R. 2013. Efficiency of advanced wastewater treatment plant system and laboratory-scale micelle-clay filtration for the removal of ibuprofen residues. J Environ Sci Health B. 48(9):814-821.

[19] Buser, H., Poiger, T., and Muller, M.D. 1999. Occurrence and environmental behavior of the chial pharmaceutical drug ibuprofen in surface waters and in wastewater. Environ. Sci. Technol. 33, 2529-2535.

[20] Lischman, L., Smyth, S.A., Sarafin, K., Kleywegt, S., Toito, J., Peart, T., et al. 2006. Occurrence and reductions of pharmaceuticals and personnel care products and estrogens by municipal wastewater treatment plants in Ontario, Canada. Sci Total Environ. 367, 544-558.

[21] Han, S., Choi, K., Kim, J., Ji, K., Kim, S., Ahn, B., Yun, J., Choi, K., Khim, J.S., Zhang, X., and Giesy, J.P. 2010. Endocrine disruption and consequences of chronic exposure to ibuprofen in Japanese medaka (*Oryzias latipes*) and freshwater cladocerans *Daphnia magna* and *Moina macrocopa*. Aquatic Toxicology 98, 256-264.

[22] Smook, T., Zho, H., and Zytner, R.G. 2008. Removal of ibuprofen from wastewater - comparing biodegradation in conventional, membrane bioreactor and biological nutrient systems. Water Science & Technol. 57, 1-8.

[23] Hutt, A.J., and Caldwell, J. 1983. The metabolic chiral inversion of 2-arylpropionic acids- a novel route with pharmacological consequences. J. Pharm. Pharmacol. 35, 693-704.

[24] Metcalf and Eddy, Inc. 2003. Wastewater Engineering, Treatment and Reuse, McGraw Hill, New York, NY, USA.

[25] American Public Health Association. 2005. Standard Methods for the Examination of Water and Wastewater. 21st Edt. American Water Works Association. Water Environment Federation. Washington DC.

[26] Yasui, H., and Shibata, M. 1994. An innovative approach to reduce excess sludge production in the activated sludge process. Water Sci. Technol. 30(9), 11-20.

[27] Ferreira, A.P., Cunha, C.L.N., and Roque, O.C.C. 2008. Avaliação da microfauna no efluente final para monitoramento da qualidade ambiental em estações de tratamento de esgotos do tipo lodos ativados. Gaia scientia 2, 51-59.

[28] Moura, A., Tacão, M., Henriques, I., Dias, J., Ferreira, P., and Correia, A. 2009. Characterization of bacterial diversity in two aerated lagoons of a wastewater treatment plant using PCR–DGGE analysis. Microbiol. Res. 164(5), 560-569.

[29] Beruetta, L., Gallo, B., and Vicente, F. 1995. A review of Solid Phase Extraction: Basic principles and new developments. Chromatographia 40, 474-483.

[30] Ternes, T.A. 1998. Occurrence of drugs in German sewage treatment plants and rivers. Water Res. 32(11), 3245–3260.

[31] Soulet, B., Tauxe, A., and Tarradellas, J. 2002. Analysis of acidic drugs in Swiss wastewaters. Int. J. Environ. Anal. Chem. 82, 659-667.

[32] Subedi, B., Du, B., Chambliss, C.K., Koschorreck, J., Rüdel, H., Markus Quack, M. et al. 2012. Occurrence of pharmaceuticals and personal care products in German fish tissue: A national study. Environ. Sci. Technol. 46(16), 9047-9054.

[33] Koutsouba, V., Heberer, T., Fuhrmann, B., Schmidtbaumler, K., Tsipi, D., and Hiskia, A. 2003. Determination of polar pharmaceuticals in sewage water of Greece by gas chromatography-mass spectrometry. Chemosphere 51(2), 69-75.

[34] Weigel, S., Berger, U., Jensen, E., Kallenborn, R., Thoresen, H., and Hühnerfuss, H. 2004. Determination of selected pharmaceuticals and caffeine in sewage and seawater from Tromsö/Norway with emphasis on ibuprofen and its metabolites. Chemosphere 56, 583-592.

[35] Zorita, S., Mårtensson, L., and Mathiasson, L. 2009. Occurrence and removal of pharmaceuticals in a municipal sewage treatment system in the south of Sweden. Sci. Total Environ. 407, 2760-2770.

[36] Klavarioti, M., Mantzavinos, D., and Kassinos, D. 2009. Removal of residual pharmaceuticals from aqueous systems by advanced oxidation processes. Environ. Int. 35(2), 402-417.

[37] Daughton, C.G., Ternes, T.A. 1999. Pharmaceutical and personal care products in the environment: Agents of subtle change? Environ. Health Persp.107, 907-938.

[38] Vieno, N.M., Tuhkanen, T., and Kronberg, L. 2005. Seasonal variation in the occurrence of pharmaceuticals in effluents from a sewage treatment plant and in the recipient water. Environ. Sci. Technol. 39(21), 8220-8226.

[39] Monteiro, S., and Boxall, A.A. 2010. Occurrence and fate of human pharmaceuticals in the environment. In reviews of environmental contamination and toxicology. Whitacre D.M. Ed., 202, 53–154, Springer, New York, NY, USA.

[40] Radjenović, J., Petrović, M., and Barceló, D. 2009. Fate and distribution of pharmaceuticals in wastewater and sewage sludge of the conventional activated sludge (CAS) and advanced membrane bioreactor (MBR) treatment. Water Res. 43(3), 831–841.

[41] Hijosa-Valsero, M., Matamoros, V., Martín-Villacorta, J., Bécares, E., and Bayona, J.M. 2010. Assessment of full-scale natural systems for the removal of PPCPs from wastewater in small communities. Water Res. 44(5), 1429–1439.

[42] Tixier, C., Singer, H.P., Oellers, S., and Müller, S.R., 2003. Occurrence and Fate of Carbamazepine, Clofibric Acid, Diclofenac, Ibuprofen, Ketoprofen, and Naproxen in Surface Waters. Environ. Sci. Technol. 37(6), 1061–1068.

[43] Daneshvar, A., Svanfelt, J., Kronberg, L., Prévost, M., and Weyhenmeyer, G.A. 2010. Seasonal variations in the occurrence and fate of basic and neutral pharmaceuticals in a Swedish river-lake system. Chemosphere 80(3), 301-309.

[44] Ying, G.G., Kookana, R.S., and Kolpin, D.W. 2009. Occurrence and removal of pharmaceutically active compounds in sewage treatment plants with different technologies. J. Environ. Monitoring 11, 1498-1505.

[45] European Medicines Agency. 2008. Guideline on the environmental risk assessment of medicinal products for human use. Doc. Ref. EMEA/VHMP/DEP/4447/00. EMEA. London.

Author' biography with Photo

Corresponding Author: Aldo Pacheco Ferreira, Researcher.

Aldo Pacheco Ferreira was born and raised in Rio de Janeiro, Brazil. He graduated from the University Gama Filho, with a bachelor degree in Biology. He earned a doctorate in Biomedical Engineering. He is a researcher at Oswaldo Cruz Foundation, Sergio Arouca National School of Public Health, Center for the Study of Worker's Health and Human Ecology, Rio de Janeiro, Brazil. He is author of 79 papers in science citation index journals.