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Autor de correspondencia:

Londoño Cañas, Y. A.
PhD
Correo electrónico:
yudy.londono@udea.edu.co

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Challenges of Water Treatment Systems to Reduce Exposure Scenarios and Involuntary Ingestion of Drugs Through Drinking Water

Yudy Andrea Londoño Cañas[1]
Nancy Johana Pino Rodriguez[1]
Gustavo Antonio Peñuela Mesa[1]

1. Universidad de Antioquia, Colombia

Abstract

This critical review is focused on the discussion of the presence of pharmaceuticals and personal care products (PPCPs) in raw and drinking water and the low efficiency of drinking water treatment plants on the removal of these micropollutants. The production of high-quality and safe drinking water is an important issue that represents one of the most critical challenges in the last years. The presence of Micropollutants, as PPPCs, and involuntary intake through drinking water entail significant health risks for the population. The high consumption of drugs by the population for the treatment of diseases and infections has exacerbated environmental and bacterial resistance problems in different contexts. These types of problems do not occur at a local level but rather at a global level. An example of that is the pandemic of COVID-19, which has had a large impact in the world, increasing the consumption of a drug group used to face the coronavirus disease. In this way, the probability to find these drugs in raw and drinking water is increased because of the risk of the virus mutation due to the development of resistant strains through continuous exposure to drugs.

The drinking water treatment system could be another barrier for controlling the spread and involuntary intake of drugs. However, the limited studies in this field suggest that conventional drinking water systems have a low efficiency to remove them. Therefore, it is necessary to increase the knowledge about the presence of these drugs in water sources for human consumption and the possibilities of drinking water treatment systems to avoid the involuntary ingestion of these drugs through drinking water.

Keywords: Pharmaceutical and personal care products; Drinking Water Treatment Plants; Human health.

Desafíos de los Sistemas de Tratamiento de Agua para Reducir Escenarios de Exposición e Ingesta Involuntaria de Fármacos a Través del Agua Potable

Resumen

Esta revisión crítica se centra en la discusión de la presencia de productos farmacéuticos y de cuidado personal (PPCP) en el agua cruda y potable y la baja eficiencia de las plantas de tratamiento de agua potable en la eliminación de estos microcontaminantes. La producción de agua potable segura y de alta calidad es un tema importante que representa uno de los desafíos más críticos de los últimos años. La presencia de Microcontaminantes, como PPPC, y su ingesta involuntaria a través del agua potable suponen importantes riesgos para la salud de la población. El elevado consumo de medicamentos por parte de la población para el tratamiento de enfermedades e infecciones ha exacerbado problemas ambientales y de resistencia bacteriana en diferentes contextos. Este tipo de problemas no ocurren a nivel local sino a nivel global. Un ejemplo de ello es la pandemia de COVID-19, que ha tenido un gran impacto en el mundo, aumentando el consumo de un grupo de medicamentos utilizados para enfrentar la enfermedad del coronavirus. De esta forma, se aumenta la probabilidad de encontrar estos fármacos en agua cruda y potable y, por tanto, también se incrementa el riesgo de mutación del virus y desarrollo de cepas resistentes a través de la exposición continua a los fármacos.

El sistema de tratamiento de agua potable podría ser una barrera importante para controlar la propagación y la ingesta involuntaria de drogas. Sin embargo, los limitados estudios en este campo sugieren que los sistemas convencionales de agua potable tienen una baja eficiencia para eliminarlos. Por lo tanto, es necesario incrementar el conocimiento sobre la presencia de estas drogas en fuentes de agua para consumo humano y las posibilidades de sistemas de tratamiento de agua potable para evitar la ingesta involuntaria de estas drogas a través del agua potable.

Palabras clave: Productos farmacéuticos y de cuidado personal; sistemas de tratamiento de agua potable; Salud humana.

1. Introduction

Pharmaceutical products are a kind of emergent pollutants relatively little studied, whose presence in the environment and freshwaters systems is not necessarily new, but the concern for the possible consequences and effects on human health that these may entail (Li et al., 2021). In Latin America, the pollution scenarios for this type of substance may be more complex than in other developed countries, due to the limited or no treatment of wastewater. Even the wastewater treatment facilities of the pharmaceutical and hospital industries are very limited, therefore, the co-treatment of these effluents with domestic wastewater has been adopted as a common practice or, in some cases, they are discharged directly to rivers without any treatment (Santos et al., 2020).

On the other hand, the insufficiency and low coverage of health services growth drugs self-medication, especially in developing countries, increasing their consumption and thus favoring the presence of these compounds in waste effluents. These problems are exacerbated in the current context presented by the covid-19 pandemic caused by SARS-CoV-2, a zoonotic pathogen that emerged in 2019, and the use of a group of specific drugs, such as remdesivir, hydroxychloroquine, chloroquine, ivermectin, azithromycin, and acetaminophen, which are used for the treatment of patients with symptoms or critical condition due to virus infection (Chen et al., 2021). Through this pandemic time, even some patients with ordinary influenza are also taking the above-mentioned or similar drugs because of panic to get sick by covid. Furthermore, these drugs are still being consumed.

Excessive consumption of these drugs by the population sharply increase the concentration levels of these pollutants in wastewater, because these compounds are not fully assimilated by the body, with the risk of accumulating in natural waters and, as a consequence, in drinking water if these are not properly treated (Sousa, Ribeiro, Barbosa, Pereira, & Silva, 2018; Yu, Wang, Yao, & Zhou, 2024).

Recent publications have highlighted a wide range of pharmaceutical products present in surface waters, as well as in drinking water, around the world (Pulicharla, Proulx, Behmel, Sérodes, & Rodriguez, 2021; Yu et al., 2024). Wastewater treatments are a crucial factor in reducing drug releases to the environment. However, these systems are mainly designed for the removal of conventional pollutants (BOD, nitrogen, and phosphorus). On the other hand, Pharmaceutical compounds, tend to have a very stable structure, low volatility, different hydrophobicities between the different compounds, complex structures, and are present in extremely low concentrations, therefore, their elimination is usually a challenge (Adomat & Grischek, 2024; Santos et al., 2020).

Drinking water treatment systems are important to prevent health risks associated with ingesting drugs in water. However, the literature is still limited in this field, and some current research suggesting that the conventional drinking treatment processes are not fully efficient in removing of micropollutants (De Boer et al., 2019; Pulicharla et al., 2021; Santos et al., 2020; Sohn et al., 2024; Sousa et al., 2018). This scenario represents a huge risk for the population which requires special attention because many pharmaceutical products can be inadvertently ingested through drinking water, increasing the health public issues for the extended exposition to these drugs. Hence, it is urgent to evaluate the pollution levels and risks of the pharmaceuticals in the freshwater systems.

On the other hand, it is important to focus the research to understand the dynamics of these micropollutants through each process that conforms to the drinking water treatment system, meanly the conventional treatment processes such as coagulation, flocculation, filtration and chlorination, which must be evaluated to identify the micropollutants removal efficiencies. It is for that, the purpose of this review is to analyze the incidence of pharmaceutical products in natural waters, especially drugs used for the treatment of patients with symptoms caused by covid 19, and the role of drinking water treatment systems as a barrier to prevent prolonged exposure of the population to these drugs due to their involuntary intake through drinking water. This review seeks not only to alert about a panorama of urgent attention which must be approached from the research but also aims to guide researchers in this field of knowledge to assess new approaches that need to be implemented in the drinking water treatment system according to the current water quality dynamics.

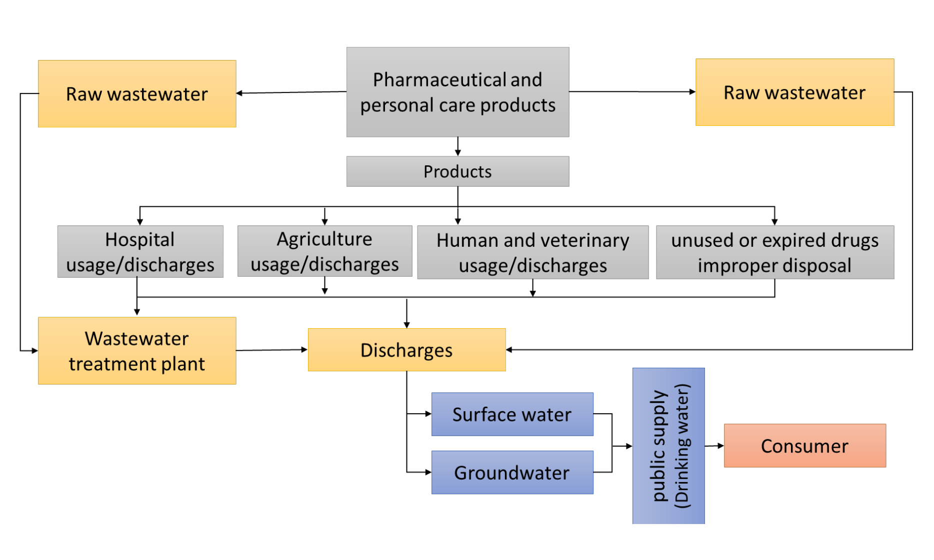
2. Sources and Pathways of PPCPs in the environment

The term “emerging pollutants” refers mainly to organic pollutants from anthropogenic activities, which have been detected in different bodies of water (Radović, Grujić, Petković, Dimkić, & Laušević, 2015; Stuart, Lapworth, Crane, & Hart, 2012). Emerging pollutants are compounds of a chemical nature and diverse origin, natural or synthetic. These products are used regularly by people, without perceiving the possible effects or consequences that they may have on the environment. Emerging contaminants include, among other chemicals, rugs, pesticides, surfactants, plasticizers, industrial additives, and a special group denominated pharmaceutical and personal care products- PPCPs. The PPCPs group includes different types of drugs for human or animal used and the personal care products include such as fragrance ingredients, sunscreen UV protectors, preservatives from multiple sources, general classes of disinfectants, mosquitoes, and other insect repellents, and soaps and shampoos (Krishnan et al., 2021).

A huge variety of PPCPs are being produced and consumed worldwide, with an annual production of over one million tons (Zhao et al., 2021), which can enter the environment through more than a few pathways. These pathways have been identified as industrial effluent, hospital discharges, runoff from fields into surface waters, aquaculture facilities, and runoff into the soil through animal farming (Yang, Sik Ok, Kim, Kwon, & Tsang, 2017). Nevertheless, the discharge of wastewater, industrial and municipal, inadequately treated has been reported as the major source of contamination of aquatic systems (Chan, Chong, Law, & Hassell, 2009; Geissen et al., 2015). These discharges contain a large number of substances, including compounds of several chemical nature (such as organic micropollutants or emerging pollutants), which have been constantly used throughout history in domestic and industrial activities.

Pharmaceutical product residues or their metabolites are excreted in urine and feces and released into sewage systems reaching Wastewater Treatment Plants and/or water sources (He et al., 2015). On the other hand, unused or expired drugs can end up in the environment due to improper disposal in toilet or kitchen drains (Aydin & Talinli, 2013; Poynton & Vulpe, 2009). Consequently, the release of these residual effluents into the environment favors the presence of a great variety of emerging pollutants as PPCPs in different natural water currents and even in drinking water (Wilkinson, Hooda, Barker, Barton, & Swinden, 2017). Figure 1 is a schematic representation of the sources and Pathways of PPCPs in the environment.

Figure 1. *Schematic representation of the sources and Pathways of PPCPs in the environment (Krishnan et al., 2021)*



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3. Occurrence of PPCPs in fresh and drinking water.

Thus, the occurrence of PPCPs in aquatic environments, especially surface water, groundwater, and drinking water has been reported in the last few years (Yang et al., 2017). The identification and quantification of these emerging micropollutants, into these environmental matrices, have been possible thanks to the development of methodologies and sensitive analytical equipment to detect and quantify them in the last 20 years (Ben, Qiang, Pan, & Chen, 2009; Yamamoto et al., 2011). Currently, more than 100,000 substances have already been classified as potentially dangerous by different international organizations, including the European Union and the United States Environmental Protection Agency (EPA) (Geissen et al., 2015).

In recent years, pharmaceutical products and estrogens have taken on special relevance, since their presence in water bodies (Sousa et al., 2018; Stuart et al., 2012; Ying, Zhao, Zhou, & Liu, 2013), and their persistence in Drinking Water Treatment Plants (Sanganyado & Gwenzi, 2019; Stackelberg et al., 2004) have been recognized as a concern. This fact requires special attention that potable water intake is one of the direct exposure pathways for the human to PPCPs concentrations (Jiang, Qu, Zhong, et al., 2019). This is the reason the spread PPCPs into the aquatic environments in the world has been evaluated through rigorous studies. The main results reported of these organic micro-pollutants presence in surface water (rivers and lakes) groundwater and drinking water are summarized in Table 1. It can see 23 PPCPs which included some of the most representative types of these micropollutants such as analgesics, stimulants, antibiotics, anti-inflammatory, anticonvulsant, mosquitoes, and insect repellants, and others.

The results reported for the different studies show a common group of compounds that are frequently detected in samples of stream water and raw-water, and unfortunately, the concentrations that they reach in the natural water analyzed are distressing. Drugs with highest concentrations level identified are Ibuprofen (5.9 – 17600 ng/L), Diclofenac (1250 – 7761ng/L), Naproxen (6.64

– 59300ng/L), Trimethoprim (5.51 –13600ng/L), Erythromycin (2806 ng/L), Clarithromycin (0.5– 2403ng/L) and Sulfamethoxazole (0.2– 1820 ng/L). Two types of drugs commonly used to treat covid -19 have been detected in raw water to important concentrations. They are Acetaminophen (15.2– 114.3ng/L) and Azithromycin (21–16633ng/L), however, for the rest of the drugs, there is still no data available on their presence in the water.

These drugs are highly used and even many of them are on the list of over-the-counter drugs. Therefore, it is easy to understand that high population consumption of these pharmaceuticals' products could increase their concentrations levels in the natural water. However, the chemical nature and physicochemical properties of each compound are determining factors of the behavior of these micropollutants into de aquatic environment.

***Table 1.** Drug concentrations were reported in natural waters (groundwater, surface water, river water, or lake water) and drinking water.*

PPCP type	Representative compounds	Raw water (ng/L)	Treated water (ng/L)	Location	Reference
Analgesics	Acetaminophen	15.2	_	Taihu región, China	(Lin, Yu, & Chen, 2016)
		17.1	_	Hamilton Harbor, Canada	(Kim & Homan, 2020)
		39.4	18.3	Quebec; water source: Lake St-Charles, Canada	(Pulicharla et al., 2021)
		95.6	22.3	Saint-Foy; water source: St. Lawrence River, Canada	(Pulicharla et al., 2021)
		31.4	23.4	Beauport; water source: Montmorency River, Canada	(Pulicharla et al., 2021)
		114.3	21.1	Levis; water source: St. Lawrence River, Canada	(Pulicharla et al., 2021)
		36.8	24.1	Charny; water soxurce: Chaudière River, Canada	(Pulicharla et al., 2021)
	Antipyrine	3.8	_	Taihu región, China	(Lin et al., 2016)
Stimulants	Caffeine	9.6	1.0	Taihu región, China	
		20.3		Hamilton Harbor, Canada	(Kim & Homan, 2020)
		39.4	13.4	Quebec; water source: Lake St-Charles	(Pulicharla et al., 2021)
		136-916	_	Yellow River German	(Yu et al., 2024)
		96.2	35.9	Saint-Foy; water source: St. Lawrence River	(Pulicharla et al., 2021)
		36.3	14.1	Beauport; water source: Montmorency River	(Pulicharla et al., 2021)
		99.4	5.4	Levis; water source: St. Lawrence River	(Pulicharla et al., 2021)
		46.3	10.9	Charny; water source: Chaudière River	(Pulicharla et al., 2021)
		115	<LOD	Elbe river water, water treatment in Dresden, Germany	(Adomat & Grischek, 2024)
Antibiotics	Erythromycin	2806	_	Surface water in Spain	(Sousa et al., 2018)
	Clarithromycin	2403	_	Surface water in Spain	(Sousa et al., 2018)
	Clarithromycin	11	<LOD	Elbe river water, water treatment in Dresden, Germany	(Adomat & Grischek, 2024)
	Clarithromycin	0.5	_	Taihu región, China	(Lin et al., 2016)
	Lincomycin	1.5	_	Taihu región, China	(Lin et al., 2016)
	Roxithromycin	3.5	_	Taihu región, China	(Lin et al., 2016)
	Sulfamethoxazole	23	1.8	Taihu región, China	(Lin et al., 2016)
		1820	_	Surface water in Taiwan	(Sousa et al., 2018)s
		0.2–1500	_	in Llobregat River and Sant Joan Despí (Spain)	(Sousa et al., 2018)
		1.4	_	Hamilton Harbor, Canada	(Kim & Homan, 2020)
		1.9	1.5	Quebec; water source: Lake St-Charles	(Pulicharla et al., 2021)
		3.3	1.9	Saint-Foy; water source: St. Lawrence River	(Pulicharla et al., 2021)
		2.1	1.7	Beauport; water source: Montmorency River	(Pulicharla et al., 2021)
		4.8	1.8	Levis; water source: St. Lawrence River	(Pulicharla et al., 2021)
		2.8	1.7	Charny; water source: Chaudière River	(Pulicharla et al., 2021)
	Azithromycin	21-68	_	Groundwater, in Serbia	(Radović et al., 2015)
		16633	_	Surface water in Spain	(Sousa et al., 2018)
	Tiamulin	2.1	_	Taihu región, China	(Lin et al., 2016)
	Trimethoprim	10.6	_	Taihu región, China	(Lin et al., 2016)
		5.51	_	Hamilton Harbor, Canada	(Kim & Homan, 2020)
		7-212	_	Surface wáter, Danube River and tributaries in Serbia	(Radović et al., 2015)
		13600	_	In Beijing	(Sousa et al., 2018)

Table 1. *Drug concentrations were reported in natural waters (groundwater, surface water, river water, or lake water) and drinking water.*

PPCP type	Representative compounds	Raw water (ng/L)	Treated water (ng/L)	Location	Reference
Anti-inflammatory	Ibuprofen	34.6	_	Hamilton Harbor, Canada	(Kim & Homan, 2020)
		126	_	Surface water (the Three Gorges Reservoir Area, China	(Al-Baldawi et al., 2021)
		186	<LOD	Elbe river water, water treatment in Dresden, Germany	(Adomat & Grischek, 2024)
		8.5	5.3	Quebec; water source: Lake St-Charles	(Pulicharla et al., 2021)
		11.4	6.5	Saint-Foy; water source: St. Lawrence River	(Pulicharla et al., 2021)
		5.9	<LOD	Beauport; water source: Montmorency River	(Pulicharla et al., 2021)
		11.1	5.4	Levis; water source: St. Lawrence River	(Pulicharla et al., 2021)
		7.2	5.2	Charny; water source: Chaudière River	(Pulicharla et al., 2021)
		17600	_	in South African surface waters	(Sousa et al., 2018)
		1830	_	in Finland, the Rakkolanjoki River	(Sousa et al., 2018)
		>1317	_	In the Lis River, Portugal	(Sousa et al., 2018)
	Diclofenac	1250	_	Iraı' Reservoir, Brazil	(Al-Baldawi et al., 2021)
		1410	_	Surface water (the Three Gorges Reservoir Area, China	
		27	<LOD	Elbe river water, water treatment in Dresden, Germany	(Adomat & Grischek, 2024)
		7761	_	Surface water in Spain	(Sousa et al., 2018)
	Indomethacin	7.6	1.2	Taihu región, China	(Lin et al., 2016)
	ketoprofen	9220	_	In South African surface waters	(Sousa et al., 2018)
	Naproxen	6.64	_	Hamilton Harbor, Canada	(Kim & Homan, 2020)
		297	_	Surface water (the Three Gorges Reservoir Area, China	(Al-Baldawi et al., 2021)
		59300	_	In South African surface waters	(Sousa et al., 2018)
		1687	_	In Finland, the Rakkolanjoki River	(Sousa et al., 2018)
Anticonvulsant	Carbamazepine	25-94	_	Surface wáter, Danube River and tributaries in Serbia	(Radović et al., 2015)
		24	<LOD	Elbe river water, water treatment in Dresden, Germany	(Adomat & Grischek, 2024)
		9-41	_	Groundwater, in Serbia	(Radović et al., 2015)
		2.2	1.8	Quebec; water source: Lake St-Charles	(Pulicharla et al., 2021)
		2.2	1.9	Saint-Foy; water source: St. Lawrence River	(Pulicharla et al., 2021)
		1.9	1.8	Beauport; water source: Montmorency River	(Pulicharla et al., 2021)
		2.9	1.9	Levis; water source: St. Lawrence River	(Pulicharla et al., 2021)
		6.5	2.2	Charny; water source: Chaudière River	(Pulicharla et al., 2021)
		0.8	_	Taihu región, China	(Lin et al., 2016)
		16.3	_	Hamilton Harbor, Canada	(Kim & Homan, 2020)
		1705	_	In Finland, the Rakkolanjoki River	(Sousa et al., 2018)
metamizole metabolites	4-FAA	37-186	_	Surface wáter, Danube River and tributaries in Serbia	(Radović et al., 2015)
		22-150	_	Groundwater, in Serbia	(Pulicharla et al., 2021)
	4-AAA	79-512	_	Surface wáter, Danube River and tributaries in Serbia	(Pulicharla et al., 2021)
		20-105	_	Groundwater, in Serbia	(Pulicharla et al., 2021)
Antipsychotic	Sulpiride	1.9	_	Taihu región, China	(Lin et al., 2016)
Mosquito and insect repellants	DEET	30	_	Taihu región, China	(Lin et al., 2016)
Treat heart rhythm	Disopyramide	3.0	_	Taihu región, China	(Lin et al., 2016)

LOD – limit of detection

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How it is showed a considerable number of monitoring studies of PPCPs reports important traces of these micropollutants in water bodies worldwide. Indisputably many of PPCPs can reach the aquatic environment and can be identified at different concentrations. However, despite these efforts, many holes remain still in our understanding of the transformation, and the fate of PPCPs in the environment due to the diversity and different physicochemical properties in different aquatic environments (Yuan, Hu, Li, & Yu, 2020) and also the diversity and different physicochemical properties of each PPCPs. Many PPCPs have been reported with low removal rates through wastewater treatment plants based on the biological process, which shows their low biodegradability and high persistence. Drugs such as Ibuprofen, Diclofenac, Trimethoprim, Erythromycin, and Sulfamethoxazole are poorly eliminated through an aerobic, anaerobic, or in both biological systems (Alvarino, Suarez, Lema, & Omil, 2018; Londoño & Peñuela, 2017). Their high persistence and consumption could be the main reasons for the accumulation of these micropollutants in the environment.

On the other hand, the presence of these drugs in drinking water is an emerging concern. Commonly used pharmaceuticals have been detected in drinking water such as ibuprofen, carbamazepine, or diclofenac (Delgado, González, & Martin, 2011). Nevertheless, Information about the presence of PPCPs in drinking water is still limited mainly because the presence and concentration of these micropollutants are not routinely monitored due to the expense necessary for complex laboratory analysis, and most of these compounds are not currently regulated (Kim & Homan, 2020).

However, although many of these compounds have not been regulated, it does not mean that there is not a risk due to their presence in water, which should be evaluated. Especially at the current, when the world begins to face a challenging scenario regarding the presence of these PPCPs in water. The hight use and consumption of drugs to control human and veterinary diseases could imply a sudden increase in the concentrations of these compounds in the aquatic environment and consequently in drinking water. Therefore, the population could be continuously exposed to different kind of drugs due to their involuntary intake through drinking water

4. Related Risk of PPCPs occurrence in the aquatic environment and drinking water.

The risk due to the presence of PPCP in the aquatic environment continues to be an open subject for evaluation and analysis. Researchers around the world continue to debate the PPCPs impacts, although they are usually present in waters at trace concentrations (ng/L to µg/L), These concentrations are enough to cause great threats to ecosystems or organisms exposed (Lin et al., 2016) only indomethacin, caffeine and sulfamethoxazole were found in effluent, albeit at concentrations less than 2 ng L À1. The results of principal component analysis suggested that three main purification processes, oxidation, coagulation combined with sedimentation and filtration combined with bio-degradation, influenced the removal performance of PPCPs. The ecotoxicological and human health risk assessment confirmed that drugs detected in effluent posed no potential toxicity and also suggested that two PPCPs (roxithromycin and sulfamethoxazole. Most of them could generate a risk of adverse effects in the different trophic levels or human health. The main concern is the long-term exposure to these compounds and their possible synergistic effects between them or with other micropollutants (García-Santiago, Franco-Uría, Omil, & Lema, 2016)

In the specific case for the drugs, despite their low concentrations, the incidental exposure to them and their toxicity should be evaluated, as the undesirable therapeutic effects of these substances as well. The continuous introduction of these substances into the environment should not go unnoticed, some researchers are already beginning to warn of the risks that the uncontrolled release of drugs into the water and the environment (Kumar et al., 2020). The emerging concern is related to the risk of virus mutation and the development of resistant strains through continuous drug exposure (To see Figure 2).

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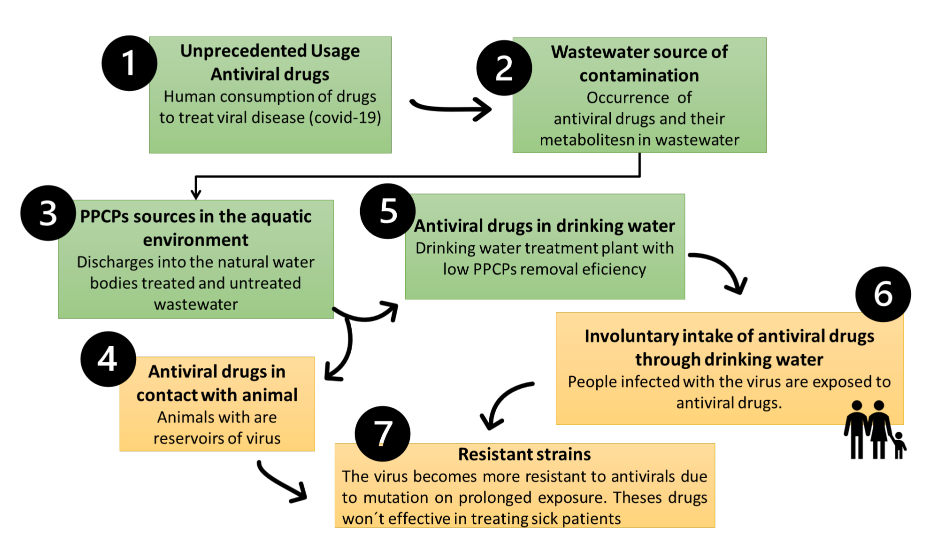
Figure 2. *Sources of virus resistance to antiviral drugs through Environmental Waters, and possibly drinking waters.*



Involuntary intake of antiviral drugs through drinking water is an important issue. Through the pandemic, many people can get sick from the virus, and they could not have symptoms and consequently, they are not on medication. But the virus, in another way, could be in prolonged exposure to low concentrations of these drugs thanks to their presence in the drinking water. This fact could be one of the ways of how the virus becomes more resistant to antivirals, it could be one cause that benefits its mutation. Under this context and due to the problems triggered by the pandemic problems, the drinking water treatment plants could play a key role how as a barrier to preventing public health issues related to exposure of the population to these drugs. However, there is limited information about the efficiency of this process in the removal of PPCPs.

5. Approaches and challenges of water treatment systems for human consumption

The efforts to control and prevent the widespread occurrence, persistence and adverse effects posed by PPCPs in the aquatic environment begin to be addressed by the public directives of international organizations. Although to date there is no specific regulation for the presence of PPCPs in water, the Europe Union set a precedent to establish the Priority Substances list and Emerging Pollutants, through Directive 2013/39 / EU and the Watch List of substances published by Implementing Decision 2015/495 / EU (Sousa et al., 2018)demands a better knowledge of the chemical status of Earth's surface water. Water quality monitoring studies have been performed targeting different substances and/or classes of substances, in different regions of the world, using different types of sampling strategies and campaigns. This review article aims to gather the available dispersed information regarding the occurrence of priority substances (PSs. This last watch list was updated by Implementing Decision 2018/240 / EU. In both Watch, lists include 3 PPCPs types with 9 compounds which comprised the synthetic estrogen: 17-alpha-ethinyl estradiol (EE2), 17-beta-estradiol (E2) estrone (E1), antibiotics drugs: erythromycin, clarithromycin, azithromycin, amoxicillin, and ciprofloxacin, and anti-inflammatory drug: diclofenac. The achievement of these legislative advances has been allowed expanding the study, evaluation, and monitoring of these organic micro-pollutants in the aquatic environment in the last years. The goal is to identify the risks they pose to health and finally establish adequate measures for their control and management.

Consequently, this next development of new legislation and the existence of consolidated data about the occurrence of emerging pollutants, both in wastewater and drinking water, will force to focus the efforts to optimize and develop efficient water treatment systems (Sousa et al., 2018)demands a better knowledge of the chemical status of Earth's surface water. Water quality monitoring studies have been performed targeting different substances and/or classes of substances, in different regions of the world, using different types of sampling strategies and campaigns. This review article aims to gather the available dispersed information regarding the occurrence of priority substances (PSs. Particularmente, the drinking water treatment field is facing one of the most demanding challenges in the last times. The design, construction, evaluation, and control of water treatment systems must be increasingly demanding to respond to a reality based on accelerated social and economic development that

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is associated with an alarming deterioration of natural water sources (surface and underground) (Pulicharla et al., 2021).

The PPCPS removal through the drinking water process is a current issue that is imperative to do face. There are not enough researches that allow understanding the behavior of these micropollutants through the drinking water treatment process and the few studies available suggest that conventional drinking water treatment, formed by coagulation, flocculation, sedimentation, rapid filtration, and post-chlorination, is not very efficient to remove them (De Boer et al., 2019; Pulicharla et al., 2021; Santos et al., 2020; Sousa et al., 2018)aiming to understand the factors that influence their occurrence and removal in conventional drinking water treatment plants (DWTPs and the main reason is that these treatment processes are not designed to remove emerging contaminants in water (Pai, Leong, Chen, & Wang, 2020) (To see table 2).

Table 2. *PPCPs removal efficiencies during the conventional drinking water treatment Plant steps. ––(<10%); – (10–50%); + (50–80%); ++ (>80%). N.A.: not analysed*

PPCP	Coagulation and flocculation	Sedimentation	Rapid filtration	Chlorination	CDWTP	Reference
Ibuprofen	–	–	–	–	N.A.	(Jiang, Qu, Zhong, et al., 2019)
Caffeine	N.A.	N.A.	N.A.	N.A.	–	(Jiang, Qu, Liu, et al., 2019)
Erythromycin	N.A.	N.A.	N.A.	N.A.	++	(Jiang, Qu, Liu, et al., 2019)
Roxithromycin	N.A.	N.A.	N.A.	N.A.	++	(Jiang, Qu, Liu, et al., 2019)
Naproxen	N.A.	–	+	N.A.	N.A.	(Mckie, Andrews, Andrews, & Barcelo, 2016)
Diclofenac	–	N.A.	–	N.A.	N.A.	(Mckie et al., 2016)
Carbamazepine	––	––	––	––	N.A.	(Jiang, Qu, Zhong, et al., 2019)
Caffeine	–	–	–	–	N.A.	(Jiang, Qu, Zhong, et al., 2019)
Diclofenac	–	–	–	–	N.A.	(Mckie et al., 2016)
Sulfamethoxypyri-dazine	++	++	++	++	N.A.	(Yang et al., 2017)
Trimethoprim	N.A.	N.A.	N.A.	N.A.	++	(Jiang, Qu, Liu, et al., 2019)
Triclosan	++	++	++	++	N.A.	(Yang et al., 2017)
Metoprolol	––	––	––	––	N.A.	(Yang et al., 2017)
Acetaminophen	–	N.A.	++	++	N.A.	Yang et al. 2017)
	–	–	–	–	N.A.	(Mckie et al., 2016)
	N.A.	N.A.	N.A.	N.A.	++	(Jiang, Qu, Liu, et al., 2019)
Azithromycin	N.A.	N.A.	N.A.	N.A.	N.A.	(Mckie et al., 2016)
Ketoprofen	–	N.A.	–	N.A.	N.A.	(Mckie et al., 2016)
	N.A.	N.A.	N.A.	N.A.	+	(Jiang, Qu, Liu, et al., 2019)

* CDWT: conventional drinking water treatment plant

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According to the literature review (Table 2), through the conventional system for the PPCPs removal, the coagulation, flocculation, and Sedimentation processes function inefficiently. This efficiency improves a little bit in Rapid filtration and Chlorination without being completely efficient for all the PPCPs analyzed. Compounds such as Ibuprofen, Carbamazepine, Caffeine (CF), Diclofenac, and Acetaminophen continue to lead their persistence through each of these stages. Some studies report that the mechanisms which could be involved in the PPCPs removal processes through the CDWTP are the associated adsorption to clay particles, electrostatic interactions between micropollutants and coagulants, the photodegradation process by sunlight (Pai et al., 2020), and other factors such as the weak acid hydrolysis coefficient (pKa) and the octanol-water partition coefficient (Know) (Jiang, Qu, Liu, et al., 2019). In recent research has focused on the last two factors which could be related to the greater removal efficiency of these micropollutants through the CDWTP (Pai et al., 2020). It is inferred that higher pKa is conducive to PPCPs exchange into ionic states, then they can be easily absorbed by particles and removal by flocculation or filtration and through hydro-phobic interaction, the removal of other target contaminants can be increased. (Jiang, Qu, Liu, et al., 2019)

6. Alternatives for eliminating organic micropollutants in water purification systems.

With the purpose to avoid drug inadvertent ingestion for the population, it is necessary to advance in search of new alternatives which can be coupled to the conventional drinking water treatment system. Unfortunately, the challenges in the water quality are increasing more and more, therefore, robust systems are required to remove traces of persistent compounds. A balance must be sought between ensuring water quality, which is harmless for the population, but at the same time, the system must be economically viable and sustainable over time so that the largest possible population can be covered and that it truly aimed to achieve the goal 6 of the 2030 agenda of the Sustainable Development Goals.

6.1. Advanced oxidation processes -AOPs

In the last two decades, the high number of publications obtained from Google Scholar and Scopus databases shows growing interest in AOP research because of the need to achieve the removal of organic micropollutants from water. It is estimated that, in the near future, AOPs will constitute one of the most used technological resources in the treatment of water contaminated with substances that are not treatable by conventional techniques due to their high chemical stability and therefore low biodegradability (Giwa et al., 2021).

These important advances have made it possible to consider the AOPs as an alternative that can be couple the conventional drinking water treatment system to improve its low efficiencies on the drug's removal. The AOPs processes are based on the generation of highly reactive non-selective oxidative radical species, such as hydroxyl (• OH), peroxide (• OHH), superoxide (• O_2^-) radicals, and singlet oxygen (• O) that attack and rapidly oxidize a wide spectrum of organic compounds present in water, in a non-selective way (De Boer et al., 2019). According to the specific way used to produce oxidation agents, AOPs can be classified into photolysis, photocatalytic oxidation, Fenton oxidation, Ultrasonic irradiation, electrochemical oxidation, and so on (Wang & Zhuan, 2020). Some advantages of this processes are descried in the figura 3.

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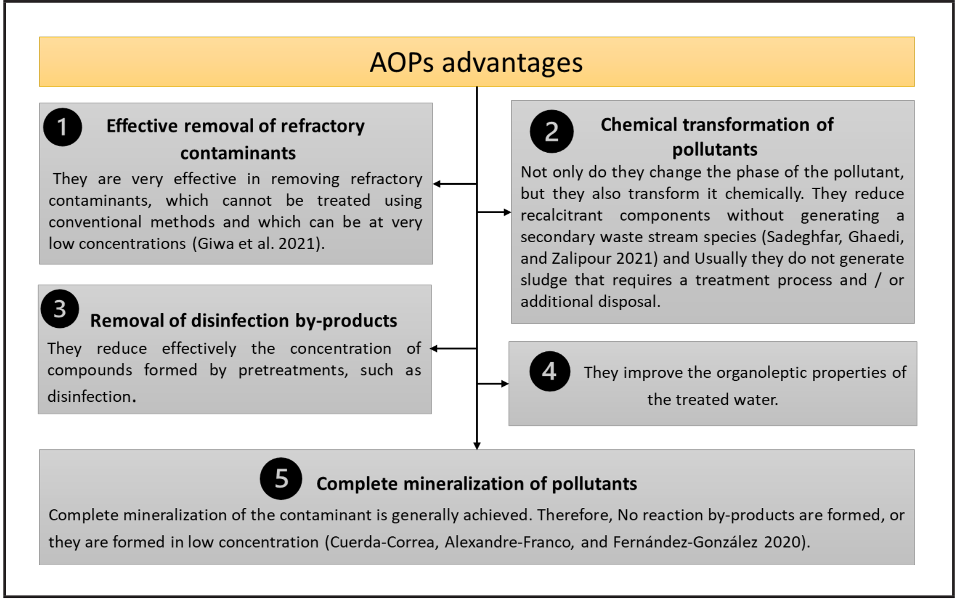
Figure 3. *Advanjtages of AOPs for water treatment (Cuerda-Correa, Alexandre-Franco, & Fernández-González, 2020; Giwa et al., 2021; Sadeghfar, Ghaedi, & Zalipour, 2021)the application of advanced oxidation processes (AOPs*



Despite the important advantages that AOPs offer, some disadvantages could be limited their use and application, these disadvantage lies in their high cost because of the use of expensive reagents (for example, H_2O_2) and energy consumption (generation of O_3) (Cuerda-Correa et al., 2020). Therefore, the main challenges of these processes would be focused on reducing the gaps between costs and also their operational complexity in such a way that they can be considered an alternative stage coupled to the conventional drinking water treatment system.

6.2. Granular activated carbon (adsorption processes)

Granular activated carbon (GAC) is a common adsorbent that has been widely used in water treatment and can be prepared from various raw materials such as sludge, coconut shells, wood char, lignin, petroleum coke, bone char, peat, sawdust, carbon black, rice hulls, peach pits, fish residues, fertilizer waste, waste rubber tire, etc (Jeirani, Niu, & Soltan, 2017)pharmaceutical and personal care products (PPCPs. The GAC has unique characteristics, for which it has gained so much interest, how it is its large surface-to-volume ratios, porosity, and its high degree of surface reactivity toward various organic compounds as well (Rao, Kumar, Dhodapkar, Pal, & Cadaval, 2021)important for complete removal of PPCPs from wastewater prior to discharge or reuse. Present study demonstrates adsorption using granular-activated carbon (GAC. Studies have reported that these characteristics can be optimized according to the activation parameters used in the physical, chemical, or electrochemical activation, such as the choice of activating agent, pyrolysis or activation temperature, impregnation ratio, and so on (Jeirani et al., 2017)pharmaceutical and personal care products (PPCPs. The optimization of the activation parameter can improve the GAC physicochemical properties and consequently the highest uptake of certain pollutants. It is for that reason, the optimization of the activation parameters of the GAC combined with its commercial availability and affordable cost has made it a good alternative for the removal PPCPs from the water (Rao et al., 2021)important for complete removal of PPCPs from wastewater prior to discharge or reuse. Present study demonstrates adsorption using granular-activated carbon (GAC

6.3. Biological drinking water treatment (BioDWT)

The biological drinking water treatment systems consist of the application of the microorganisms for biochemical oxidation and degrading the pollutants in the contaminated water. The application of these biological systems can also contribute to producing biologically stable water and prevent the growth of microorganisms in the water distribution system (Abu Hasan, Muhammad, & Ismail, 2020). The usage of biological processes for drinking water treatment dates since the '80s, however, the current application is still limited (Abu Hasan et al., 2020). Some configurations using biological processes, such as Biological activated carbon, Trickling filter, Membrane bioreactor, and others, have been reported as an alternative to be coupled to the conventional drinking water system.

Advances in the study, application, and optimization of biological processes coupled with drinking water treatment systems could make a significant contribution to the production of safe drinking water. These systems could operate with good efficiencies, not only in the removal of organic micropollutants, but also in the removal of conventional organic matter, and consequently, in the reduction of disinfection products generated after the chlorination process.

7. Conclusions

The production of high-quality and safe drinking water is one of the most critical challenges in the last years. The high deterioration of water sources carries significant health risks for the population as a consequence of the involuntary intake of contaminants in drinking water. Specifically, the presence of PPCPs in raw and drinking water and the low efficiency of drinking water treatment plants on the removal of these micropollutants have been discussed in this review paper. The main conclusion obtained is directed towards research approaches in drinking water, which need to focus on in determining the presence of micropollutants that even to low concentrations have great impacts on public health. On the other hand, it is important to expand the frontier of knowledge about the incidence of each of the physicochemical processes of water purification in the removal of these substances, and on the proposal and evaluation of alternatives for optimization of this conventional process.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to affect the work reported in this article.

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