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STATE OF THE ART ON THE OCCURRENCE AND REMOVAL OF IBUPROFEN USING MEMBRANE TECHNOLOGY

ESTADO DEL ARTE SOBRE LA OCURRENCIA Y REMOCIÓN DE IBUPROFENO UTILIZANDO TECNOLOGÍA DE MEMBRANAS

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Resumen: La presencia de Contaminantes Emergentes (CE) en el ambiente y especialmente en el agua, es debida principalmente al uso diario y creciente de productos de cuidado personal, farmacéuticos y compuestos disruptores endocrinos. Los CE, aun en concentraciones del orden de nanogramos por litro (ng/L), son capaces de generar serios daños potenciales en la salud y en los ecosistemas. El ibuprofeno es un CE del grupo farmacéutico, ampliamente utilizado y de venta libre, lo cual hace que sea de fácil acceso. Esta investigación, realiza una recopilación de algunos estudios a nivel mundial que han reportado la presencia del ibuprofeno a niveles de traza, en el agua superficial, subterránea, efluentes y afluentes de las plantas de tratamiento de agua residual e incluso en el agua potable; así como los porcentajes de remoción que se han obtenido al utilizar tratamientos avanzados, la tecnología de membranas.

Palabras clave: Ibuprofeno, membranas, nanofiltración, ocurrencia, osmosis inversa, remoción.

Abstract: The presence of emerging contaminants (ECs) in the environment and especially in water is mainly due to the daily and increasing use of personal care products, pharmaceuticals, and endocrine disrupting compounds. ECs, even in concentrations of the order of nanograms per liter (ng/L), can generate serious potential damage to health and ecosystems. Ibuprofen is a widely used and over-the-counter EC of the pharmaceutical group, which makes it easily accessible. This research makes a compilation of some studies worldwide that have reported the presence of ibuprofen at trace levels in surface water, groundwater, effluents, and effluents from wastewater treatment plants and even in drinking water, as well as the removal percentages that have been obtained by using advanced treatments such as membrane technology.

Keywords: Ibuprofen, membranes, nanofiltration, occurrence, reverse osmosis, removal.

1. INTRODUCTION

The impacts on ecology, the environment and water sources have arisen as a result of excessive population growth and anthropogenic activities; water is one of the most affected resources in terms of availability and quality losses. Among the main sources of pollution are: wastewater, agricultural and urban run-off, livestock development, industrial waste, effluent from treatment plants, accumulation of toxic sediments, uncontrollable use of pesticides, power generation, among others.

Water quality research is commonly focused on nutrients, microbial pollutants, heavy metals and priority pollutants. However, recent research reveals the presence of a multitude of organic pollutants that significantly affect water quality (Rodriguez-Narvaez et al., 2017); began to be studied in the mid-1990s to focus on chemicals that were "recently discovered" in the environment, had no regulatory standards associated with them, and however, they were at least potentially toxic to wildlife and even humans, this group of chemicals is now recognized as Emerging Pollutants (CE) (Poynton & Robinson, 2018).

Among the ECs are pharmaceuticals (PhAC), which are a set of developing ecological pollutants, which are used extensively and progressively as part of human and veterinary medication. They include compounds of environmental interest such as antibiotics, legal and illicit drugs, analgesics, steroids, beta-blockers, etc. (Fatta-Kassinos et al., 2011). It is estimated that approximately 3000 different substances are used as pharmaceuticals; however, only a few have so far been investigated in the environment (Richardson, 2008). They have been detected in natural waters (surface and groundwater), treated effluents, sediments and sludge from waste water treatment plants (PTAR) and even in water intended for human consumption (Jaffrézic et al., 2017).

Of the PhACs that have been most frequently detected in the environment, we find ibuprofen, a drug widely used as antipyretic, analgesic and anti-inflammatory (NSAID); over-the-counter, being the third most popular worldwide (Zur et al., 2011); studies have reported its presence in drinking water (Aristizabal-Ciro et al., 2017), influents and effluents of PTAR (Madera-Parra et al., 2018; Pérez-Parada et al., 2012), in untreated wastewater (Gibson et al., 2007) and in surface water (Ascar et al., 2013; Babay et al., 2014; Félix-Cañedo et al., 2013a; Suazo et al., 2017).

Currently conventional drinking water treatment plants (PTAP) are insufficient to remove traces of EC and what is worse are not regulated by water quality standards, it has been proven by the scientific community that the exposure of humans to such pollutants may be capable of altering the endocrine system, blocking or disrupting the hormonal functions of organisms, generating irregularities of the immune system, decrease in fertility, and may even increase the incidence of different types of cancer (Maroneze et al., 2014). The presence of ibuprofen in drinking water is potentially related to growth impairment in human embryonic kidney cells (Pomati et al., 2006).

Different techniques are currently being implemented for the removal of EC in water, this research makes a review on the use of membrane technology as a viable and sustainable alternative for the elimination of ibuprofen in different concentrations, which can be replicated in areas where solutions to these problems have to be implemented.

2. DATA MINING

To collect information, search sources were used in the Scopus bibliographic database, both for review and research articles, using the keywords: "Emerging Contaminants", "Pharmaceutical Products", "Endocrine Disrupting", Wastewater", "Drinkwater", "Surface Water", "Determination", "Occurrence and "Membrane Technology"; the highest concentration of articles found from the
In 2016, taking into account the most recent publications, the responses were removed and the most relevant were chosen in the EC study. Using VOSviewer software, it was possible to build and display bibliometric networks

(Fig.1) , where it can be seen that most articles make relevance to the detection method, sources and pharmaceuticals.

It is important to note that almost all the information on emerging pollutants in the EC and PhAC review documents is available only for European and North American countries (Lange et al., 2012). Consequently, it is difficult to assess differences in occurrence patterns between different geographical regions (Tran et al., 2018). The number of studies is also increasing in Asia, mainly in China, thanks to the growing awareness, there is still a notable knowledge gap in South American and African countries (Ebele et al., 2017).

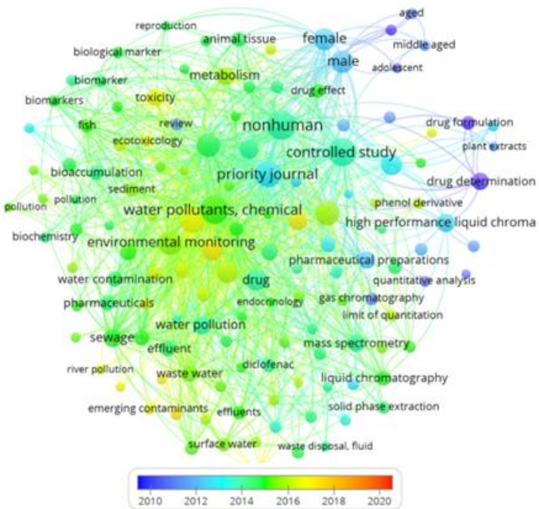

Fig. 1. Bibliometric Assessment

3. OCCURRENCE IN THE WATER

Pharmaceutical compounds PhACs are widely used due to their numerous medical, industrial, agricultural and domestic applications; in recent years their presence the environment has been of concern due to possible threats to ecosystems and human health, studies have reported their presence in different water matrices, this is due to the potential threats they can enter the environment through various routes, such as: domestic, industrial, agricultural and hospital wastewater; as well as transport through the natural hydrological cycle.

Ibuprofen is a pharmaceutical compound that is part of the PhAC that have been most frequently detected in the environment, then some cases are presented.

3.1 Drinking Water and Supply Sources

The occurrence of PhAC in drinking water is a matter of vital importance since it involves the health of humans, therefore, its presence must be evaluated and monitored from the sources of supply to its distribution, as well as: reservoirs, reservoirs, surface waters, PTAP, among others.

Several sources have reported the presence of pharmaceutical compounds PhAC, worldwide in drinking water, among these, ibuprofen is one of the most detected due to its massive use, for example, in the metropolitan area of Turin, Italy, concentrations above 3 ng/L were found, taking into account that the source of supply concentrates a large amount of pollution due to contact with sewage and hospital water (Papagiannaki et al., 2021); Canada, in 17 sampling points determined that ibuprofen is one of the most frequently detected PhAC in drinking water (Kleywegt et al., 2011); in Colombia the concentration detected is much higher than in other countries consulted, since the reservoirs that are used as a source of supply for drinking water, have contact with domestic, industrial and agricultural wastewater without any type of treatment (Aristizabal-Ciro et al., 2017). Table 1 shows some research carried out worldwide on the occurrence of ibuprofen in drinking water and environmental problem.

Table 1: Occurrence of ibuprofen in drinking water

Country	Concentration (ng/L)	Reference
Italy	3.77	(Papagiannaki et al., 2021)
China	1.28	(Wu et al., 2022)
Taiwan	55.6	(Pai et al., 2020)
France	1.3	(Vulliet et al., 2011)
Canada	12	(Kleywegt et al., 2011)
United States	10.2	(Padhye et al., 2014)
Brazil	10	(Pompei et al., 2019)
Poland	39	(Kot-Wasik et al., 2016)
Nigeria	49.6	(Waleng & Nomngongo, 2022)
Colombia	7 - 62	(Aristizabal-Ciro et al., 2017)

3.2 Waste Water Treatment System

The Waste Water Treatment Plants, PTARs are among the main sources of EC in surface waters. This is mainly associated with the low throughput of conventional technologies for the disposal of quantities at EC trace levels. However, the scenario is more critical in developing countries as PTARs are practically non-existent, and therefore their discharges are made directly on water sources and agricultural areas.

3.2.1 Afluentes y efluentes de las PTAR

Research shows that concentrations pharmaceutical compounds of PhAC entering waste water treatment plants PTAR are very high, especially of antibiotics and analgesics. Thus, in PTARs different processes are used to eliminate as many toxic substances that may occur in the tributaries before being discharged to the bodies of water, however, the vast majority

are conventional and cannot effectively eliminate the concentrations of these substances at trace levels, which is generating direct contamination in water sources. A study carried out in China investigated the occurrence in the tributaries of two PTAR, of a group of PhAC used for the treatment of various diseases, among which was the COVID-19, determining that ibuprofen was the drug that was detected with the highest concentration, as well as in the influent after its treatment (Liu et al., 2022). Likewise, another study conducted in South Africa reported that ibuprofen was the PhAC detected with the highest concentration in both the tributary and the effluent, thus establishing that after a conventional treatment the removal is insufficient, and therefore contributes to the pollution of the river Msunduzi (Matongo et al., 2015). In Krakow, Poland, the presence of eleven pharmaceutical compounds frequently used PhAC was studied, ibuprofen being one of the substances with the highest concentration in the tributary and effluent of the PTAR studied (Nosek et al., 2014). Moreover, in a study conducted in Korea, which evaluated four Waste Water Treatment Plant, PTARs using different biological treatment processes for the elimination of contaminants, the results showed that in the process the coagulation process there was an adverse effect on the elimination of ibuprofen (Son et al., 2021). In Chile, water samples were evaluated before and after treatment by a PTAR near the Metropolitan Region, determining that the concentration of ibuprofen was 10 a
100 times higher than other pharmaceutical compounds PhAC's like ketoprofen and naproxen, in addition, the research showed that the highest concentrations found in surface water were very close to the PTAR discharge site, indicating that the treatment process is insufficient to remove these pollutants effectively contaminants (Ascar et al., 2013).

Table 2 shows some of the research carried out worldwide on the occurrence of ibuprofen in the PTAR influent and effluent.

Table 2: Ibuprofen occurrence in PTAR influent and effluent

Country	Tributary (ng/L)	Tributary (ng/L)	Reference
China	178–2647	0–204	(Liu et al., 2022)
South Africa	117600	58710	(Matongo et al., 2015)
Poland	2496	<42	(Nosek et al., 2014)
Switzerland	15670-22820	0-780	(Larsson et al., 2014)
Korea	76700–174000	530–2910	(Son et al., 2021)
Spain	316 ± 9.52	81.0 ±8.0	(Afonso-Olivares et al., 2017)
India	11000-217000	170	(Praveenkumarreddy et al., 2021)
Portugal	350-37100	70-10800	(Silva et al., 2021)
Germany	32000 ± 800	400	(Sossalla et al., 2021)
Costa Rica	500 - 10000	90 - 8000	(Ramírez-Morales et al., 2020)
Chile	2850 - 47720	2800 - 40000	(Ascar et al., 2013)
Colombia	100 - 700	2100 - 100	(Arrubla et al., 2016)

3.3 Surface Water

Currently many water sources are contaminated worldwide, which represents a serious concern for human health and the environment. So, it is necessary to monitor the presence of of emerging pollutants EC, since once they enter the rivers, they are responsible for dispersing them to other bodies of water, including aquifers, estuaries and marine systems. Climate change has also contributed to the distribution of the EC into the environment, as extreme storms and floods are generated, can release pollutants through surface runoff and also through sediment resuspension in rivers which increases the CE load on the water.
(Richardson & Kimura, 2017).

Several studies around the world have reported the presence of pharmaceutical compounds PhAC in surface waters, in Buenos Aires, Argentina, several sources were studied, in areas close to a large number of industrial, municipal and domestic facilities, that discharge their wastewater into rivers and streams, determination of high concentrations of PhAC, including ibuprofen (Elorriaga et al., 2013). Also, in the Metropolitan Region of Chile, water samples were collected from different sites of the Maipo River, marked by urban settlements and agricultural activities, also determining high concentrations of ibuprofen (Suazo et al., 2017). Similarly, in the Metropolitan Area of Mexico City, the presence and distribution of a group of 17 EC in surface water sources were determined, where 11 pollutants were detected, including ibuprofen (Félix-Cañedo et al., 2013 in addition, ibuprofen was reported in Santiago de Cali Colombia on the Cauca River (Madera-Parra et al., 2018).

Table 3 shows some of the research carried out worldwide on the occurrence of ibuprofen in surface waters.

Table 3: Occurrence of ibuprofen in surface waters

Counntry	Concentration (ng/L)	Reference
Argentina	400–13000	(Elorriaga et al., 2013)
Chili	2300	(Suazo et al., 2017)
Mexico	15 - 45	(Félix-Cañedo et al., 2013)
Colombia	894	(Madera-Parra et al., 2018)
India	1834	(Gopal et al., 2021)
Norway	<20-2500	(Paruch & Paruch, 2021)
Czech Republic	1600	(Skocovska et al., 2021)
China	7.9-590	(Yao et al., 2018)
Spain	2660	(Mandaric et al., 2018)

3.4 Seawater

Sea water is also being significantly affected by the presence of emerging pollutants EC, which is largely due to the incorporation of wastewater with and without treatment, in addition to the anthropic influence on coastal areas which offer entertainment areas, fishing, tourism among others. Several authors have reported this problem, for example, in Brazil in the Bay of All Saints, the occurrence of EC was studied in both shallow and deep waters, because these receive more than 7367 m3 of wastewater badly treated per day, raising concerns about high concentrations of PhAC, including ibuprofen (Pereira et al., 2016). Thus same, a study conducted in the north coast of Portugal determined the presence of several pharmaceutical compounds PhAC, where ibuprofen and its two metabolites (carboxybuprofen and hydroxyibuprofen) recorded the highest concentrations in sea water samples from the beach of Castelo do Queijo, this is because nearby PTARs discharge their effluents at this specific point (Lolić et al., 2015). Table 4 below shows some of the research carried out on the presence on the occurrence of ibuprofen in seawater.

Table 4: Occurrence of ibuprofen in seawater

Country	Concentration (ng/L)	Reference
Brazil	326.1 - 2094	(Pereira et al., 2016)
Portugal	222	(Lolić et al., 2015)
Turkey	<15 - 2130	(Korkmaz et al., 2022)
United Kingdom	0.8 - 697	(Niemi et al., 2022)
South Africa	170	(Ngubane et al., 2019)
Spain	16	(Gros et al., 2012)
France	1500	(Togola & Budzinski, 2008)
Singapore	41 - 121	(J. Wu et al., 2010)
Taiwan	2.5 – 57.1	(Fang et al., 2012)

4. IBUPROFEN REMOVAL USING MEMBRANE TECHNOLOGY

Membrane technology treatments are based on the use of hydrostatic pressure to remove suspended solids and high molecular weight solutes and allow the passage of water and low weight solutes (Rodriguez-Narvaez et al., 2017), membranes with different pore sizes (Microfiltration (MF), 1-0.1 µm; Ultrafiltration (UF), 0.1-0.01 µm; Nanofiltration (NF), 0.01-0.001 µm), as well as semipermeable selective membranes (reverse osmosis (RO), pore size < 0.001 µm and direct osmosis (FO)) (Maroneze et al., 2014). Their use has increased considerably, one of the great advantages of these filtration systems is that they are capable of retaining a large number of polluting substances in waters, including CE (Maroneze et al., 2014); however, they do not allow the degradation of these, so those pollutants are concentrated in the form of solid waste, requiring further treatment, and therefore increasing the costs of the process (Homem & Santos, 2011). Treatments with membranes are very promising, especially with new new research in the development of antifouling and autocurative membranes (Richardson, 2008).

Properties of membrane materials and contaminants, such as pore size, hydrophobia, functional groups, pKa, in addition to treated water quality, are some of the complex factors influencing elimination (Rodriguez-Narvaez et al., 2017).

The following Table 5 shows some of the research that has been done worldwide with respect to ibuprofen removal using membrane technology.

Table 5: Percentage of ibuprofen removal using membrane technology

Country	Technology	% Rem.	Ref.
Brail	RO	98	(Licona et al., 2018)
Australia	RO	95	(Alturki et al., 2010)
China	RO	94.8	(Li et al., 2018)
Spain	RO	99	(Urtiaga et al., 2013)
Palestine	UF/RO	99.9	(Khalaf et al., 2013)
Brazil	NF	90	(Licona et al., 2018)
Spain	NF	81.2	(Maryam et al., 2020)
Netherlands	NF	99	(Verliefde et al., 2009)
Australia	NF	100	(Nghiem et al., 2006)
Australia	NF	99	(Alturki et al., 2010)
United States	NF	100	(Bellona et al., 2010)
Spain	NF	99	(Garcia-Ivars et al., 2017)

Country	Technology	% Rem.	Ref.
China	NF	93.3 ± 0.3	(Ge et al., 2017)
Saudi Arabia	FO	98.2	(Valladares Linares et al., 2011)
Singapore	FO	93	(Jin et al., 2012)
United States	FO	99.9	(Holloway et al., 2014)

5. REGULARISATIONS OF THE EC

As time passes and emerging pollutants CE detection techniques in water bodies have become more sensitive, research has shown that the presence of these compounds can lead significant potential for human health and the environment at either trace levels, it is for this reason that strict regulatory decisions are absolutely necessary to control and mitigate this situation effectively.

In the Latin American context, there are still no specific regulatory standards for assessing the toxicity of emerging pollutants (EC). Therefore, those that exist at the global level to provide a frame of reference will be mentioned.

In 1995, the European Union established 10 ng/L and 10 µg/kg as the maximum permitted concentrations of pharmaceutical compounds (PhAC) and personal care products in surface water and soil. In 2001, through the Water Framework Directive (WFD), it developed a list of dangerous substances published in Decision 2455/2001/EC, which later became Annex X of the directive with the presence of 33 substances in which pharmaceutical products were not included. Therefore, these were not within an adequate surveillance program (Caviedes Rubio et al., 2017).

However, EC discharge limits in EU wastewater are not regulated, and some directives and guidelines have been published in recent years (Espíndola & Vilar, 2020). A new 2013/39/EU was launched in 2013, recommending monitoring and treatment options for a group of 45 priority substances. Decision 2015/495 of 20 March 2015 was also issued. Substances to be controlled in surface waters of the European Union include 3 hormones, 4 pharmaceutical compounds, 8 pesticides, one personal care product and one industrial product. This Decision was updated in 2018 by Decision 2018/840/EU, which removed 5 substances from the watch list (diclofenac, oxadiazon, triallate, 2-ethylhexyl-4-methoxycinnamate and 2,6 -di-terc-butyl-4-methylphenol) due to high quality monitoring data achieved; and 3 new substances (amoxicillin, ciprofloxacin and metaflumizone) were included.

In the UK, the NORMAN network has identified more than 1000 emerging pollutants (CE) (Geissen et al., 2015); these substances include pharmaceuticals, illegal or abused drugs, personal care products, endocrine disruptors, fire retardants, etc. (Farré et al., 2008). In Switzerland, an amendment for municipal wastewater treatment plants was approved, requiring a minimum disposal of 80% for some priority compounds (amisulpride, carbamazepine, citalopram, clarithromycin, diclofenac, hydrochlorothiazide, metoprolol, venlafaxine, benzothiazole, candesartan, irbesartan and mecoprop) (Starling et al., 2019). This measure is part of a broader effort to address growing concerns about the EC's presence in the environment.

In the United States, each state is responsible for updating its legislation regarding surface water quality (Starling et al., 2019). However, the Environmental Protection Agency (EPA) is responsible for national standards

of drinking water quality. It also developed a monitoring program, the Unregulated Pollutant Monitoring Rule (UCMR), to collect data on substances suspected of being present in drinking water (Espíndola & Vilar, 2020).

Currently, very little information is available globally on the maximum allowable limits for ibuprofen in different water sources. However, in Australia there is a regulation regulating the maximum permissible value in drinking water, known as DWG (Guideline Water Value), which is 0.4 ppm (400 ng/L) (Natural Resource Management Ministerial Council et al., 2008). This legislation establishes an important framework to ensure the safety of drinking water and protect public health from ibuprofen contamination.

6. CONCLUSIONS

As analytical methods for quantifying pollutants evolve, the presence of PhAC in the environment becomes more evident due to the direct discharge of mostly untreated wastewater, the use of agrochemicals, industrial wastes, among others; on the different bodies of water, such as: rivers, lakes, streams, seas, reservoirs; which make the quality of these affected. This could compromise the supply of drinking water and therefore human health, as few technologies are used to remove EC.

Among the most promising technologies are membrane treatments, which, as seen in this research, removal rates are very high compared to conventional methods that are currently inefficient at removing contaminants entering water sources. These membrane treatments offer a more effective and advanced solution to address growing concerns about the presence of emerging contaminants in water.

It is therefore necessary for environmental authorities, within their regulations, to include mandatory guidelines on the introduction of advanced treatments for drinking water; as well as constant monitoring and maximum permissible limits on different bodies of water. These measures are essential to protect public health and ensure water quality in the future.

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