

Emerging pollutants from pharmaceutical industry wastewater and their treatment by ozonation

Los contaminantes emergentes de las aguas residuales de la industria farmacéutica y su tratamiento por medio de la ozonización

Juliana Andrea Jaimes-Urbina¹
Javier Augusto Vera-Solano²

¹Universidad de Pamplona (Colombia). Email: jandreaajames11@gmail.com;
orcid: <https://orcid.org/0000-0002-3566-4427>

²Universidad de Pamplona (Colombia). Email: javier.vera@unipamplona.edu.co;
orcid: <https://orcid.org/0000-0002-3415-146x>

Received: 08-08-2019 Accepted: 18-02-2020

How to cite: Jaime-Urbina, Juliana; Vera-Solano, Javier (2020). Emerging pollutants from pharmaceutical industry wastewater and their treatment by ozonation. *Informador Técnico*, 84(2), 249-262. <https://doi.org/10.23850/22565035.2305>

Resumen

La industria farmacéutica es en la actualidad un valioso elemento de sanidad a nivel mundial. La manufactura de medicamentos y la limpieza de equipos, generan un agua residual con contaminantes emergentes de difícil eliminación con tratamientos tradicionales, provocando impactos ambientales sobre los ecosistemas. El siguiente artículo analiza el tratamiento con ozono en las aguas residuales de la industria farmacéutica. Se realizó una revisión de la literatura científica sobre las aguas residuales de la industria farmacéutica, la implementación de tratamientos tradicionales, los impactos medioambientales que ocasionaban los vertidos de dicha industria, y específicamente acerca de la implementación del ozono para remover los residuos farmacéuticos de los cuerpos de agua. Los resultados sugieren que el tratamiento de ozonización es eficiente en la remoción de compuestos farmacéuticos, especialmente de antiinflamatorios, antibióticos y estrógenos.

Palabras clave: contaminante emergente; medicamentos; residuos farmacéuticos; ozonización.

Abstract

The pharmaceutical industry is currently a valuable element of health worldwide. The manufacture of medicines and the cleaning of equipment generate wastewater with emerging pollutants that are difficult to eliminate with traditional treatments, causing environmental impacts on ecosystems. The following article discusses ozone treatment in pharmaceutical industry wastewater. A review of the scientific literature was carried out on wastewater from the pharmaceutical industry, the implementation of traditional treatments, the environmental impacts caused by discharges from said industry, and specifically on the implementation of ozone to remove pharmaceutical waste from water bodies. The results suggest that the ozonation treatment is efficient in the removal of pharmaceutical compounds, especially anti-inflammatories, antibiotics, and estrogens.

Keywords: emerging pollutant; medicines; pharmaceutical waste; ozonation.

1. Introduction

The pharmaceutical industry is one of the sectors of the general economy that is exclusively dedicated to the manufacture, distribution, marketing, and preparation of pharmaceutical chemical products. This sector is made up of various private and public organizations, whose objective and purpose are to satisfy the health needs of humans and animals through a wide range of drugs (Remington; Gennaro, 1990). In the 20th century, medicine eliminated many diseases, thus increasing life expectancy, due to the discovery of tetanus and diphtheria vaccines (Torres, 2010). A study by Lichtenberg (2014) found that innovation in the pharmaceutical sector increased life expectancy by up to 1.73 and 3.7 years in countries with the highest demand for drugs. Thus, with the creation of medicines, it is possible to cure diseases such as measles, malaria, and hepatitis C, and they are even diseases that can be eradicated, for example, polio, smallpox, and rinderpest (Spanish Confederation of Business Organizations [CEOE], 2019).

In the pharmaceutical industry, the water used is the raw material and is called “water for pharmaceutical use” with different types: purified water, highly purified water, and water for injection (Carpiuc, 2015). To better illustrate the use of water in the manufacture of medicines, in the granulation process, purified water is required (Instituto Nacional de Medicamentos, 2014). However, water is used in the sanitation processes of equipment, containers, and primary packaging, therefore, residual water is obtained, characterized by containing residues of chemical products, such as leftover drugs and/or detergents used in the cleaning (Martínez *et al.*, 2018). After the above, the World Health Organization (2019) affirms that because of the various procedures carried out in the pharmaceutical industry, a great diversity of pharmaceutical waste manages to mix with bodies of water, through the effluents of the manufacturing or production facilities. Consequently, these wastes have become a matter of growing concern to the public, since they could reach drinking water sources.

Wastewater from this industry presents variability in its quantity and components (Tuset, 2019). In this sense, and since there are different modalities in the operations, the generation of waste is varied in concentration and composition (Ramos; Espinosa; López; Pellón, 2005). Similarly, the composition of the water discharged into the environment varies depending on the process by which it is derived (Ramos, 2009). It is then intuited that the amount of pharmaceutical waste dumped may be low, but its continuous entry into the ecosystem can increase the concentration of pollutants in water bodies, which generates a long-term risk for aquatic and terrestrial organisms (Klavarioti; Mantzavinos; Kassinos, 2009). In this way, it can be established that the main problem is the lack of both techniques and technologies, which allow, in addition to treating, to know the components and concentrations of wastewater for this industry (Ramos, 2009).

In recent years, residues of more than 150 medicines for human and animal use have been found in environments as remote as the Arctic (Rodríguez, 2013). For example, in the study carried out by Schwaiger, Ferling, Mallow, Wintermayr, and Negele (2004), they determined that at low concentrations of diclofenac (1 µ/L) alterations begin to be observed in rainbow trout, detecting alterations in the kidneys and gills, in addition to the accumulation of the compound studied in their organs. Likewise, the presence of high concentrations of propranolol in water can interfere with the ability of fish to exchange oxygen with the environment (Owen *et al.*, 2007).

The unawareness of the components that are present in the wastewater of the pharmaceutical industry makes it difficult to apply a certain treatment (Martínez *et al.*, 2018). In short, biological treatment processes are considered the most economical and usual for wastewater treatment (Arslan-Alaton; Caglayan, 2006). However, Akmehmet-Balcioğlu and Ötker (2003) claim that the presence of certain compounds prevents a complete elimination through biological treatments. For example, the presence of antibiotics and disinfectants in industrial discharges affects the effectiveness of the biological treatment of wastewater (Ramos, 2009). Likewise, the discharge of untreated effluents makes it difficult to eliminate certain compounds through conventional biological treatment processes (Gharbani *et al.*, 2010). In this regard, ozone processes have the ability to eliminate toxic pollutants and the so-called “emerging pollutants”, which include pharmaceutical waste (Ramos, 2009).

and of the cleaning industry (Pinheiro; Salla; Bolaños, 2018) up to turn them into products that are less harmful to human health and the aquatic environment (Quiroga; Quero-Pastor; Acevedo, 2015). The use of ozone has been shown to be effective in effectively removing pharmaceutical products from wastewater (Lester; Mamane; Zucker; Avisar, 2013).

Water is a good that belongs to everyone, but many times it is not taken into account. Everyday tons and tons of chemical compounds that destroy aquatic ecosystems are thrown into rivers, and one of the industries that contributes to this phenomenon is pharmaceuticals. To try to mitigate the impacts produced by this type of pollution, advanced oxidation treatments appear, including ozonation. That is why, from the perspective of the systematic review, it was analyzed and reflected on how ozonation is a simple and respectful tool that can be used for the good of the environment.

Up to this point, it is stated that the treatment of wastewater from the pharmaceutical industry is an issue that must be thoroughly investigated insofar as the discharge of water from this industry generates environmental problems of great magnitude. According to all the above, the following question is the central axis of this bibliographic review article. How does the ozonation technique contribute to the reduction of pollution due to the generation of emerging pollutants related to the pharmaceutical industry?

2. Emerging pollutants (EP)

In the same way as remnants of different types of pollutants are found in urban wastewater, the presence of remains of drugs, pesticides, and other substances is also observed, which are called emerging pollutants (EP), compounds that are discharged into the water and that are not regulated. Emerging pollutants, also called micro-pollutants, are chemical compounds that are the product of human activities carried out in daily life, such as personal hygiene or health care, which can cause negative effects on the ecosystem, generating alterations on the environment. These are substances of different origin and chemical composition of which relatively little is known regarding the impact they have on the environment and on humans, substances that are known with the name of emerging pollutants (Ramírez; Chicaiza; Ramos; Álvarez; 2019).

They are normally released into the environment in small amounts, but over time, by their intensive and widespread use, they build up in the environment. Currently, they are also called pollutants of emerging interest, that are not necessarily new chemical products and generally include pollutants that have often been present in the environment, but whose presence, importance, and effects (toxicity) are being evaluated (Arbeláez, 2015). Of all the emerging pollutants, those that possibly arouse the greatest concern are drugs, so their study is among the priority lines of research of the main organizations dedicated to the protection of public and environmental health (Informacion Farmacoterapeutica de la Comarca [INFAC], 2016). Most of the polluting cases have not been regulated, which is why they are candidates for future regulations, depending on studies that show the potential effects on health and the monitoring of their occurrence (Verlicchi; Galletti; Petrovic; Barceló, 2010). Emerging contaminants in water include drugs, perfluorinated compounds, hormones, drugs of abuse, personal care, and hygiene products. We can also find them in pesticides, drugs for both human and animal use, antiseptics, flame retardants, and surfactants also known as tensioactive. Consequently, the main source of entry of these compounds into the aquatic environment is through sewage, although it is also worth highlighting the role of agriculture and livestock as sources of diffuse contamination of pesticides and antibiotics, respectively.

3. Pharmaceutical industry

The pharmaceutical industry is one of the great economic sectors in charge of developing and selling thousands of tons of pharmaceutical chemicals that today are essential consumer goods not only for humanity but also for animals. It is an advanced sector since for the creation of their products they invest significant sums of money in

research with the aim of developing cures against diseases. It is appropriate to highlight that like any industry for the development of its drugs and medicines, there are processes that have inputs and outputs. In the case of this industry, the inputs are the raw material for the preparation of drugs and the outputs are the products and by-products of the transformation process added to the production waste.

3.1. Medicines

The concept of drug or medicine is a term that should be used exclusively to denote the active principle, not the pharmaceutical product. As “active ingredient” is generally used primarily when referring to the formulation and manufacturing operations. It is recommended that the term “drug” be used to refer to those situations in which the active ingredient is in contact with biological systems. A drug can also be designated as a pharmaceutical product used for the prevention, diagnosis, or treatment of a disease (Arias, 1999). Medicines are basically made up of two components, the active ingredients, and the excipients. The former can be one or more and are essentially responsible for producing the medicinal effect in the body. The latter are inactive substances that are added to the active principle to be able to administer the drugs (Asociación Española de Medicamentos Genéricos [AESEG], 2013). In certain cases, some drugs contain adjuvants that are responsible for the drugs being easily absorbed (Martínez; Turégano, 2014). In addition to the active ingredients and formulation adjuvants, pigments and colorants are also sometimes components of the drug (Kümmerer, 2001).

3.2. Pharmaceutical product waste

The generation of waste by pharmaceutical manufacturing varies depending on the characteristics and concentrations used in production, even at the time of year in which it is found. It is conceived that the main residues are originated by the cleaning of equipment, apart from the compounds used in the cleaning process added to the effluent (Martínez *et al.*, 2018). As stated by Trecco *et al.* (2011), during the development and production of pharmaceutical products, a large amount of sanitary waste is generated, the nature of these wastes being very varied, since they can contain biological, radioactive, pure chemical and acid waste, among others. Although it is difficult to identify the characteristics of effluents from pharmaceutical industries, it is inferred that wastewater, originating from organic synthesis plants, has a high concentration of chemical oxygen demand (COD) and salinity (Gadipelly *et al.*, 2014).

Hospitals are a great source of emerging pollutants. According to Grisales, Ortega, and Rodríguez (2012), it is due to various activities, such as laboratory waste, patient excretion, research activities, among others. Pharmaceutical products that are discarded by hospital sources are those that are generally in charge of treating more serious pathologies (Moreno-Ortiz *et al.*, 2013). Uncontrolled hospital discharges introduce antibiotics, cytotoxic agents, and disinfectants from health centers, being important sources for bodies of water (Grisales *et al.*, 2012); (Kümmerer, 2001). Antineoplastics (cytotoxic) are used for the treatment of cancer (Moreno-Ortiz *et al.*, 2013), this product has been detected in concentrations between 5 and 50 g/L in hospital discharges (Kümmerer, 2001). Pharmaceutical products can generate residues, after being consumed, as stated by Snyder, Vanderford, and Drewes (2009), since they are excreted by the human being, presenting two cases, the compound is either completely or partially metabolized. It is estimated that after the consumption stage, in excretion there are residues between 30 % and 90 % of the ingested dose (Mudgal *et al.*, 2013). Antibiotics can be disposed of up to 90% by humans after consumption, thus allowing these compounds to reach wastewater and spread through the environment (Akmehmet-Balcioğlu; Ötker, 2003).

4. Advanced oxidation process (AOP)

Advanced oxidation chemical processes use (chemical) oxidants to reduce levels of chemical oxygen demand (COD) and biological oxygen demand (BOD), and the biodegradability index can be expressed as (BOD/COD). In this case, the biodegradability index is directly related to the concentration of organic matter present in the water and its separation of organic components and oxidizable inorganic components. Processes can totally oxidize organic materials such as carbon (C) and water (H₂O), although it is often not necessary to operate these processes up to this level of treatment. These are based on physicochemical processes capable of producing profound changes in the chemical structure of pollutants, involving the generation and use of powerful transient species, mainly the hydroxyl radical (OH⁻). In addition, the generation of radicals is generated from oxygen, hydrogen peroxide, and supported catalysts, so the reaction by-products are only water and carbon dioxide (Bes; Silva; Bengoa, 2018).

Among the main advanced oxidation process technologies, Table 1 shows the Fenton processes, which consists of the addition of iron salts in the presence of hydrogen peroxide (H₂O₂) in an acid medium, for the formation of OH⁻ radicals. The combination of H₂O₂ and iron salts is called the Fenton reagent. Electrochemical oxidation occurs through anodic reactions in which oxygen is transferred from the solvent (water) to the products to be oxidized and ozonation, which is an advanced oxidation technology, that is not exclusive to water purification since it has numerous applications for wastewater treatment because it improves its biodegradability making conventional biological treatment easier (Patiño; Arroyave; Marín, 2012).

Table 1.

Main technologies of advanced oxidation processes

Advanced oxidation technologies	
Ozonation	Sub/supercritical water oxidation
Ozone/hydrogen peroxide	Vacuum Ultraviolet photolysis (VUV)
Fenton processes	Ultraviolet/hydrogen peroxide
Electrochemical oxidation	Ultraviolet ozone
Non-thermal plasma	Photolysis/Fenton
Ultrasound	Heterogeneous photocatalysis

Source: own elaboration.

5. Treatment of pharmaceutical wastewater by applying ozone

The presence of drugs in the environment has been investigated by different professionals. It is estimated that approximately half of the water from the pharmaceutical industries in the world is discharged without specific treatment (Enick; Moore, 2007; Lange *et al.*, 2006), which generates the presence of pharmaceutical waste in ecosystems. In 1970, the presence of cardiovascular drugs, analgesics, and contraceptives in US sewage was reported for the first time (Tambosi; Yamanaka; José; Muniz; Schröder, 2010). The importance of detecting these products is due to the fact that the pharmaceutical compounds released into the environment may be toxic, affecting any level of the biological hierarchy (cells, organs, organisms, population, ecosystems, or ecosphere) (Klavarioti *et al.*, 2009). For their part, conventional treatments are limited by the different characteristics and components that pharmaceutical wastewater presents. The presence of these residues in the environment and in aquatic systems constitute a serious problem since they are extremely resistant to biological degradation and usually escape intact to the treatment of conventional plants (Oller; Malato; Sánchez-Pérez, 2011). In this

way, by means of the ozonation technique, drug residues present in wastewater, in the case of drugs such as ibuprofen, diclofenac, and propofol, among others, are eliminated, and the biodegradability of pharmaceutical wastewater is improved (Huang *et al.*, 2020). Table 2 indicates the generalized use that allows the continuous discharge of the same and their products.

Table 2.

Drugs present in wastewater that have been treated by means of the ozonation technique

Drug	Systematic name
Ibuprofen	(RS) -2- (4- (2-methylpropyl) phenyl) propanoic acid
Paracetamol	N-acetyl-4-aminophenol
Diclofenac	Diclofenac 2- (2,6-dichloroanilino)
Propofol	(2,6-Bis (1-methylethyl) phenol))
Codeine	3-methylmorphines

Source: own elaboration.

Wastewater treatment plants (WWTPs) are generally inefficient, as certain pharmaceutical compounds exit treatment unaffected, leading to subsequent treatments (Klavarioti *et al.*, 2009). A combination recommended by Mascolo *et al.*, (2010) is to integrate ozonation into the biological process, since they consider that the biological process reduces the load of pollutants and ozonation would oxidize the remaining products.

It is appropriate to indicate that ozone is a colorless gas, with a strong odor, with high oxidizing power, it is the triatomic form of oxygen (Teixeira, 2002), which is used as a homogeneous advanced oxidation process (AOP) and is the second most powerful oxidant (fluorine exceeds it due to its oxidation potential) (Grisales *et al.*, 2012). Its use has allowed a notable improvement in the taste, color, filtration characteristics, and biodegradability of water (Muñoz; Malato; Rodríguez; Domènech, 2008), in addition to inhibiting the growth of fungi and algae, and reducing turbidity (Ponce, 2005). It is generally used to eliminate the pollutants present in the water. In the same sense, its process can be carried out by direct reaction. Ozone is available as molecular ozone and reacts with organic compounds dissolved in water or through the reaction of these organic compounds with OH- radicals, generated from the decomposition of ozone when it dissolves in water (indirect reaction) (Quiroga *et al.*, 2015). It is necessary to emphasize that ozone in an aqueous solution can react with most pollutants that are in industrial wastewater in two different ways: 1) by direct reaction of molecular ozone or 2) by reaction of the species formed by the decomposition of ozone in water (free radicals) (Masten; Davies, 1994; Hoigné; Bader, 1977).

The ozonation process allows the degradation of toxic organic compounds, thus increasing the biodegradability of the effluent, since ozone is an effective oxidant, and it is also capable of reducing the concentrations of many pharmaceutical products (Bahr *et al.*, 2007; Kim; Tanaka, 2010; Snyder; Wert; Rexing; Zegers; Drury, 2006). Some studies show that the compounds have a great reactivity with ozone, for example, antibiotics and contraceptives, are rapidly transformed with ozone. Likewise it has been shown that anti-inflammatories containing amino groups and anti-epileptics with double chain show a high reaction with ozone (Grisales *et al.*, 2012). Various studies emphasize the importance of ozone treatment of traces of pharmaceutical residues in wastewater. Table 3 indicates some of these investigations such as Quiroga *et al.*, (2015) where they refer to ozonation as an advanced treatment for the elimination of drugs, or the pilot study carried out by Huber *et al.* (2005) on the oxidation of pharmaceutical products during the ozonation of municipal wastewater effluents.

Table 3.

Other studies on ozone treatment of drugs present in wastewater

Item	Author, year
Advanced treatments for drug removal in surface waters	Quiroga <i>et al.</i> , (2015)
Ozonation of pharmaceutical compounds: Rate constants and elimination in various water matrices	Benitez; Steel; Real and Roldán (2009)
Oxidation of pharmaceuticals during ozonation of municipal wastewater effluents: A pilot study.	Huber <i>et al.</i> (2005)
Review of technologies for wastewater treatment including some drugs	Miceli-Montesinos; Nájera-Aguilar; Rojas-Valencia; Quintero-López and Orantes-García (2014)
Treatment of Industrial Effluents by Oxidative Processes in the presence of ozone	Almeida; Assalin; Rosal; Duran (2004)
Technologies for the elimination of colorants and pigments present in wastewater. A Review	Barrios; Gaviria; Agudelo; Cardona (2015)
Emerging pollutants and their impact on health	Reinoso; Serrano; Orellano (2017)
Hydrochemistry and emerging pollutants in urban industrial wastewater of Morelia, Michoacán	Robledo-Zacarías; Velázquez-Machuca; Montañez-Soto; Pimentel-Equihua; Vallejo-Cardona; López-Calvillo; Venegas-González (2017)

Source: own elaboration.

6. Drug persistence

The presence of pharmaceutical products in a water source can vary from one place to another depending on the type of products and the volume of the discharge in the water bodies. Consequently, the persistence of these pollutants in nature depends, among other factors, on the characteristics of the drugs, the volume excreted, and the characteristics of the environmental compartments. For example, fat-soluble drugs can accumulate in animal fat tissue and enter the food chain (ethinylestradiol is a potential candidate to bioaccumulate in large predators (Mudgal *et al.*, 2013). In some of these drugs, their persistence during wastewater treatment has been confirmed, detecting concentrations, for example, of iopromide, above 20 mg L⁻¹. Thus, diatrizoate, iopromide, iopomidol and amidotrizoic acid were quantified in concentrations of µg L⁻¹ (Ramos, 2009). The persistence of these compounds in wastewater may be due to their mixtures and physicochemical characteristics, as well as their origin. Although these substances are present in water in low concentrations, they can have an important footprint on ecosystems, in general, the presence of pharmaceutical remains in the environment and in aquatic systems, constitute a serious problem, since they are extremely resistant to biological degradation, being sometimes ineffective treatments with conventional biological reactors of wastewater treatment plants.

7. Methodology

To locate the bibliographic documents, several documentary sources were used. A systematic review was carried out focused on the articles that could shed light on the treatment of emerging pollutants found in pharmaceutical wastewater through ozonation treatment. The units of analysis were all those documents on the subject found in the Google scholar, Redalyc, Scielo, Redib, and ScienceDirect databases. The algorithms or search criteria included the following descriptors: ozonation, pharmaceutical waters, emerging pollutant, drugs, pharmaceutical waste, and pharmaceutical wastewater treatment. These descriptors were combined in various ways at the time of search to broaden the search criteria. When searching for documents in each of the databases, 68 articles were preselected, 56 of which were chosen according to the inclusion and exclusion criteria. Articles that did not refer to thematic nuclei and/or those that were not in indexed journals were not

taken into consideration for the analysis. For the organization of the documents, an Excel matrix was made with the following data: name, author, doi or URL, objective, description, methodology, results, conclusions, journal, country, discipline, search algorithm, and search engine. Finally, a global analysis of each of the articles was carried out by means of which the essential points of the analysis were identified, questions, results, and conclusions were formulated.

In Figure 1 it can be seen the distribution of the articles reviewed since 2010, it should be noted that 2013 and 2015 were the years in which more publications on the subject were found in the review carried out.

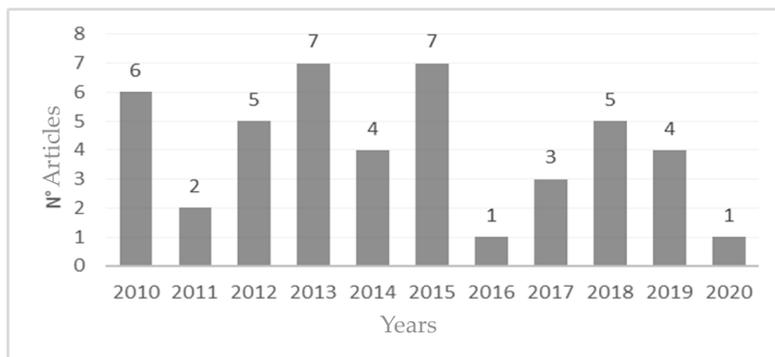


Figure 1. Distribution of articles since 2010
Source: Own elaboration.

In Figure 2 the number of documents by language can be seen. In the case of our systematic review, thirty-three (33) articles were found in English with the highest number, followed by Spanish with twenty-two (22) and one (1) article in Portuguese.

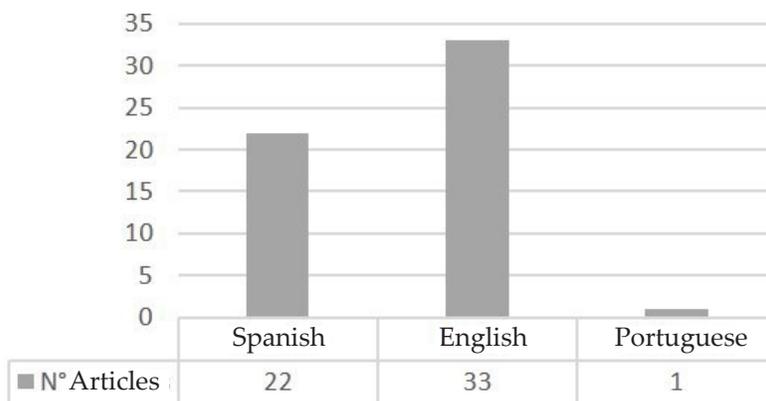


Figure 2. Number of articles reviewed by language
Source: Own elaboration.

Table 4 shows the main indexed scientific journals from which the information for the review was extracted, identifying international journals from countries such as Germany, Korea, Turkey, Italy, among others.

Table 4.

Main journals by country used in the review

Journal	Country
Journal of hazardous materials	Egypt
Water Science and Technology	Germany
Science of the Total Environment	Korea
Chemosphere.	Turkey
Toxicology Letters	United Kingdom
Journal of Bioremediation & Biodegradation	Italy
Water Research	Greece
Environmental Toxicology: An International Journal	U.S.A.
Regulatory Toxicology and Pharmacology	Denmark

Source: own elaboration.

The review also revealed the academic disciplines that have carried out a greater number of studies in relation to drug treatments through ozonation, among them we have toxicology and chemical engineering, followed by the environment, eco chemistry and civil engineering.

8. Most relevant results

Among the most frequent drugs in pharmaceutical wastewater and that have undergone treatment through ozonation, we can find diclofenac, ibuprofen, amoxicillin, paracetamol, carbamazepine. Metoprolol, phenacetin, codeine, sulfachlorpyridazine, sulfadimethoxine, sulfamerazine, sulfamethazine, sulfathiazole, and trimethoprim.

As a result of the review, it was possible to show how ozonation in a high number of studies turns out to be effective when we talk about the ability to eliminate toxic pollutants from pharmaceutical wastewater. It should also be mentioned that the concentration level of drug residues depends on the source where they are being generated, since we can find them not only in the pharmaceutical industry, but in activities as simple as personal hygiene, livestock, cleaning, and disinfection activities among others. The ozonation process is highly beneficial for the mitigation of the contamination of surface water bodies with medicines since it allows the biodegradation of the effluent, ozone being a highly effective oxidant, also contributing to inhibit the growth of algae and fungi in them. Similarly, it should be noted among the results of the review is that the high persistence of emerging residues in wastewater is notably mentioned in several of the documents, which often leads to generating relevant impacts such as the affectation of the aquatic fauna present in surface water.

9. Conclusions

Emerging residues are currently arousing great interest for new studies and research, since their presence in the environment can produce potentially harmful alterations for humans and animals, and very little is known about them, so it is necessary to increase the research level regarding these. Conventional wastewater treatments have proven to be inefficient in the removal of pharmaceutical pollutants, which is why it is necessary to seek and investigate new advanced treatments in wastewater, which help to efficiently eliminate or reduce the percentage of pollution that this type of pollutant generates to the environment.

The ozonation technique aims to provide environmental, health, and economic advantages for the elimination of pollution. With the use of advanced tertiary treatments, it is possible to extract emerging or micropollutant compounds, especially pharmacological substances that today have the viable risk of threatening the quality of water for human consumption. It is essential to reduce the use of chemical products, for example, with the use of minimal doses of drugs to protect the health of the aquatic environment and reduce the costs that can be generated from water purification, especially in the pharmaceutical industries adapting to the characteristics and specifications of its effluents, thus preventing these pollutants from reaching the waste or drinking water treatment plants. This is due to the fact that the presence of drugs or emerging pollutants in the bodies of water, generates an environmental problem of great magnitude, since these products usually intervene in the trophic chains of the species present there, modifying part of their physiology, their behavior, and even, in the case of bacteria, making them resistant.

10. References

- Arbeláez, Paula (2015). *Contaminantes emergentes en aguas residuales y de río y fangos de depuradora* (tesis doctoral). Universitat Rovira I Virgili, Tarragona, España.
- Arias, Tomás (1999). *Glosario de medicamentos: Desarrollo, evaluación y uso*. Washington, D.C.: Organización Panamericana de la Salud.
- Almeida, Edna; Assalin, Márcia; RosaI, Maria; Durán, Nelson (2004). Tratamento de efluentes industriais por processos oxidativos na presença de ozônio. *Química Nova*, 27(2), 818-824.
<https://doi.org/10.1590/S0100-40422004000500023>
- Asociación Española de Medicamentos Genéricos (2013). *¿Qué es un principio activo?* Recuperado de:
<https://www.engenerico.com/que-es-un-principio-activo/>
- Akmehmet-Balcioğlu, Işıl; Ötker, Merih (2003). Treatment of pharmaceutical wastewater containing antibiotics by O₃ and O₃/H₂O₂ processes. *Chemosphere*, 50(1), 85–95.
[https://doi.org/10.1016/S0045-6535\(02\)00534-9](https://doi.org/10.1016/S0045-6535(02)00534-9)
- Arslan-Alaton, Idil; Caglayan, Ali (2006). Toxicity and biodegradability assessment of raw and ozonated procaine penicillin G formulation effluent. *Ecotoxicology and Environmental Safety*, 63(1), 131–140.
<https://doi.org/10.1016/j.ecoenv.2005.02.014>
- Bahr, Carsten; Schumacher, Jochen; Ernst, Mathias; Luck, Francis; Heinzmann, B.; Jekel, Martin (2007). SUVA as control parameter for the effective ozonation of organic pollutants in secondary effluent. *Water Science and Technology*, 55(12), 267–274.
<https://doi.org/https://doi.org/10.2166/wst.2007.418>
- Barrios-Ziolo, L.F.; Gaviria-Restrepo, L.F.; Agudelo, E.A.; Cardona-Gallo, S.A. (2015). Technologies for the removal of dyes and pigments present in wastewater. A review. *DYNA*, 82 (191), 118-126.
[10.15446/dyna.v82n191.42924](https://doi.org/10.15446/dyna.v82n191.42924)
- Benítez, Javier; Acero, Juan; Real, Francisco; Roldán, Gloria (2009). Ozonation of pharmaceutical compounds: Rate constants and elimination in various water matrices. *Chemosphere*, 77(1), 53-59.
<https://doi.org/10.1016/j.chemosphere.2009.05.035>
- Bes, Sarai; Silva, Adrián; Bengoa, Christophe (2018). *Manual técnico sobre procesos de oxidación avanzada aplicados al tratamiento de aguas residuales industriales*. España: CYTED.
- Carpiuc, Lucia (19 de julio de 2015). *Agua de uso farmacéutico*. Recuperado de:
<https://vdocuments.mx/agua-de-uso-farmacutico.html>

- Reinoso, Julieta; Serrano, Clara; Orellana Danilo (2017). Contaminantes emergentes y su impacto en la salud. *Revista de la Facultad de Ciencias Médicas de la Universidad de Cuenca*, 35(2), 55-59.
- Confederación Española de Organizaciones Empresariales (5 de abril de 2019). *La industria farmacéutica y sus contribuciones a la salud mundial*. Recuperado de:
<https://www.ceoe.es/es/contenido/actualidad/noticias/la-industria-farmaceutica-y-sus-contribuciones-a-la-salud-mundial>
- Enick, Oana; Moore, Margo (2007). Assessing the assessments: pharmaceuticals in the environment. *Environmental Impact Assessment Review*, 27(8), 707-729.
<https://doi.org/10.1016/j.eiar.2007.01.001>
- Farmacontaminacion. Impacto ambiental de los medicamentos (2016). Información Farmacoterapéutica de la Comarca [INFAC], 24(2), 59-64.
- Forero, Jorge; Ortiz, Olga; Ríos, Fabián (2005). Aplicación de procesos de oxidación avanzada como tratamiento de fenol en aguas residuales de refinería. *Ciencia Tecnología y Futuro*, 3(1), 97-109.
- Gadipelly, Chandrakanth; Pérez-González, Antía; Yadav, Ganapati; Ortiz, Inmaculada; Ibáñez, Raquel; Rathod, Virendra; Marathe, Kumudini (2014). Pharmaceutical industry wastewater: Review of the technologies for water treatment and reuse. *Industrial and Engineering Chemistry Research*, 53(29), 11571-11592.
<https://doi.org/10.1021/ie501210j>
- Gharbani, P.; Khosravi, M.; Tabatabaie, S.; Zare, K.; Dastmalchi, S.; Mehrizad, A. (2010). Degradation of trace aqueous 4-chloro-2-nitrophenol occurring in pharmaceutical industrial wastewater by ozone. *International Journal of Environmental Science and Technology*, 7, 377-384.
<https://doi.org/10.1007/BF03326147>
- Grisales, Dayana; Ortega, Joela; Rodríguez, Tatiana (2012). Remoción de la materia orgánica y toxicidad en aguas residuales hospitalarias aplicando ozono. *DYNA*, 79(173), 109-115.
- Huber, Marc; Göbel, Anke; Joss, Adriano; Hermann, Nadine; Löffler, Dirk; McArdell, Christa; Ried, Achim; Siegrist, Hansruedi; Ternes, Thomas; Gunten, Urs von (2005). Oxidation of Pharmaceuticals during Ozonation of Municipal Wastewater Effluents: A Pilot Study. *Environmental Science & Technology*, 39(11), 4290-4299.
<https://doi.org/10.1021/es048396s>
- Hoigné, J.; Bader, H. (1977). Ozonation of Water: Selectivity and Rate of Oxidation of Solutes. *Ozone: Science & Engineering*, 1, 73-85.
<https://doi.org/10.1080/01919517908550834>
- Huang, Yuanxing; Jiang, Jiewen; Ma, Luming; Wang, Yaowei; Liang, Manli; Zhang, Zhiguo; Li, Liang. (2020). Iron foam combined ozonation for enhanced treatment of pharmaceutical wastewater. *Environmental Research*, 83, 109-205.
<https://doi.org/10.1016/j.envres.2020.109205260>
- Instituto Nacional de Medicamentos (2014). *Farmacopea argentina* (7 ed.) Recuperado de:
http://www.anmat.gov.ar/webanmat/fna/flip_pages/Farmacopea_Vol_IV/files/assets/basic-html/toc.html
- Kim, Ilho; Tanaka, Hiroaki (2010). Use of ozone-based processes for the removal of pharmaceuticals detected in a wastewater treatment plant. *Water Environment Research*, 82(4), 294-301.
[doi: 10.2307/25679780](https://doi.org/10.2307/25679780)

- Klavarioti, Maria; Mantzavinos, Dionissios; Kassinos, Despo (2009). Removal of residual pharmaceuticals from aqueous systems by advanced oxidation processes. *Environment International*, 35(2), 402–417. <https://doi.org/10.1016/j.envint.2008.07.009>
- Kümmerer, Klaus (2001). Drugs in the environment: Emission of drugs, diagnostic aids and disinfectants into wastewater by hospitals in relation to other sources - A review. *Chemosphere*, 45(6–7), 957–969. [https://doi.org/10.1016/S0045-6535\(01\)00144-8](https://doi.org/10.1016/S0045-6535(01)00144-8)
- Lange, Franziska; Cornelissen, Sjeff; Kubac, David; Sein, Myint M.; Sonntag, Justus von; Hannich, Christoph B.; Sonntag, Clemens von (2006). Degradation of macrolide antibiotics by ozone: a mechanistic case study with clarithromycin. *Chemosphere*, 65(1), 17–23. <https://doi.org/10.1016/j.chemosphere.2006.03.014>
- Lester, Yaal; Mamane, Hadas; Zucker, Ines; Avisar, Dror (2013). Treating wastewater from a pharmaceutical formulation facility by biological process and ozone. *Water Research*, 47(13), 4349–4356. <https://doi.org/10.1016/j.watres.2013.04.059>
- Lichtenberg, Frank (2014). Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000-2009. *Health Policy and Technology*, 3(1), 36-58. <https://doi.org/10.1016/j.hlpt.2013.09.005>
- Masten, Susan; Davies, Simón (1994). The use of Ozonation to degrade organic contaminants in wastewaters. *Environmental Science & Technology*, 28 (4), 180-186. <https://doi.org/10.1021/es00053a718>
- Martínez, Fernando; Molina, R.; Rodríguez, Ivan; Pariente, Isabel; Segura, Yolanda; Melero, Juan (2018a). Techno-economical assessment of coupling Fenton/biological processes for the treatment of a pharmaceutical wastewater. *Journal of Environmental Chemical Engineering*, 6(1), 485–4. <https://doi.org/10.1016/j.jece.2017.12.008>
- Martínez, Francisco; Turégano, Juan (2014). *Ciencia para el Mundo Contemporáneo: Guía de Recursos Didácticos*. Recuperado de: http://www3.gobiernodecanarias.org/aciisi/cienciasmcmc/web/pdf/u5_salud_y_enfermedad.pdf
- Mascolo, Giuseppe; Laera, Giuseppe; Pollice, Alfieri; Cassano, Daniela; Pinto, Appio; Salerno, Carlo; Lopez, Antonio (2010). Effective organics degradation from pharmaceutical wastewater by an integrated process including membrane bioreactor and ozonation. *Chemosphere*, 78(9), 1100–1109. <https://doi.org/10.1016/j.chemosphere.2009.12.042>
- Moreno-Ortiz, Victor; Martínez-Núñez, Juan; Kravzov-Jinich, Jaime; Pérez-Hernández, Luis; Moreno-Bonett, Consuelo; Altagracia-Martínez; Marina (2013). Los medicamentos de receta de origen sintético y su impacto en el medio ambiente. *Revista Mexicana de Ciencias Farmacéuticas*, 44(4), 17–29. 261
- Mudgal, Shailendra; De Toni, Arianna; Lockwood, Sarah; Salès, Katherine; Backhaus, Thomas; Halling Bent (2013). *Study on the environmental risks of medicinal products Executive*. Francia: Bio Intelligence Service.
- Muñoz, Ivan; Malato, Sixto; Rodríguez, Amadeo; Domènech, Xavier (2008). Integration of environmental and economic performance of processes. Case study on advanced oxidation processes for wastewater treatment. *Journal of Advanced Oxidation Technologies*, 11(2), 270–275. <https://doi.org/10.1515/jaots-2008-0211>
- Miceli-Montesinos, Auzania; Nájera-Aguilar, Hugo; Rojas-Valencia, María; Quintero-López, Luz; Orantes-García, Carolina (2014). Revisión de Tecnologías para el tratamiento de aguas residuales incluyendo algunos fármacos. *Espacio I+D Innovación más Desarrollo*, 3(5), 73-96. [doi: 10.31644/IMASD.5.2014.a04](https://doi.org/10.31644/IMASD.5.2014.a04)

- Oller, Isabel; Malato, S.; Sánchez-Pérez, José (2011). Combination of advanced oxidation processes and biological treatments for wastewater decontamination—a review. *Science of the Total Environment*, 409(20), 4141–4166.
<https://doi.org/10.1016/j.scitotenv.2010.08.061>
- Organización Mundial de la Salud (2019). *Agua, Saneamiento e Higiene: Productos farmacéuticos en el agua potable*. Recuperado de:
https://www.who.int/water_sanitation_health/emerging/info_sheet_pharmaceuticals/es/
- Owen, Stewart; Giltrow, Emma; Huggett, Duane; Hutchinson, Thomas; Saye, JoAnne; Winter, Matthew; Sumpter, John (2007). Comparative physiology, pharmacology and toxicology of β -blockers: mammals versus fish. *Aquatic Toxicology*, 82(3), 145–162.
<https://doi.org/10.1016/j.aquatox.2007.02.007>
- Patiño, Kelly; Arroyave, Sandra; Marín, Juan (2012). Oxidación Electroquímica y Ozonización Aplicadas al Tratamiento de Aguas de Lavado de la Producción de Biodiesel. *Informacion tecnologica*, 23(2), 41-52.
<http://dx.doi.org/10.4067/S0718-07642012000200006>
- Martins Pinheiro, A., Salla, M. R., & Bolanos Rojas, M. L. (2019). Tratamiento de aguas residuales provenientes de industria de productos de limpieza y desinfectantes por ozonización convencional y catalítica. *Ingeniare. Revista chilena de ingeniería*, 27(2), 223-235.
- Ponce, Efraín. (2005). *Diseño de un tren de potabilización para una planta generadora de agua embotellada* (tesis de pregrado). Universidad de las Américas Puebla, Mexico.
- Quiroga; José; Quero-Pastor, Maria; Acevedo, Asunción (2015). Tratamientos avanzados para la eliminación de fármacos en aguas superficiales, *Revista de Salud Ambiental* (Espec. Congr.), 15, 12-64.
- Ramírez, Lenin; Chicaiza, Sabrina; Ramos, Allan; Álvarez, Cesar (2019). Detección de antibióticos betalactámicos, tetraciclinas y sulfamidas como contaminantes emergentes en los ríos San Pedro y Pita del cantón Rumiñahui. LA GRANJA. *Revista de Ciencias de la Vida*, 30(2), 88-102.
- Ramos, Caridad; Espinosa, Maria; López, Matilde; Pellón, Alexis (2005). Tratamiento de las aguas residuales provenientes de la industria de medicamentos. *Revista CENIC. Ciencias Químicas*, 36(1), 39–44.
- Ramos, Caridad (2009a). Medicamentos de consumo humano en el agua, propiedades físico-químicas. *Revista Cubana de Higiene y Epidemiología*, 47(2), 1-18.
- Remington, Joseph; Gennaro, Alfonso (1990). *Remington's Pharmaceutical Sciences* (18 ed.) Easton, Pensilvania: Mack Publishing Company.
- Robledo Zacarías, V. H., Velázquez Machuca, M. A., Montañez Soto, J. L., Pimentel Equihua, J. L., Vallejo Cardona, A. A., López Calvillo, M. D., & Venegas González, J. (2017). Hidroquímica y contaminantes emergentes en aguas residuales urbano industriales de Morelia, Michoacán, México. *Revista internacional de contaminación ambiental*, 33(2), 221-235.
- Rodríguez, Rita (2013). *Influencia de los fármacos presentes en el agua residual sobre la resistencia de la bacteria Escherichia coli y su eliminación por oxidación avanzada* (tesis doctoral). Universidad Politécnica de Madrid, España.
- Schwaiger, Julia; Ferling, Hermann; Mallow, U.; Wintermayr, H.; Negele, Rolf (2004). Toxic effects of the non-steroidal anti-inflammatory drug diclofenac: Part I: histopathological alterations and bioaccumulation in rainbow trout. *Aquatic Toxicology*, 68(2), 141–150.
<https://doi.org/10.1016/j.aquatox.2004.03.014>

- Snyder, Shane; Wert, Eric; Rexing, David; Zegers, Ronald; Drury, Douglas (2006). Ozone oxidation of endocrine disruptors and pharmaceuticals in surface water and wastewater. *Ozone: Science and Engineering*, 28(6), 445–460.
<https://doi.org/10.1080/01919510601039726>
- Snyder, S.; Vanderford, B. J.; Drewes, J. (2009). *State of knowledge of endocrine disruptors and pharmaceuticals in drinking water*. Estados Unidos: Water Environment Research Foundation.
- Tambosi, José; Yamanaka, Leonardo; José, Humberto; Muniz, Regina de Fátima; Schröder, Horst (2010). Recent research data on the removal of pharmaceuticals from sewage treatment plants (STP). *Química Nova*, 33(2), 411–420.
- Teixeira, Claudia (2002). *Estudo comparativo de tipos diferentes de processos oxidativos avançados* (tesis doctoral). Universidade Estadual de Campinas, Brasil.
- Torres, Amariyls (2010). Medicamentos y transnacionales farmacéuticas: impacto en el acceso a los medicamentos para los países subdesarrollados. *Revista Cubana de Farmacia*, 44(1), 97–110.
- Trecco, Cecilia; Castello, Vanesa; Kedikian, Romina; Sobrero, Cecilia; Sisti, Ada; Oviedo, Sergio (2011). Efficient management of waste within the best practices of the pharmaceutical industries. *Producción + Limpia*, 6(2), 32–46.
- Tuset, Sergio (11 de febrero de 2019). *Tratamiento de aguas residuales en la industria farmacéutica* [Mensaje en un blog]. Recuperado de:
<https://blog.condorchem.com/tratamiento-de-aguas-residuales-en-la-industria-papelera/>
- Verlicchi, Paola; Galletti, Alessio; Petrovic, Mira; Barceló, Damiá (2010). Hospital effluents as a source of emerging pollutants: An overview of micropollutants and sustainable treatment options. *Journal of Hydrology*, 389(3-4), 416-428.