

Article

Removal of Pharmaceuticals from Wastewater: Analysis of the Past and Present Global Research Activities

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Abstract: Water pollution is a worldwide problem. Water consumption increases at a faster rate than population and this leads to a higher pollution rate. Sustainable Development Goals (SDG) include proposals aimed at ensuring the availability of clean water and its sustainable management (Goal 6), as well as the conservation and sustainable use of oceans and seas. The current trend consists in trying to reconcile economic growth with sustainability, avoiding the negative externalities for the environment generated by human activity. More specifically, the objective of this article is to present the evolution of the research regarding the removal of polluting pharmaceuticals that are discharged into wastewater. To do that, a bibliometric analysis of 2938 articles comprising the period 1979–2020 has been carried out. This analysis includes productivity indicators in the scientific field: journals, authors, research institutions and countries. In addition, keyword analysis allows the identification of four main axes of the research regarding the removal of pharmaceutical residues found in wastewater. The first group of articles is aimed at identifying the pharmaceuticals present in polluting effluents. The second and third groups of articles focus on presenting the procedures that enable the treatment of emerging contaminants, either from a biological point of view (second group) or a physicochemical point of view (third group). The fourth group refers to water quality and its possibilities to be reused. Finally, there is a growing trend of worldwide scientific publications, which justifies the importance of polluting residues management, especially those of pharmaceutical origin, in order to achieve a more sustainable society.



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1. Introduction

Emerging contaminants (EC) comprise a wide variety of organic compounds, mainly of synthetic origin, introduced in the environment through different anthropogenic activities and classified as potentially dangerous due to their negative impact on the environment as well as their adverse effects on living beings [1–3]. Among these, the most remarkable contaminants are pharmaceuticals, endocrine-disrupting compounds, disinfection by-products, hygiene and personal care products, surfactants, flame retardants, industrial compounds, domestic products, agrochemicals and microplastics [4–8].

This study is focused on pharmaceuticals, which represent one of the most significant groups [9] because of an increase in their consumption caused the rise in the global population [10]. Among pharmaceuticals, it is important to highlight analgesics, lipid regulators, antibiotics, diuretics, non-steroidal anti-inflammatory drugs, stimulants, antiseptics, beta-blockers, antimicrobials, as well as their metabolites and transformation products [8]. These contaminants are introduced in the environment during their production through

wastewater coming from urban areas and hospitals. Some of their potentially negative effects on the environment are their high and chronic toxicity on the biota, the proliferation of antibiotic-resistant microorganisms, endocrine disruption in animals and humans, as well as the presence of pharmaceuticals and metabolites derived from them in different aquatic ecosystems [11–15].

In this context, wastewater flows represent primary reservoirs for all types of EC, mainly pharmaceuticals. Conventional wastewater treatment plants are not able to completely eliminate these contaminants, which therefore remain in their effluents and are finally discharged into the aquatic ecosystems previously mentioned [2,16]. Metabolites and degradation by-products, like most pharmaceuticals, are not biodegradable and remain in water even after being treated with conventional processes. Consequently, they tend to bioaccumulate in the environment [15,17].

In this respect, different water treatment technologies have been developed over the years and have proven to be effective in order to remove or degrade those pharmaceuticals present in wastewater. These treatments can be classified into biological, physical and chemical processes [15,18,19].

This study aims at analyzing the evolution of scientific production on removal of pharmaceuticals from wastewater during the period 1979–2020, examining the most widely used processes for that treatment. To the authors' knowledge, this is the first study of this nature and it is therefore appropriate to carry out a bibliometric analysis on this subject so as to know the research trend in scientific community over the last four decades as well as potential future trends. Table 1 includes the 10 most cited articles in relation to the aim of this study.

Table 1. Main articles reviewed in relation to the objective of the research topic.

Year	Article Title [Reference]	Journal	Author(s)	Cites
2009	Pharmaceuticals and endocrine disrupting compounds in U.S. drinking water	Environmental Science and Technology	Benotti M.J., Trenholm R.A., Vanderford B.J., Holady J.C., Stanford B.D., Snyder S.A.	1147
2004	Behavior of pharmaceuticals, cosmetics and hormones in a sewage treatment plant	Water Research	Carballa M., Omil F., Lema J.M., Llombart M., García-Jares C., Rodríguez I., Gómez M., Ternes T.	1123
2007	Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking, and waste waters	Water Research	Kim S.D., Cho J., Kim I.S., Vanderford B.J., Snyder S.A.	987
2009	The removal of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs during wastewater treatment and its impact on the quality of receiving waters	Water Research	Kasprzyk-Hordern B., Dinsdale R.M., Guwy A.J.	915
2004	Persistence of pharmaceutical compounds and other organic wastewater contaminants in a conventional drinking-water-treatment plant	Science of the Total Environment	Stackelberg P.E., Furlong E.T., Meyer M.T., Zaugg S.D., Henderson A.K., Reissman D.B.	756
2003	Ozonation: A tool for removal of pharmaceuticals, contrast media and musk fragrances from wastewater?	Water Research	Ternes T.A., Stüber J., Herrmann N., McDowell D., Ried A., Kampmann M., Teiser B.	752
2006	Biological degradation of pharmaceuticals in municipal wastewater treatment: Proposing a classification scheme	Water Research	Joss A., Zabczynski S., Göbel A., Hoffmann B., Löffler D., McArdell C.S., Ternes T.A., Thomsen A., Siegrist H.	742

Table 1. Cont.

Year	Article Title [Reference]	Journal	Author(s)	Cites
2009	Fate and distribution of pharmaceuticals in wastewater and sewage sludge of the conventional activated sludge (CAS) and advanced membrane bioreactor (MBR) treatment	Water Research	Radjenović J., Petrović M., Barceló D.	735
2007	Role of membranes and activated carbon in the removal of endocrine disruptors and pharmaceuticals	Desalination	Snyder S.A., Adham S., Redding A.M., Cannon F.S., DeCarolis J., Oppenheimer J., Wert E.C., Yoon Y.	719
2003	Occurrence and fate of carbamazepine, clofibrac acid, diclofenac, ibuprofen, ketoprofen, and naproxen in surface waters	Environmental Science and Technology	Tixier C., Singer H.P., Oellers S., Müller S.R.	708

2. Materials and Methods

A bibliometric analysis has been applied to a sample of 2938 documents, published between 1979 and 2020, which were obtained from Scopus database. The documents that have been selected include final versions of articles, books and chapters dealing with the topic of removal of pharmaceuticals from wastewater.

Bibliometric analysis has been proven reliable in different fields of study [20–22] and has been applied to more than 3200 researches. By means of this analysis, it is possible to present a group of indicators of scientific production, such as: evolution of the number of scientific articles published; productivity of authors, institutions and countries; total number of papers published on each subject; total number of citations per author; productivity of main journals dealing with this subject; h-index and SJR impact factor of main documents. Most of these indicators have been presented through collaboration network maps, of both authors and countries, although they have proven particularly useful when it comes to identifying new research trends based on the use of keywords and semantic structure of researches [23–25]. In order to analyze keywords, they were classified taking into consideration a similar meaning but a different spelling. However, keywords like “article” or “review” were excluded, as they did not contribute to data analysis.

VOSviewer software, version 1.6.11. (Leiden University, Leiden, the Netherlands), was used in order to create and analyze networks through co-authorship and co-citation maps. In this regard, VOSviewer has become a highly useful tool for bibliometric analysis [26,27].

Table 2 presents the main stages of the analysis that has been carried out and those aspects that were considered for the selection of the sample, the bibliographic database and the software used for the creation and graphic representation of the information. After identifying the main terms used by researchers in order to refer to the subject of study, the documents obtained were analyzed by combining the different search fields in Scopus database. The fields “title”, “abstract” and “keyword” presented an accurate selection of the documents related to this subject. The reason why Scopus database was chosen is that it contains a high volume of scientific documents (70 million documents) undergoing the process of peer review in which more than 5000 editors participate [28]. This database presents an efficient and rapid documentation management thanks to its management tools [29], in contrast to other databases [30].

Table 2. Stages of bibliometric analysis process.

Stages of the Process	Selection Criteria	Results
1. Pre-analysis	1.1. Search and analysis of the terms “pharmaceutical”, “wastewater” and “removal” in Scopus database. 1.2. Verification of the publication period and the papers’ coincidence with the conceptual term and research field.	(TITLE-ABS-KEY (“pharmaceutical”) and TITLE-ABS-KEY (wastewater) and TITLE-ABS-KEY (removal)) and DOCTYPE (ar or bk or ch) and PUBYEAR <2021 SCOPUS—2940 document results between 1974 and 2020.
2. Data exploitation (categorization and coding)	2.1. Analysis of the amount and typology of the documents contained in SCOPUS database.	SCOPUS—2938 document results. Two documents were removed from 1974 and 1978. Indicators and bibliometric maps with VOSViewer - Networking maps of relationship between authors
3. Processing of the outcome	3.1. Assessment of the type of analysis, indicators and tools for scientific mapping through VOSViewer	- Co-occurrence of keywords - Evolution of the publication of documents on this subject. - Identification of the main lines of research.

Source: own elaboration.

3. Results and Discussion

3.1. Evolution of Scientific Production

Table 3 shows the main characteristics of the research on removal of pharmaceuticals from wastewater (RPW). This study analyzes the entire scientific production, with the exception of two documents published in 1974 and 1978. Consequently, the study period starts in 1979 and finishes in 2020. The analysis covers 42 years and is divided into 6 periods, of seven years of research each.

Table 3. Removal of pharmaceuticals from wastewater (RPW): major characteristics.

Period	A	AU	C	TC	TC/A	J
1979–1985	4	8	4	3	0.75	2
1986–1992	14	44	9	11	0.79	8
1993–1999	21	64	15	76	3.62	14
2000–2006	133	414	30	1128	8.48	56
2007–2013	709	2202	66	20,059	28.29	213
2014–2020	2057	6590	91	83,147	40.42	432

A = articles per period; AU = number of authors; C = number of countries, TC = total citations in articles; TC/A = total citations per article; J: number of journals per period.

The first period analyzed (1979–1985) includes a total of four publications on RPW while the last period (2014–2020) contains a total of 2057 publications. This growing trend is not only shown in the number of researches on RPW but also in the rest of variables considered in the table. A total of 8 authors of scientific production participate in the first period of analysis (1979–1985), which means 0.09% of total authors in the sample. The number of authors in the last period (2014–2020) amounts to 6590, which represents 77.13% of the sample. In addition, the average of authors per article, which is obtained by associating number of authors with publications per period, ranges from 2 in the first period to 3.20 in the last period.

There is a total of 93 countries participating in the research on RPW. The first period specified in the table (1979–1985) includes 4 countries, which represents 4.30% of the sample. The last period (2014–2020) includes the participation of all the countries in the sample, with the exception of two of them, which means 97.85% of the sample. A total of 104,424 citations are recorded within the time frame analyzed. Three citations are registered between 1979 and 1985 while the number of citations in the period 2014–2020 amounts

to 83,147. Hence, the average of citations per article rises from 0.75, in the first period, to 40.42 in the last period. The number of journals taking part in this research is 574. The lowest value is registered in the first period (1979–1985) with 2 journals, which means 0.35% of the sample. However, the highest value is found in the two last periods, 2007–2013 and 2014–2020, with a total of 213 and 432 journals respectively. The representation value according to the total sample of journals is 37.11% for the period 2007–2013 and 75.26% for the last period (2014–2020). Finally, the average of articles per journal increases from 2 articles in 1979–1985 to 4.76 in the last period.

The total sample of publications analyzed in this study comprises 2938 documents. The first period specified in Table 3 (1979–1985) includes four publications, which represent 0.14% of the sample. The second period, from 1986 to 1992, includes 14 researches, which means a representation of 0.48%. The third period, 1993–1999, includes 21 documents and represents 0.71% of the sample analyzed. From 2000 to 2006, the number of publications rises to a total of 133 and represents 4.53% of the sample obtained. There are 709 researches in the period 2007–2013, which means a representation of 24.13% in the sample. The last period analyzed (2014–2020), with a representation of 70.01% of the sample, includes a total of 2057 publications.

Scientific production up to the year 2000 has not been analyzed in detail due to the fact that before 2000 the problem of environmental pollution by drugs was very rarely addressed by scientists, also due to the lack of highly sensitive analytical equipment in most countries in the world. Therefore, Figure 1 represents the research published annually from 2000 to the present. The greatest variation percentage (200%) is found in 2001, when the number of publications changes from two to six. The following year is 2003, with a variation of 150%: from eight to twenty publications. The first year registering more than 100 annual publications is 2011. The highest number of publications is produced in 2020, with a total of 417 researches.

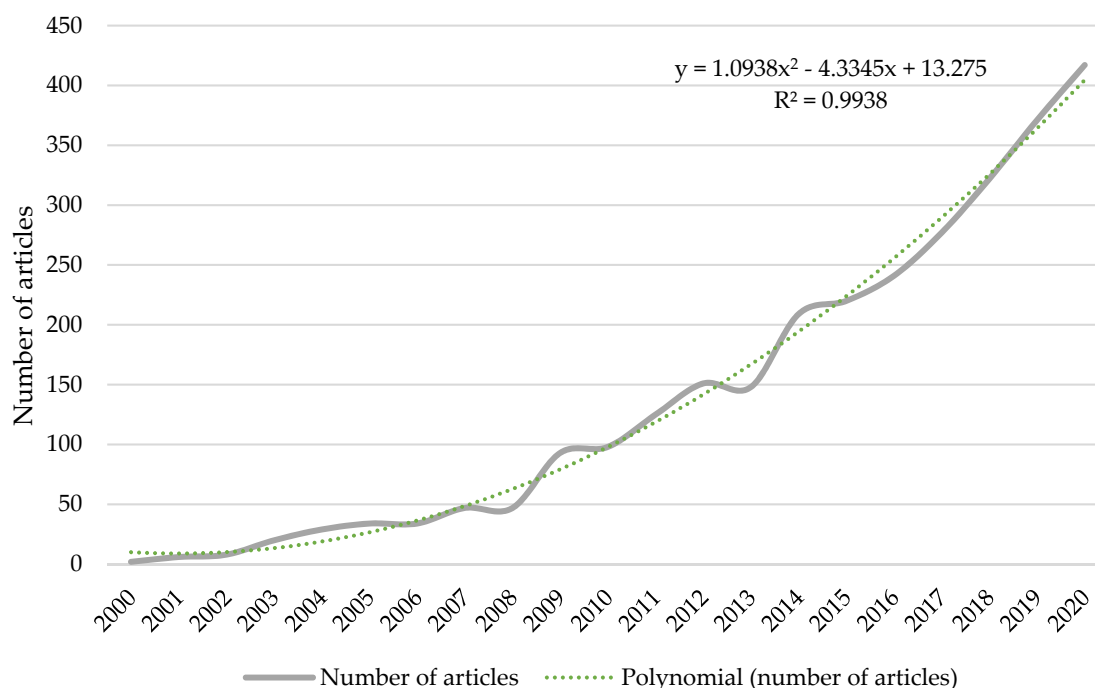


Figure 1. Number of published documents from 2000 to 2020.

3.2. Analysis of Scientific Production per Subject Category

Scopus database allows classifying the analyzed sample in different categories, depending on the interest of the authors and the publishers. Variables such as the type of journals in which it is published, main keywords, the title of the research or the object of

study make it possible for the database to frame the research in a single category or in several at the same time. In this case, the researches included in the sample have been classified into 23 categories. The evolution of the main categories, together with the number of publications that are included annually under each of them, is represented in Figure 2.

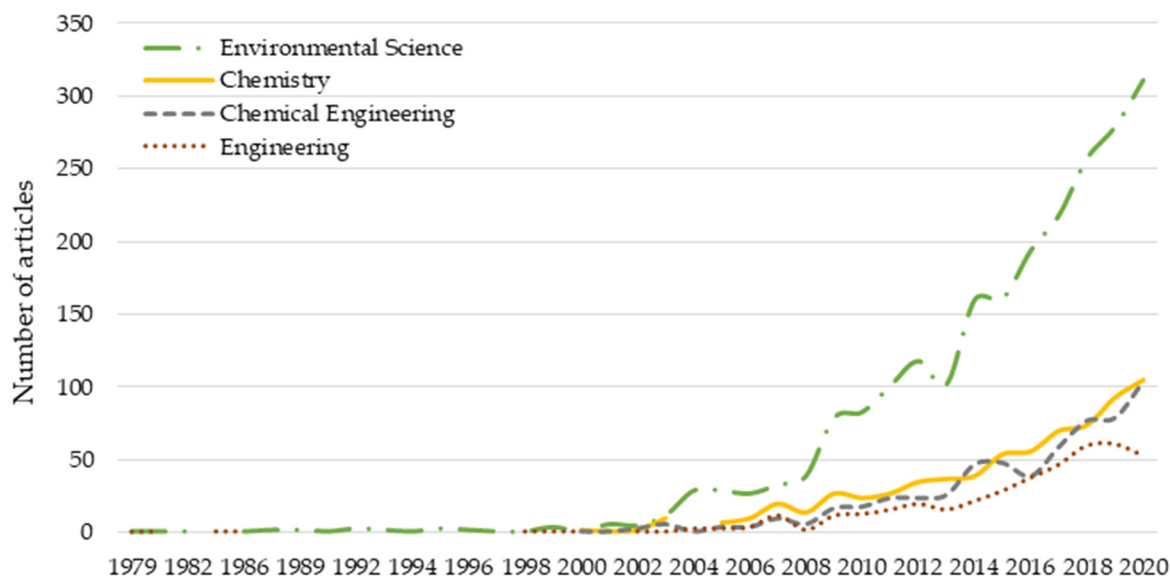


Figure 2. Comparison of growth trends of the main subject areas in the period studied.

The category with the highest representation is environmental science. This category leads the classification, as it contains 2270 researches and represents 43.35% of the sample analyzed. In addition, it stands out as a reference in the researches that have been carried out, as it contains publications from 42 years of scientific production, with the exception of 1985, when no documents were registered. Regarding the percentage variation experimented along the periods analyzed, the period 2000–2006 presents the highest value (679%), changing from 14 to 109 researches. The following discipline is chemistry, with a total of 710 publications and 13.56% of representation in the sample. The first document was published in 1980, but it was not considered annually in the researches carried out until 2005. The highest variation percentage is included in the period 2000–2006, with a value of 1500%, ranging from 2 to 32 documents. The category chemical engineering is in the third position. This discipline contains 602 published researches and represents 11.50% of the sample. Its first publication was registered in 1980 and, although occasionally considered in several researches (1992, 1996 and 1998), it was taken again into annual consideration as a subject category from 2000. As a result, the highest variation percentage (900%) is located in the period 2000–2006, changing from 2 to 20 researches. Engineering is in the fourth place, with a total of 419 publications and 8.00% of representation. The first research under this discipline, like the two previous disciplines, was carried out in 1980 and contains two additional researches in this first period (1979–1985). Since 1998, it has become established as the main category where annual researches are classified. Its highest number of publications is registered in 2018, with a total of 60 documents, and the highest variation percentage (600%) is produced in 2007–2013, changing from 13 to 91 researches.

Each publication is classified into one or more subject categories, depending on the authors' and publisher's interest. In this case, there is a total of 5236 documents classified into 23 disciplines. This value exceeds the sample analyzed (2938 researches). A total of 4001 researches belong to the four main categories mentioned, which represents 76.41% of the sample. The rest of subject categories (19) are not taken into consideration in Figure 2, as they account for less than 5% of the sample.

3.3. Identification of Most Prolific Journals on RPW

The sample of 2938 documents has been published in a total of 574 journals. Table 4 shows the 20 most prolific journals, which include 1555 articles and represent 52.93% of the sample. This table covers the number of publications included in each of those journals, the total number of citations [31], the average of citations per article, the h-index [32], the country to which those journals belong and the impact factor according to Scimago Journal Rank [33]. Regarding the publications included in the sample, several elements have been analyzed: h-index of documents, publication date of the first article and the most recent publication issued by each journal in the table. The journals are American and European, with the last one representing 80% of the journals included in the table. More specifically, the most significant journals are those from the Netherlands and United Kingdom. With regard to the quartile to which they belong, 15 journals belong to the first quartile, meaning 75% of the journals included in the table; four journals are classified under the second quartile (20%) and one journal is included in the third quartile (5%).

Table 4. Most active journals on RPW from 1979 to 2020.

Journal	A	TC	TC/A	H Index Articles	H Index Journal	SJR	C	1st Article	Last Article
<i>Water Research</i>	241	26,696	110.77	87	285	2.932(Q1)	Netherlands	1988	2020
<i>Science of the Total Environment</i>	208	9833	47.27	53	224	1.661(Q1)	Netherlands	2004	2020
<i>Journal of Hazardous Materials</i>	132	8224	62.30	53	260	2.010(Q1)	Netherlands	2003	2020
<i>Chemosphere</i>	126	5839	46.34	46	228	1.530(Q1)	UK	2003	2020
<i>Water Science and Technology</i>	126	2829	22.45	31	131	0.471(Q2)	UK	1982	2020
<i>Environmental Science and Pollution Research</i>	118	2170	18.39	27	98	0.788(Q2)	Germany	2007	2020
<i>Chemical Engineering Journal</i>	100	3550	35.50	36	198	2.315(Q1)	Netherlands	2009	2020
<i>Desalination and Water Treatment</i>	69	536	7.77	13	51	0.327(Q2)	USA	2009	2019
<i>Bioresource Technology</i>	59	2447	41.47	32	273	2.430(Q1)	Netherlands	1992	2020
<i>Environmental Science and Technology</i>	49	6897	140.76	36	373	2.704(Q1)	USA	2003	2020
<i>Journal of Environmental Chemical Engineering</i>	44	707	16.07	16	60	0.927(Q1)	UK	2014	2020
<i>Journal of Environmental Management</i>	40	774	19.35	16	161	1.321(Q1)	USA	2004	2020
<i>Environmental Technology United Kingdom</i>	35	317	9.06	12	71	0.485(Q2)	UK	1992	2020
<i>Separation and Purification Technology</i>	34	990	29.12	15	155	1.209(Q1)	Netherlands	2007	2020
<i>Water Switzerland</i>	33	155	4.70	7	42	0.657(Q1)	Switzerland	2012	2020
<i>Environmental Pollution</i>	31	1721	55.52	16	211	1.968(Q1)	UK	2009	2020
<i>Journal of Chemical Technology and Biotechnology</i>	29	431	14.86	13	111	0.661(Q1)	UK	1996	2020
<i>Water Environment Research</i>	28	537	19.18	10	69	0.301(Q3)	USA	2005	2019
<i>Desalination</i>	27	3133	116.04	21	169	1.814(Q1)	Netherlands	1980	2018
<i>Journal of Water Process Engineering</i>	26	172	6.62	8	35	0.808(Q1)	UK	2014	2020

A = number of articles; TC = total citations for all articles; TC/A = number of citations per article; SJR = Scimago journal rank (quartile); C = country; UK = United Kingdom; USA = United States of America.

Water research is at the top of the table. This journal from the Netherlands has the highest volume of publications (241), total citations (26,696), h-index in publications (87) and impact factor (2.932). It has a long background, since it issued its first publication in the first period and still continues conducting researches in this field. The publication *Behavior of Pharmaceuticals, Cosmetics and Hormones in a Sewage Treatment Plant* [34] has a total of 1113 citations and, consequently, becomes the most cited publication in the journal and the second most cited document of the sample. The journal *Science of the Total Environment* occupies second position. This journal, which is also from the Netherlands, includes 208 researches, a total of 9833 citations, an average of 47.27 citations per article and an h-index of 224. It belongs to the first quartile, with an impact factor of 1.661, and currently continues publishing on RPW. The *Journal of Hazardous Materials*, also coming from the

Netherlands, occupies the third position in the table. Among its main characteristics, it is important to highlight 132 published researches, a total of 8224 citations received, an average of 62.30 publications per article and an h-index value of 260. *Environmental Science and Technology* is the journal appearing in the tenth position. This American journal stands out for having the highest values regarding the average of citations (140.76) and the h-index of the journal (373).

Regarding the dates of publication, the journals *Water Science and Technology* and *Desalination* are the only ones publishing researches in the first period analyzed (1979–1985). In the case of the British Journal, *Water Science and Technology*, the publication was issued in 1982 under the title “Single Sludge Nitrogen Removal from Industrial Wastewater” [35]. The second journal, from the Netherlands, published the article “Experience with Plate-and-Frame Ultrafiltration and Hyperfiltration Systems for Desalination of Water and Purification of Wastewater” in 1980 [36], which makes it the first journal in the table that published a research belonging to this study field. In addition, the *Journal of Environmental Chemical Engineering* and the *Journal of Water Process Engineering* should be highlighted, as they have a short research background and both have published their first research in 2014. This journal is followed by *Water Switzerland*, being the third journal with the shortest background. This Swiss journal is in the 15th position among the most prolific ones and in the 12th position in the ranking of the last period analyzed, despite carrying out its first publication in 2012.

3.4. Productivity of Most Relevant Authors from 1979 to the Present Day

The current sample has been produced by a total of 8542 authors. Table 5 shows the 10 most prolific authors, who represent 0.12% of total authors and 9.26% of the sample of researches. The table shows the main characteristics of the authors, like published researches, number of citations received, average of citations, institution to which they belong or h-index [37]. The origin of the authors considered in the table is varied, as it is possible to find American, Asian and European authors. However, the number of European authors is higher, accounting for 60% of the table. It is important to highlight the date in which these authors published their last researches, as all of them (with the exception of Josep Maria Bayona) have published in the last year analyzed (2020).

Table 5. Most prolific authors from 1979 to 2020.

Authors	A	TC	TC/A	Institution	C	1st Article	Last Article	H Index
Barceló, D.	50	4603	92.06	Catalan Institute for Water Research	Spain	2003	2020	32
Bester, K.	31	586	18.90	Aarhus Universitet	Denmark	2007	2020	14
Yu, G.	31	1448	46.71	Tsinghua University	China	2010	2020	20
Rodríguez-Mozaz, S.	28	1552	55.43	Catalan Institute for Water Research	Spain	2012	2020	20
Snyder, S.A.	26	4861	186.96	The University of Arizona CSIC-Instituto de	USA	2004	2020	20
Bayona, J.M.	25	2480	99.20	Diagnóstico Ambiental y Estudios del Agua (IDAEA)	Spain	2005	2016	23
Deng, S.	24	1281	53.38	Tsinghua University CSIC-Instituto de	China	2010	2020	16
Matamoros, V.	24	2352	98.00	Diagnóstico Ambiental y Estudios del Agua (IDAEA)	Spain	2005	2020	21
Petrovic, M.	23	3773	164.04	Catalan Institute for Water Research	Spain	2003	2020	20
Huang, J.	21	1233	58.71	Tsinghua University	China	2010	2020	16

A = number of articles; TC = total citations for all articles; TC/A = number of citations per article; C = Country; USA = United States of America.

Damià Barcelò, who is at the top of the list, belongs to the Catalan Institute for Water Research. This Spanish author has 50 publications, a total of 4603 citations and an average of 92.06 citations per publication. He stands out for being the author with the broadest research background, together with Mira Petrovic, and for having the highest h-index, with a value of 32. His first research on this study field is called Analysis and Removal of Emerging Contaminants in Wastewater and Drinking Water [38], with a total of 499 citations. The author Kai Bester is in the second position. This Danish author registers 31 researches on RPW, a total of 586 citations, an average of 18.90 citations per document and an h-index of 14. He belongs to Aarhus Universitet and he continues publishing on this research field at present. Shane A. Snyder, in the fifth position, is the author with the highest value of total citations (4861) and average of citations (186.96), as in 2009 he published the most cited research of the sample analyzed [39]. This author comes from the University of Arizona (USA) and has 26 researches and an h-index of 20. Sara Rodríguez-Mozaz is in the fourth position. She stands out for having a short research experience, as she first published on this research line in 2012. A total of 28 documents have been published in nine years, with 1552 citations, an average of citation of 55.43 and an h-index of 20. This Spanish author, along with Mira Petrovic, does not appear in Scopus with the same values as those shown in the table. This is due to the fact that, despite being the same researchers, their publications have been divided into two different signatures: one of them takes into account the accent marks over the surnames and another one that does not. In fact, Figure 3 includes these authors with both signatures registered in Scopus. The rest of authors have very similar values, this is, publications between 20 and 30, a total of citations of 1000–2000 and an h-index of 16–20. Finally, regarding the institutions to which the main authors belong, the most significant ones, representing 70% of the authors in the table, are: Tsinghua University, Spanish National Research Council (CSIC) -Institute of Environmental Assessment and Water Research (IDAEA), and the Catalan Institute for Water Research.

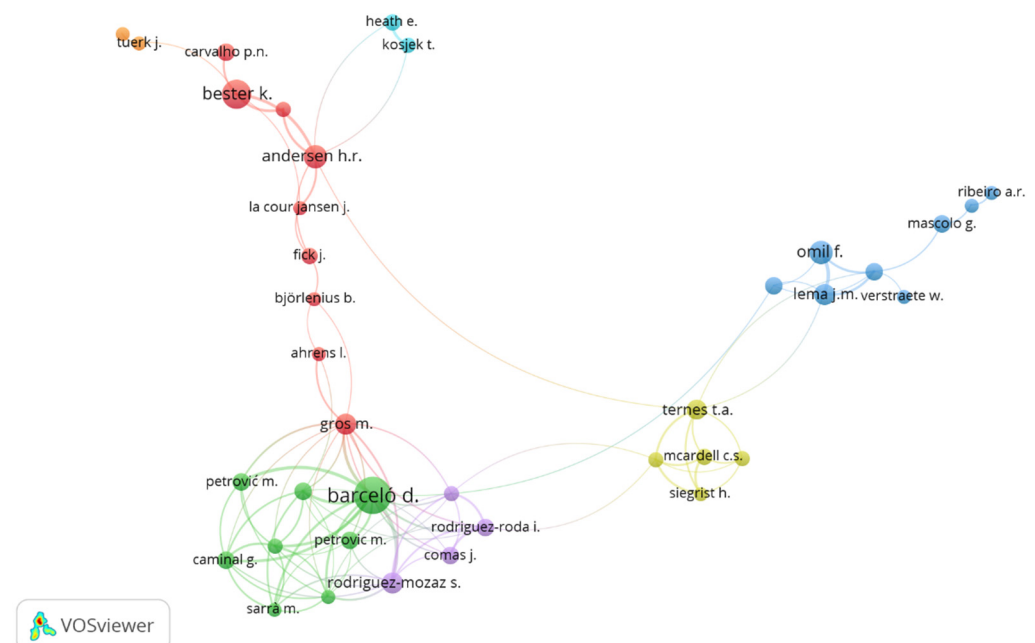


Figure 3. Network of cooperation based on co-authorship of the main authors.

The tool VOSviewer allows representing graphically the collaboration relationships established between countries, authors, institutions, etc. A map of collaboration between the main authors (from co-authorship) is represented in Figure 3. In order to produce the chart, the 108 most prolific authors, from which only 38 have a cooperation relationship of research on RPW, have been included. The collaboration groups are identified by means

of different colors. The size of the circles indicates the volume of documents belonging to each author whereas the line width joining the authors makes reference to the collaboration network with other authors.

The first and largest cluster is represented in red. This collaboration group is led by one of the most prolific authors, Kai Bester. Some of the authors composing the cluster are Henrik Rasmus Andersen, with 20 researches, Meritxell Gros, with 17 documents, Pedro N. Carvalho, with 11 publications, and Berndt Björleinius, with 7. As observed in the representation, most of the authors do not collaborate with each other, but publish specific researches with some of the authors. For instance, Pedro N. Carvalho collaborates with Kai Bester [40], Henrik Rasmus Andersen publishes with Kai Bester [41] and Henrik Rasmus Andersen investigates with Jes la Cour Jansen [42]. However, no joint research collaboration is found between these authors. The green cluster is led by the prolific authors Damia Barcelò and Mira Petrovic. This collaboration group is formed by seven Spanish authors, including Glòria Caminal and Montserrat Sarrà. The purple cluster includes the prolific author Sara Rodríguez-Mozaz and some other Spanish authors like I. R. Rodríguez-Roda or Joaquim Comas. As shown in the figure, these authors also have a cooperation relationship with the authors from the green cluster. It is because of this that, although belonging to different groups, they have joint researches [43–45]. Thomas A. Ternes, with 14 researches, Christa S. McCardell, with 10 researches, and Adriano Joss, with 9 documents, are included in the yellow cluster. One of the researches conducted by these authors is “Oxidation of Pharmaceuticals during Ozonation of Municipal Wastewater Effluents: A Pilot Study” [46], although numerous researches on RPW are registered [47–49]. The dark blue cluster is composed by Francisco Omil, with 20 publications, Lema, J. M., with 17 researches, Giuseppe Mascolo, with 11, Ana R. Lado Ribeiro, with 9, and Willy Henry Verstraete, with 8. The nationality of this collaboration group is varied, as it contains, among others, Italian, Portuguese, Spanish and Belgian authors. The orange cluster represents the close collaboration between the Turkish author Ilda Vergili and the German author Jochen Tuerk [50,51]. Finally, the light blue cluster represents the close cooperation between Ester Heath and Tina Kosjek [52–55]. Both authors are Slovenian and belong to the same institution (Jozef Stefan Institute).

3.5. Characteristics of Main Institutions

Table 6 shows the 10 most prolific institutions in the time frame analyzed (1979–2020). The table shows the country to which these institutions belong, number of publications, total of citations received, average of citations per document and h-index. In addition, the international activity developed by these institutions is taken into account. Consequently, the collaboration index of the publications and the citations received for national and international documents are specified. The total sample of institutions is 6432 and, therefore, these 10 institutions represent 0.16% of the total. However, they cover 562 researches, which represents 19.13% of the sample. Nationalities are varied, although Spanish and Chinese are the commonest.

CSIC-Institute of Environmental Assessment and Water Research IDAEA [56] is at the top of the list. This Spanish institution overtakes the rest in number of documents (80), total of citations (5847), average of citations (73.09) and h-index (42). The Ministry of Education in China is in the second position in the table. This Chinese institution registers 75 researches, a total of 2042 citations, an average of 27.23 citations per article and an h-index of 26. Despite not containing any journal or author of French origin, it is remarkable that CNRS Centre National de la Recherche Scientifique is included in this table. Even so, as observed in its values, it has the lowest number of total citations (787), average of citations (14.57) and h-index (16). It is remarkable that 9 out of the 10 most prolific authors belong to the institutions appearing in the first, fourth, eighth and ninth positions.

Table 6. Characteristics of the most outstanding institutions.

Institution	C	A	TC	TC/A	H Index	IC (%)	TCIC	TCNIC
CSIC-Instituto de Diagnóstico Ambiental y Estudios del Agua IDAEA	Spain	80	5847	73.09	42	38.75%	44.68	91.06
Ministry of Education China	China	75	2042	27.23	26	20.00%	41.53	23.65
Universitat de Girona	Spain	71	4481	63.11	36	43.66%	38.16	82.45
Tsinghua University	China	68	2776	40.82	27	26.47%	39.94	41.14
CNRS Centre National de la Recherche Scientifique	France	54	787	14.57	16	44.44%	13.92	15.10
Chinese Academy of Sciences	China	51	2159	42.33	28	33.33%	45.88	40.56
Harbin Institute of Technology	China	47	1045	22.23	18	21.28%	29.90	20.16
Catalan Institute for Water Research	Spain	44	3179	72.25	23	45.45%	30.35	107.17
Aarhus Universitet	Denmark	38	1159	30.50	19	68.42%	37.19	16.00
Universidade do Porto	Portugal	34	1485	43.68	18	47.06%	68.19	21.89

C = country, A = number of articles; TC = total citations for all articles; TC/A = total citations per article; IC = percentage of articles made with international collaboration; TCIC = number of citations in articles with international collaboration; TCNIC = number of citations in articles without international collaboration.

Regarding international cooperation, CSIC-Institute of Environmental Assessment and Water Research IDAEA registers 38.75%. However, the institution Aarhus Universitet has the highest value (68.42%), having conducted 12 researches with no international collaboration and 26 publications with international collaboration. On the contrary, Ministry of Education China is the institution with the lowest collaboration index (20%), with 60 national collaborations and 15 international collaborations. The rest of Chinese institutions present very similar values concerning collaboration index, with the lowest values in the table. The number of total citations for articles produced nationally and internationally is balanced, as 50% of them have more citations in the publications with international collaboration and 50% register more citations in national researches. Universidade do Porto stands out for registering the highest number of total citations for international researches (68.19) and the Catalan Institute for Water Research registers the highest number of total citations for national researches (107.17). Finally, the institution CNRS Centre National de la Recherche Scientifique possesses the lowest value of total citations for both international (13.92) and national (15.10) researches.

3.6. Main Countries in Scientific Production on RPW

Table 7 shows the characteristics of the most relevant countries in the research. It shows the researches conducted by each country, total citations received, average of citations per document, h-index and dates of the first and last research, together with the position they have in each period. These 10 countries cover 2277 publications, representing 77.50% of the sample. The current interest in this research field is remarkable, since all the countries continue publishing during the last year analyzed (2020).

Table 7. Most relevant countries in number of articles.

Country	A	TC	TC/A	H Index	First Article	Last Article	R (A)					
							1979–1985	1986–1992	1993–1999	2000–2006	2007–2013	2014–2020
China	572	13,300	23.25	59	1990	2020	0	4(1)	3(2)	5(11)	2(118)	1(440)
Spain	379	20,957	55.30	78	1995	2020	0	0	12(1)	3(14)	1(119)	2(245)
United States	351	18,837	53.67	73	1982	2020	3(1)	8(1)	5(2)	2(22)	3(107)	3(218)
India	216	3123	14.46	31	1992	2020	0	6(1)	1(3)	6(11)	5(45)	4(156)
Germany	174	11,735	67.44	54	1995	2020	0	0	4(2)	1(23)	4(52)	5(97)
Italy	132	4842	36.68	37	2002	2020	0	0	0	10(5)	6(33)	7(94)
Canada	118	3851	32.64	33	1988	2020	0	3(1)	0	22(1)	9(27)	8(89)
France	113	3784	33.49	31	2004	2020	0	0	0	12(3)	11(23)	9(87)
United Kingdom	113	4829	42.73	36	1992	2020	0	7(1)	14(1)	9(7)	8(31)	11(73)
Iran	109	1420	13.03	22	2009	2020	0	0	0	0	19(12)	6(97)

A = number of articles; TC = total citations for all articles; TC/A = number of citations per article; R = rank position by number of published articles.

China is at the top of the list with 572 publications, 13,300 total citations, an average of citations per document of 23.25 and an h-index of 59. Its first research was published in 1990 and continues working on RPW nowadays. Spain, with 379 documents, is the second country in the list. This country has the highest value of total citations (20,957) and h-index (78). Its first research was published in the third period analyzed. However, in the last period analyzed (2014–2020), it has managed to reach the second position in the list, with 245 documents. Iran, in the last position, has the lowest values regarding publications (109), total citations (1420), average of citations per document (13.03) and h-index (22). This is due to the fact that it has a short background regarding this research line, as it was the last country to publish on RPW, more specifically in 2009. On the contrary, USA, which is in the third position, is the country with the longest research background, since it registers one research in the first period analyzed (1979–1985). The countries experiencing the highest variation with respect to the number of publications during the period 2000–2006 are Spain, USA, Germany and UK. The countries with the highest variation percentage in the period 2007–2013 are China, India, Italy, Canada and France. Finally, the country with the most significant variation in the last period analyzed (2014–2020) is Iran due to the fact that it entered this line of research relatively recently.

All the countries included in the table have made valuable contributions to the scientific production on RPW. However, some countries have managed to make their researches become a reference in this study field. For the three most cited publications of the table (out of the 2277 included), the title and the country of origin have been specified. In the first place, USA reaches 1144 citations and conducted the most cited research of the sample under the title “Pharmaceuticals and Endocrine Disrupting Compounds in U.S. Drinking Water” [39]. In the second place, Spain and Germany elaborated the article “Behavior of Pharmaceuticals, Cosmetics and Hormones in a Sewage Treatment Plant” [34], which was published in 2004 and has 1113 citations. In the third place, UK registers a research with a total of 907 citations. This research was published in 2009 and is entitled “The Removal of Pharmaceuticals, Personal Care Products, Endocrine Disruptors and Illicit Drugs during Wastewater Treatment and its Impact on the Quality of Receiving Waters” [57]. The researches conducted by USA, with 1144 citations, and the one conducted by Spain and Germany, with 1113 citations, occupy the first and second positions, respectively, in the sample of 2938 documents. UK is in the fifth position in the total sample analyzed (with 907 citations).

The countries listed in the table conduct researches on RPW at both national and international levels. Table 8 includes the main characteristics of this cooperation between countries. The variables shown are: number of collaborators from each country, the five main countries of cooperation, collaboration index and total citations received in both national and international articles.

Table 8. International collaboration of the most prolific countries.

Country	NC	Main Collaborators	IC (%)	TC/A	
				IC	NIC
China	38	United States. Australia. Japan. Hong Kong. Singapore.	29.02%	35.11	18.40
Spain	50	Portugal. Italy. Germany. Brazil. United Kingdom.	38.79%	47.61	60.16
United States	44	China. Singapore. Canada. Taiwan. South Korea.	53.85%	48.02	60.25
India	37	United States. Saudi Arabia. South Korea. Japan. Oman.	27.31%	23.78	10.96
Germany	46	Spain. Switzerland. United States. China. United Kingdom.	57.47%	83.65	45.54
Italy	35	Spain. Philippines. Portugal. United States. United Kingdom.	53.79%	41.80	30.72
Canada	28	United States. China. France. United Kingdom. Spain.	42.37%	38.48	28.34
France	34	Algeria. Canada. Spain. Cuba. Germany.	46.02%	23.13	42.31
United Kingdom	37	China. Germany. United States. Spain. Australia.	69.03%	30.74	69.46
Iran	18	Italy. Jordan. Saudi Arabia. Spain. Turkey.	18.35%	11.95	13.27

NC = number of collaborators; IC = percentage of articles made with international collaboration; TC/A = number of citations per article; IC = international collaboration; NIC = no international collaboration.

China, which is at the top of the list of most prolific countries, registers a total of 38 collaborators and a collaboration index of 29.02%. USA, Australia, Japan, Hong Kong and Singapore are among the main collaborating countries. The second country in the table, Spain, presents the highest number of collaborators (50), although Germany (46) and USA (44) have very similar figures. UK presents the highest percentage of collaboration index (69.03%), followed by Germany (57.47%), USA (53.85%) and Italy (53.79%). Germany registers the highest value of average of citations for documents produced internationally, 83.65. UK registers the highest value of average of citations per article for documents produced nationally, 69.46. Finally, Iran has the lowest values for number of collaborators (18), collaboration index (18.35%), average of citations for international articles (11.95) and average of citations for national articles (13.27).

International cooperation by means of co-authorship is represented in Figure 4. Scientific production in each country is defined by the size of the circles and each cooperation group is differentiated by colors. In order to elaborate this figure, the 36 most prolific countries of the sample have been incorporated to the tool VOSviewer, obtaining a total of 5 clusters. The collaboration network is wide, as it contains countries from all the continents. As shown in the international collaboration map, Europe, in the first place, and Asia, in the second place, are the continents with more scientific contribution on RPW.

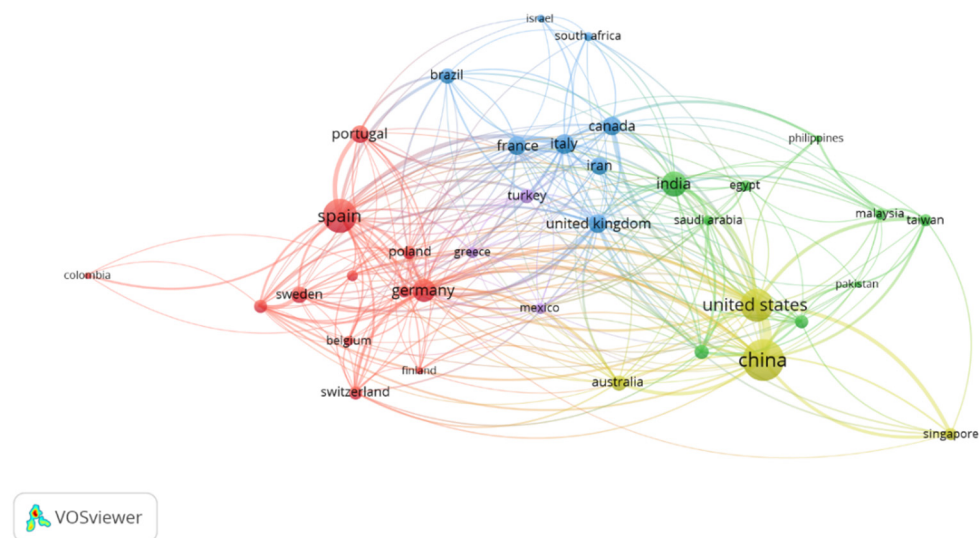


Figure 4. International cooperation based on co-authorship between countries.

The red cluster is led by Spain and Germany. It is the largest collaboration group, as it contains a total of 12 countries, including Portugal, Sweden, Switzerland, Finland, Belgium and Poland. They represent the highest per-centage of the sample analyzed, as they cover 37.51% and a total of 1102 articles. The green cluster is led by India. It is the second largest collaboration group, with a total of 9 countries. Among its members, it is possible to find Egypt, Pakistan, Saudi Arabia, Malaysia and Philippines. The scientific production represented by this collaboration group is 19.13% of the total sample and 562 publications. The blue cluster is formed by France, Italy, UK, Canada, Brazil, Iran, Israel and South Africa. It is characterized by containing the highest number of most prolific countries, with 50% of them included within the 10 countries considered in Table 7. The eight countries forming this group have a total of 723 articles and represent 24.61% of the total sample analyzed. The yellow cluster is led by USA and China. The rest of countries composing this international collaboration group are Australia and Singapore. In total, they register 1057 publications and 35.98% of the sample. Finally, the purple cluster is the most reduced one, as it is formed by only three countries (Greece, Mexico and Turkey). In total, they register 155 publications and 5.28% of the sample.

3.7. Keywords Used in Scientific Production on RPW

Keywords are used in order to define the subject of study in published researches. This information makes it possible to know the main interests generated during the time frame studied (1979–2020) and analyze the maturity of each term. Table 9 shows the 20 main keywords used along the period analyzed. The sample of 2938 documents contains a total of 17,002 keywords. However, for the following analysis, the concepts considered in the main search were excluded (wastewater, waste water, sewage, pharmaceuticals, drug, drug products, remove).

Table 9. Main keywords from 1979 to 2020.

Keyword	1979–2020		1979–1985		1986–1992		1993–1999		2000–2006		2007–2013		2014–2020	
	A	%	R (A)	%	R (A)	%	R (A)	%	R (A)	%	R (A)	%	R (A)	%
Wastewater Treatment	1701	57.9%	22(1)	25.0%	23(2)	14.3%	1(11)	52.4%	1(97)	72.9%	2(369)	52.0%	1(1221)	59.4%
Effluents	1286	43.8%	0	0.0%	62(1)	7.1%	119(1)	4.8%	4(60)	45.1%	1(408)	57.5%	2(816)	39.7%
Water Pollutants, Chemical	916	31.2%	0	0.0%	0	0.0%	266(1)	4.8%	24(19)	14.3%	7(209)	29.5%	4(687)	33.4%
Pollutant Removal	885	30.1%	0	0.0%	0	0.0%	0	0.0%	5(37)	27.8%	5(223)	31.5%	6(625)	30.4%
Waste Water Management	875	29.8%	2(3)	75.0%	2(6)	42.9%	2(10)	47.6%	3(66)	49.6%	4(267)	37.7%	7(523)	25.4%
Water Pollutant	776	26.4%	0	0.0%	0	0.0%	0	0.0%	105(8)	6.0%	33(84)	11.8%	5(684)	33.3%
Water Treatment	600	20.4%	24(1)	25.0%	24(2)	14.3%	268(1)	4.8%	7(32)	24.1%	8(199)	28.1%	13(365)	17.7%
Waste Disposal, Fluid Chemistry	574	19.5%	0	0.0%	0	0.0%	261(1)	4.8%	20(22)	16.5%	11(146)	20.6%	11(405)	19.7%
Chemistry	552	18.8%	0	0.0%	0	0.0%	0	0.0%	203(4)	3.0%	80(46)	6.5%	8(502)	24.4%
Waste Component Removal	544	18.5%	0	0.0%	0	0.0%	0	0.0%	15(25)	18.8%	9(156)	22.0%	14(363)	17.6%
Adsorption	534	18.2%	0	0.0%	11(2)	14.3%	24(2)	9.5%	26(17)	12.8%	36(82)	11.6%	10(431)	21.0%
Biodegradation	486	16.5%	0	0.0%	15(2)	14.3%	8(4)	19.0%	13(26)	19.5%	10(149)	21.0%	20(305)	14.8%
Carbamazepine	471	16.0%	0	0.0%	0	0.0%	0	0.0%	6(34)	25.6%	12(140)	19.7%	21(297)	14.4%
Pharmaceutical Preparations	465	15.8%	0	0.0%	0	0.0%	0	0.0%	38(13)	9.8%	15(125)	17.6%	16(327)	15.9%
Oxidation	446	15.2%	0	0.0%	98(1)	7.1%	10(4)	19.0%	14(26)	19.5%	18(121)	17.1%	22(294)	14.3%
Diclofenac	443	15.1%	0	0.0%	0	0.0%	0	0.0%	9(30)	22.6%	14(127)	17.9%	23(286)	13.9%
Antibiotics	429	14.6%	0	0.0%	0	0.0%	0	0.0%	40(12)	9.0%	23(103)	14.5%	17(314)	15.3%
Concentration (composition)	425	14.5%	0	0.0%	0	0.0%	0	0.0%	396(2)	1.5%	16(115)	16.2%	15(308)	15.0%
Degradation	387	13.2%	0	0.0%	57(1)	7.1%	110(1)	4.8%	34(13)	9.8%	23(100)	14.1%	21(272)	13.2%
Chemical Oxygen Demand	381	13.0%	0	0.0%	3(5)	35.7%	3(9)	42.9%	9(29)	21.8%	13(122)	17.2%	29(216)	10.5%

A = number of articles; R = rank position by number of articles published.

Wastewater Treatment, Waste Water Management and Water Treatment are the only terms with publications in the first period analyzed (1979–1985) out of the 20 main concepts used in the study on RPW. The most recent keywords have been Pollutant Removal, Water Pollutant, Chemistry, Waste Component Removal, Carbamazepine, Pharmaceutical Preparations, Diclofenac, Antibiotics and Concentration (composition). These 9 terms were first used in the period 2000–2006, therefore 35% of the most prolific terms have relatively brief maturity.

The first term of the table is wastewater treatment. This keyword contains 1701 occurrences and represents 57.9% of the sample. It contains one publication in the first period analyzed (1979–1985) [36], and 1221 in the last period (2014–2020). The second keyword of the table is effluents. This concept contains 1286 occurrences, which represents 43.8% of the total sample analyzed. This concept was first used in the second period analyzed (1986–1992), more specifically in the research “Effect of Organic Load and Reactor Height on the Performance of Anaerobic Mesophilic and Thermophilic Fixed Film Reactors in the Treatment of Pharmaceutical Wastewater” [58]. Currently, it is still in use in the last period analyzed (2014–2020), as it is in the second position with 816 occurrences. Finally, the term with the third highest number of occurrences is water pollutants, and chemical. This keyword was first used in the period 1993–1999, under the title “The influence of anaerobic pretreatment on the nitrogen removal from biosynthetic pharmaceutical wastewaters” [59]. Currently, the interest in this study field has led to an increase of 228.71% in the occurrences, as it has changed from 209 occurrences in the period 2007–2013 to a total of 687 in the last period analyzed (2014–2020).

Figure 5 has been elaborated taking into account the time frame studied (1979–2020), with the aim of analyzing the maturity of each main term used in the research line concerning RPW. In order to do so, the period represented in the time line is 2013–2017. The terms in dark blue make reference to the keywords with greater maturity, as they cover researches in the first years of the study. On the contrary, the terms in light green and yellow indicate that they have recently been incorporated into the research on RPW. In addition, the most prolific terms of each period are specified in order to complete the analysis and get to know in which exact period they were cited.

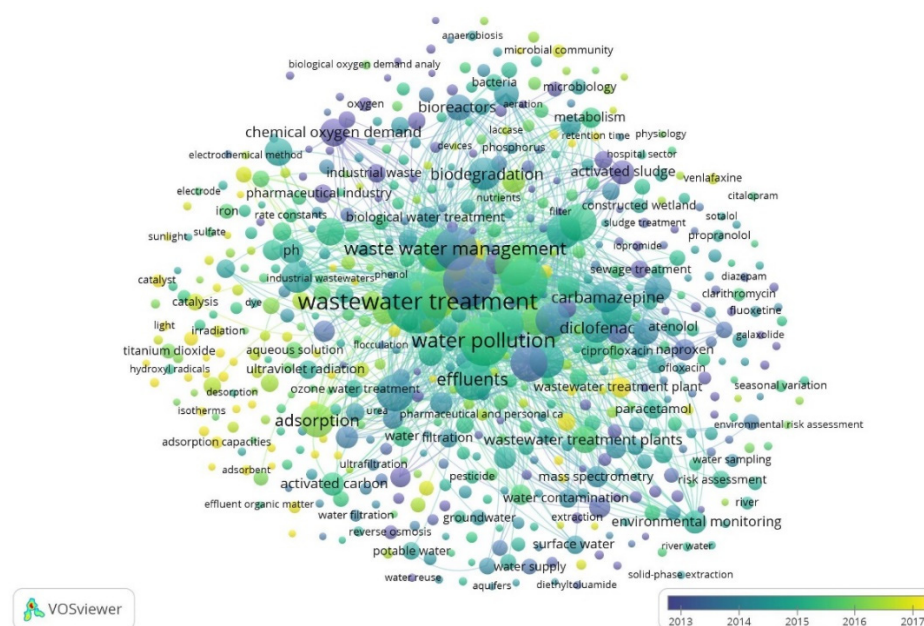


Figure 5. Timeline for main keywords used.

A total of 17,002 keywords are used in the sample containing 2938 documents. In the first period analyzed (1979–1985), researches make use of terms related to wastewater composition. The main keywords for these publications are: chemicals toxicity, cyanide, hydrogen cyanide, industrial waste and sludge. The object of study widens during the second period analyzed (1986–1992), as it incorporates chemical and biological processes to substances present in wastewater. Researches included in this period use the concepts activated sludge, activated carbon, ammonia and bacteria (microorganism) with high occurrence. Regarding the processes mentioned in the publications of this period, the terms adsorption, biodegradation and denitrification stand out for being highly repeated. During the third period analyzed (1993–1999), apart from incorporating terms related to wastewater composition (pharmaceuticals, hydrogen peroxide) and chemical processes (adsorption, oxidation, nitrification), a new interest focused on techniques that allow the reduction or removal of these substances is incorporated. The first terms found in the researches of this period related to pharmaceuticals removal processes are: effluents treatment and biological treatment of water. The following period (2000–2006) makes use of a total of 1666 keywords. In this period, the new terms incorporated into the research line refer to specific pharmaceuticals. The terms with the highest occurrence are: carbamazepin, ibuprofen, diclofenac, naproxen, diazepam, ketoprofen, ethinylestradiol, estradiol, antibiotics and non-classified pharmaceuticals. The period 2007–2013 covers a total of 7329 keywords. The researches conducted in this period can be divided into three different fields. The first of them, wastewater composition, incorporates new concepts like: paracetamol, sulfamethoxazole, pharmaceutical preparations, industrial waste and atenolol. The second of them is focused on chemical processes that are carried out in wastewater. Within this field, terms like oxidation, degradation and adsorption are used. Finally, the last line of study focuses on processes of removal or reduction of these substances in water. In this period, the

processes mentioned in the period 1993–1999 are completed, as they incorporate: process of activated sludge, water treatment with ozone, ultraviolet radiation, liquid chromatography, reverse osmosis, ozonation and filtration. This last period of study starts in 2014 and finishes in 2020. A total of 12,897 keywords are included in the 2057 researches belonging to this period. During these last seven years of research, the object of study is similar to the previous period. In the substances present in wastewater the terms iron, hormones, pharmaceutical and personal care products, ciprofloxacin, metoprolol and triclosan are included. Nine new keywords are mentioned regarding removal processes: photocatalysis, photodegradation, bioremediation, advanced oxidation process, high-performance liquid chromatography and oxidation-reduction reaction. Finally, apart from including the terms previously mentioned concerning biological, physical and chemical phenomena, some other terms, such as wastewater treatment plants and wastewater pumping plants, are also mentioned.

Figure 6 represents the map concerning the keywords used for the research on RPW based on co-occurrence. The map was elaborated taking into account the 600 most representative terms, from which 592 are considered in Figure 6. Each color makes reference to a cluster and, therefore, according to the graph, it is possible to differentiate up to 4 fields in the sample analyzed.

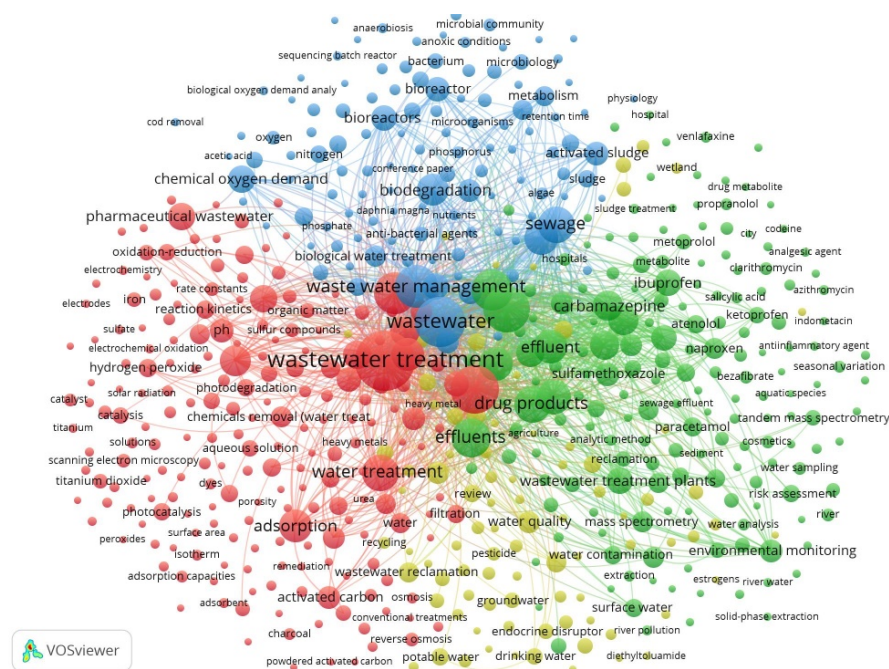


Figure 6. Main keywords network based on co-occurrence.

The red cluster is defined by the terms wastewater treatment, water treatment, adsorption and pharmaceutical wastewater. This cluster is formed by a total of 203 terms and is the largest one within the 4 that have been represented. There is a balance between the terms referring to chemical substances present in wastewater and those processes focused on removal. Consequently, among the terms forming the cluster, it is possible to find the concepts iron, titanium, hydrogen peroxide, activated carbon, oxidation-reduction, photocatalysis or chemical removal. The green cluster is the second group in number of terms (177). It is represented by the terms effluents, drug products and carbamazepine. This cluster groups the names of those pharmaceuticals that are more commonly found in wastewater, such as naproxen, paracetamol, atenolol, codeine, sulfamethoxazole, amoxicillin, ketoprofen, metoprolol, among others. This green cluster mentions the possibility of detecting them in the effluents themselves. In this way, terms like mass spectrometry, water sampling, extraction, environmental monitoring or water analysis are considered. The

third cluster is formed by a total of 121 terms and is represented in blue. The terms with the greatest number of occurrences are wastewater management, sewage, biodegradation and chemical oxygen demand. The concepts composing this cluster make reference to the biochemical processes used for the removal of emerging pollutants that have been cited, for example, bioactivity, bioconversion, aerobiosis, anaerobic growth or nitrification. The yellow cluster contains a total of 91 keywords. This is the smallest group of keywords and, among the concepts it contains, those related to water pollution can be highlighted: water potability, water quality or ground water pollution.

Finally, the relationship between the clusters is highlighted, as the researches link terms belonging to different groups of keywords. Consequently, it is possible to find numerous researches that link objects of study from two different clusters. For instance, one of them dealing with photocatalysis, in the red cluster, along with those pharmaceuticals mentioned in the green cluster [60–63].

3.8. Technologies for Pharmaceuticals Treatment

As shown in some of the clusters included in Figure 6, there is a relevant number of studies addressing the application of treatment technologies in order to improve the removal of pharmaceuticals from wastewater [15]. In this respect, as mentioned in Section 1, it is important to highlight biological, chemical and physical processes. Figure 7 shows the occurrence percentage of each of the previous treatments in the total number of documents analyzed during the period 1979–2020.

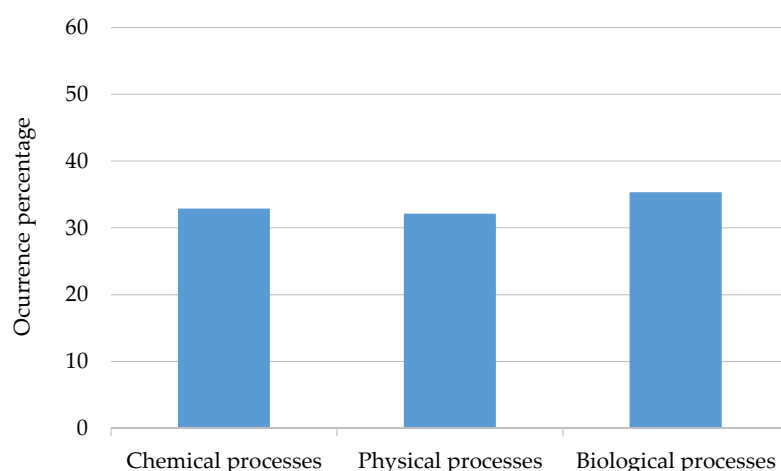


Figure 7. Treatment processes of wastewater containing pharmaceuticals.

The importance of those processes is similar. Biological processes stand slightly apart from the rest, with an occurrence percentage of 35.23%, followed by chemical and physical processes with values of 32.77% and 32.00%, respectively.

Biological treatment technologies have been widely used for the removal of pharmaceuticals present in wastewater, although its performance depends on the components to be removed, wastewater characteristics and operating conditions [7,64]. In general, the predominant mechanism of action of these treatments is biodegradation. However, some of them also work using biosorption and/or bioaccumulation if microalgae are utilized [65]. During biodegradation, high-molecular-weight contaminants are degraded into smaller molecules by microorganism, and even biomineralized into simple inorganic molecules such as water and carbon dioxide [8,66]. As for biosorption, microorganisms are immobilized on an adsorbent and the processes of sorption and biological oxidation occur [67]. Figure 8a shows the occurrence percentage of the biological processes used for pharmaceuticals treatment. They were evaluated by taking into consideration the number of times that these technologies were used as a treatment method in the articles

published in indexed journals from Scopus database (occurrence percentages for chemical and physical processes were also evaluated in this way).

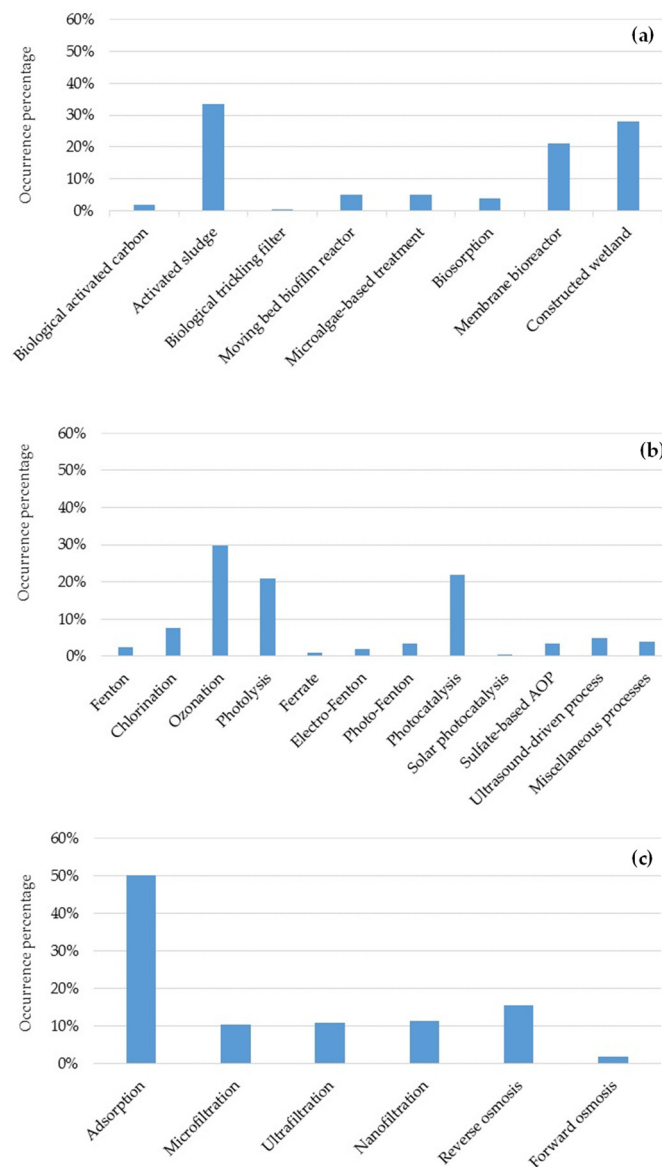


Figure 8. Treatment technologies in biological (a), chemical (b) and physical (c) processes.

It is important to highlight the process of activated sludge (33.58%), followed by constructed wetland (28.05%) and membrane bioreactor (21.08%).

Chemical treatment technologies are also used for the degradation of these contaminants, including conventional oxidation processes, such as Fenton, chlorination, ozonation and photolysis; and advanced oxidation processes (AOPs) [8]. In general, AOPs combine chemical agents, like chlorine, hydrogen peroxide or ozone with catalysts based on transition metals and metal oxides, as well as a source of energy like UV-Vis radiation, electrical current, solar radiation or ultrasounds [68]. AOPs are technologies involving the in situ generation of oxidant species which present a high reactivity to organic and inorganic matter [69,70]. Hydroxyl radical is one of the most powerful oxidant agents, as it can react in an instant and non-selective basis to organic and inorganic compounds with reactions speeds of approximately 10^7 and 10^{10} L mol⁻¹ s⁻¹, respectively [71]. Consequently, AOPs aim at generating a sufficient concentration of hydroxyl radicals which will lead to a complete conversion and mineralization of toxic organic compounds into CO₂, H₂O and inorganic

acids [72], or at least its transformation into simpler compounds, less toxic or more readily biodegradable [73,74]. Figure 8b shows the most remarkable processes, such as ozonation (29.69%) and photolysis (20.94%) among the conventional methods, and photocatalysis (21.88%) among AOPs. More specifically, photocatalysis transforms the contaminants in the presence of a catalyst (normally, semiconducting metal oxides such as TiO_2 or ZnO) activated when light is used as a source of energy.

Adsorption, with 50.24% (Figure 8c), and membrane filtration (microfiltration, ultrafiltration, nanofiltration, reverse and forward osmosis) are the most remarkable physical treatments.

Adsorption is based on the removal of contaminants carried out on the surface or pores of a solid or adsorbent material [75]. Carbonaceous materials are the most widely used adsorbents for pharmaceuticals removal due to their high porosity, broad range of functional groups, adjustable superficial functionality, high specific surface, low price, high availability and chemical resistance [76–78]. This is shown in Figure 9, where the use of activated carbon (62.23%) prevails over other adsorbents such as biochar, carbon nanotubes, clay minerals, zeolite, mesoporous materials, microporous materials, resins and metal oxides. The predominant adsorption mechanism in pharmaceuticals removal with carbonaceous materials is electrostatic interaction and, secondarily, physisorption, chemisorption and π -electron dispersions [77]. If compared to other processes, adsorption is simpler, leads to a lower sludge formation and is considered as a green process of low investment cost [79]. Adsorption processes can normally achieve nearly a complete removal, although the performance depends on the operating conditions, proportion of solid, affinity between the adsorbate and the adsorbent surface, contact time, ionic strength and competitive reactions [77]. In addition, adsorption requires a subsequent process in order to discard or regenerate the adsorbent that has been used.

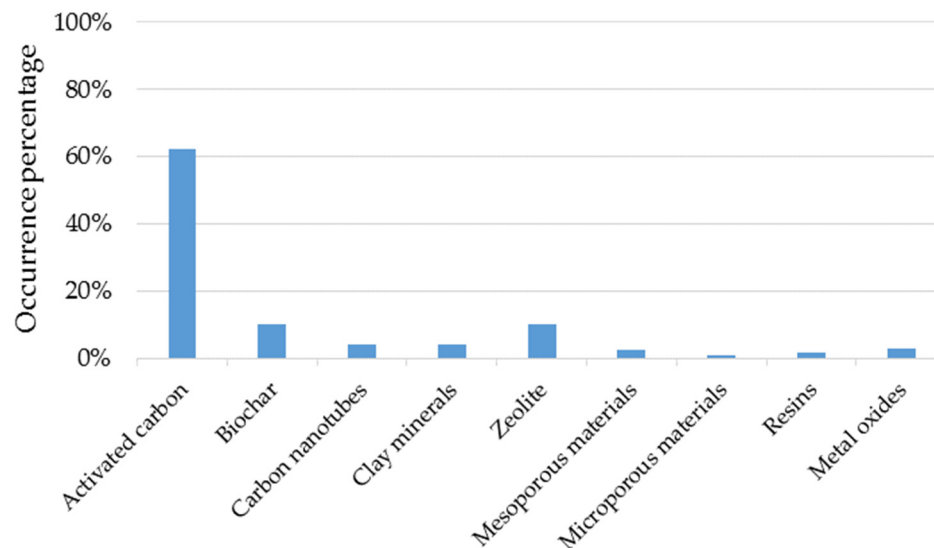


Figure 9. Adsorbents used during the adsorption process.

In membrane filtration, contaminants separation is controlled by three main mechanisms: steric exclusion (based on the separation of solutes on the basis of size), hydrophobic repulsion and electrostatic interactions between membrane and pharmaceuticals which enables their adsorption on the membrane charged surface [80]. In this respect, it is important to highlight that membranes are made of different materials with specific characteristics, such as hydrophobicity, pore size or surface charge, in order to identify the type of existing contaminant [15]. This membrane filtration process has been widely used for water treatment, achieving high percentages of pharmaceuticals removal and producing high-quality permeates [81]. However, like in adsorption, this technology also requires additional stages in order to treat the generated solid sludge contained in the existing

contaminant. In addition, in order to optimize membrane functionality, it needs to be cleaned or pre-treated periodically due to fouling phenomenon, which leads to a loss in membrane performance [82,83].

Nowadays, hybrid technologies, which combine some of the treatments previously mentioned, are being developed [84]. Most of the hybrid systems consist of biological processes followed by some physical or chemical treatment systems [8]. Ahmed et al. [8] indicated that membrane bioreactor followed by reverse osmosis, and ozonation followed by biological activated carbon have been observed to be effective in the removal of pharmaceuticals. Additionally, García et al. [18] analyzed several adsorption-biological hybrid configurations for the removal of pharmaceuticals. In light of this, they highlighted that powdered activated carbon in a conventional activated sludge reactor and powdered activated carbon in a membrane bioreactor are the most applicable hybrid technologies in this field, followed by granular activated carbon in a biofilm reactor and granular activated carbon in a conventional activated sludge reactor.

4. Conclusions

Fresh water pollution is a serious issue nowadays and SDG take it into consideration in their Goal 6. Pollution rate grows faster than population. This pollution comes from a variety of sources and this paper presents the evolution of contaminants from pharmaceutical sources. To do this, a sample of 2938 articles, from 1979 to 2020, was analyzed by means of a bibliometric analysis. Hence, the main authors, institutions, countries, journals and subject categories were identified, as well as the most widely used treatment processes for the removal of these contaminants from wastewater.

Scientific production has increased considerably in the last seven years (2014–2020). A total of 2057 articles (70%) were published during this period. Since 2014, most of the scientific production can be linked to 2030 Agenda and the 17 SDG in 2015.

Taking into consideration subject categories, *Environmental Sciences* is the most relevant one in the sample, with 43.35% of total of published articles. This is why the most prolific journals belonging to this subject category are related to environment. More specifically, 20% of articles are published in the following journals: *Water Research* (241 articles), *Science of the Total Environment* (208 articles) and *Journal of Hazardous Materials* (132 articles). The rest of journals (with a lower number of articles) are also well positioned among impact factors. In fact, 75% of the twenty most prolific journals in the world are included in the first quartile (Q1) of Scopus.

In reference to the most prolific authors and countries, five of the tenth most relevant authors are Spanish. Damiá Barceló, from the Catalan Institute for Water Research, is at the top with 50 published articles. Kai Bester (Denmark), from Aarhus University, with 31 publications, is in the second position and so is Gang Yu (China), from Tsinghua University of Beijing. However, taking into account the number of citations, Snyder, from the University of Arizona, is the author with the highest number, with a total of 4861 citations and 26 articles.

In relation to institutions and countries, it is important to remark CSIC (Spain), with 80 publications and the highest number of citations (5847), and the Ministry of Education of China, with 75 publications and 2042 citations. In this respect, four of the ten most prolific institutions by number of articles are Chinese. This is probably why China is the country with the highest number of publications (572), followed by Spain (379) and USA (351). These three countries cover 44% of worldwide scientific production.

In addition, the analysis of available information indicates that there are four main lines of research. The first line makes reference to chemicals present in water, as well as some processes used for their removal. The second cluster informs about the pharmaceuticals that are present in wastewater along with the techniques that make it possible to detect them. The third cluster deals with biochemical processes occurring in contaminated water and, finally, the fourth cluster contains concepts that are related to water potability and quality.

These treatment processes can be biological, chemical or physical. Among biological processes, the most remarkable ones are activated sludge systems, membrane bioreactor and constructed wetland. The process of photocatalysis is the most widely used among advanced oxidation ones. Ozonation and photolysis are the most commonly used conventional oxidation methods. Regarding physical processes, activated-carbon adsorption is the most widely used.

Finally, this study has proven that scientific research on pharmaceutical contaminants present in wastewater is extensive, especially in the last seven years, which will contribute to foster technical progress regarding treatment processes used to solve this environmental problem.

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