The Persistence of Refractory Pharmaceuticals in Aquatic Systems and Their Environmental Impacts

Xingqi Sheng

Ulink High School of Suzhou Industrial Park, Jiangsu China

xingqi.sheng@sz-alevel.com

Abstract. This study investigates the occurrence and persistence of pharmaceutical residues in wastewater, with particular emphasis on treatment methods including nanofiltration, microbial biodegradation, constructed wetlands, and titanium dioxide (TiO_2) photocatalysis. Most of these approaches achieve elimination rates exceeding 70% for specific pharmaceuticals. However, notable limitations remain: microbial biodegradation is highly sensitive to environmental factors such as temperature, pH, and nutrient availability, leading to variability across seasons and locations; TiO_2 photocatalysis requires ultraviolet light excitation and is hindered by light scattering, shielding effects, and interference from natural organic matter and inorganic ions. These findings underscore the urgent need for more robust and scalable solutions to mitigate the environmental risks posed by pharmaceutical contamination in aquatic systems.

Keywords: Pharmaceutical removal, waste water, Environmental risks, Photocatalysis.

1. Introduction

Pharmaceutical residues are increasingly being detected in aquatic systems as a result of wastewater treatment plants (WWTPs) that are not designed to remove such micropollutants. These residues originate from multiple sourceas, including excessive drug prescriptions, expired household medicines, hospital and clinical waste, improper disposal practices, and metabolites excreted by patients. Due to their chemical stability, high solubility, and resistance to conventional degradation, pharmaceuticals persist during wastewater treatment and subsequently enter rivers, lakes, groundwater, and even drinking water sources. Their long-term presence poses ecological risks, such as endocrine disruption in fish and amphibians, reproductive and behavioral changes in aquatic organisms, and contamination of groundwater through landfill leachate and sewer leakage. Although current concentration levels in drinking water are typically at nanograms per liter and no direct human health effects have yet been confirmed, the precautionary principle suggests that drinking water should remain free of such contaminants [1-4]. Industrial sources, including fermentation liquors, chemical process wastes, condenser effluents, and laboratory washing water, further exacerbate this issue, while biotechnological production releases ancillary substances such as buffers, chelators, and antibiotics. Recent studies indicate that 15–20% of pharmaceuticals used in hospitals may be bioaccumulative [5-8].

Despite the growing awareness of pharmaceutical contamination in aquatic systems, relatively few studies have focused specifically on their removal in wastewater treatment. Existing WWTPs lack adequate processes for eliminating pharmaceutical residues, and current research addressing advanced removal technologies remains fragmented and insufficient. This knowledge gap highlights the urgent need for a comprehensive review of available treatment methods, their efficiency, and their limitations, in order to guide future research and practical applications.

The objective of this study is to identify and assess the most effective approaches for pharmaceutical removal from wastewater. This research is significant for two main reasons. First, it underscores a critical weakness in existing wastewater treatment systems, which fail to adequately address micropollutant removal. Second, it emphasizes the lack of public awareness and regulatory oversight regarding pharmaceutical waste management. Without effective technologies and informed policy interventions, pharmaceutical contaminants will continue to accumulate in aquatic environments, posing long-term ecological and public health risks.

2. Methodology

This study employed a systematic literature review approach to identify relevant research on pharmaceutical removal in wastewater treatment. Databases including Web of Science, Scopus, ScienceDirect, and Google Scholar were searched for publications between 2000 and 2025 using the keywords "pharmaceutical removal" AND "drinking water" AND (biodegradation OR constructed wetlands OR TiO_2 OR nanofiltration). Inclusion criteria were restricted to peer-reviewed articles containing experimental data with water treatment as the primary research focus, while studies without data, unrelated topics, or meeting summaries were excluded. The initial search yielded 20 articles, of which 12 remained after the removal of duplicates. Following the screening of titles and abstracts, 10 articles were selected for further assessment. A thorough review of the full texts resulted in 9 articles that met all inclusion and exclusion criteria, and these were used as the basis for this study.

3. Results

3.1. Presentation of key findings

1. Conventional biological methods

Traditional approaches to handling pharmaceutical wastewater have long relied on biological treatment methods, both aerobic and anaerobic microorganisms are involved in breaking down pharmaceuticals and their byproducts through degradation processes.

a. Biodegradation by Microbial Cultures. Microbial communities are crucial to ecosystems, decomposing organic matter and xenobiotics like pharmaceuticals. Environmental biodegradation is especially key for pharmaceutical breakdown, particularly when WWTPs and STPs are inefficient. Naturally occurring bacteria, fungi, and algae degrade medicines through two complementary routes. In metabolic degradation, specialist bacteria such as Pseudomonas putida import the drug, employ cytochrome P450 enzymes to cleave its structure, then funnel the fragments into the tricarboxylic-acid (TCA) cycle, ultimately releasing carbon dioxide, water, and energy (ATP). When the compound cannot sustain growth, cometabolic degradation takes over: fungi like Trametes versicolor consume simple sugars and simultaneously secrete laccases and ligninolytic peroxidases that oxidise the drug extracellularly, breaking it into small, harmless molecules such as CO_2, ammonia, and sulfate. Together, these microbial strategies provide an enzyme-driven polishing step that markedly reduces pharmaceutical residues in treated effluents.

b. Constructed Wetlands. Constructed wetlands offer effective, reliable, and sustainable wastewater treatment. They have a long history of wastewater treatment, characterized by low costs, simple operation, easy maintenance, environmental friendliness, and their potential as an alternative to wastewater treatment plants. Upon entry, suspended solids and hydrophobic APIs (Active Pharmaceutical Ingredient) are rapidly removed by sedimentation and sorption to organic substrates and biofilms; ionizable species are simultaneously retarded via pH-dependent electrostatic interactions with negatively charged soil particles and root surfaces. A vertical redox gradient then governs subsequent fate: oxic microzones surrounding the rhizosphere sustain aerobic bacteria that deploy extracellular oxidases (e.g., laccases, peroxidases) to cleave aromatic moieties, while deeper anoxic layers harbour denitrifiers and sulfatereducers that cometabolise nitro- or azo-substituted pharmaceuticals using root exudates as electron donors. Concurrent phyto-transformation involves root uptake of hydrophilic residues followed by intracellular phase-I/II enzymatic reactions and sequestration within vacuoles or lignin matrices. Supplementary photolytic degradation occurs at the water– biofilm interface, enhancing removal of recalcitrant species such as ketoprofen and diclofenac. Integrated performance data indicate >70 % elimination of readily degradable pharmaceuticals (e.g., tetracycline, sulfamethoxazole), confirming the system's reliability as a sustainable tertiary treatment option. Biological treatments can be valueable ideas for people to dispose of pharmaceutical wastewater; However, these methods are susceptible to fluctuations due to natural factors such as temperature, pH, and nutrient levels. Consequently, their effectiveness will vary with the seasons and across different geographical locations. Thus, more improvements should be made to make those treatments more reasonable and usable.

2. Chemical methods

a. Titanium Dioxide (TiO2) Photocatalysis Heterogeneous photocatalysis using the semi-conductor titanium dioxide (TiO2) has proven to be a promising treatment technology for water purification. The effectiveness of this oxidation technology for the destruction of pharmaceuticals has also been demonstrated in numerous studies. For example, the most commonly investigated antiepileptic is the dibenzoazepine derivative, carbamazepine (CBZ; 5H-diben-zo [b,f]-azepine-5-carboxamide). CBZ, also used assedative for numerous mental disorders, can cause toxic effects in the liver and is a hematopoietic. Studies have reported the removal efficiency of CBZ in WWTPs as below 10 %. The degradation efficiency of UV/TiO2 for CBZ has reached 70.4% So I think it would be a good idea to put it into sewage treatment. Because when TiO2 is excited by ultraviolet light, strong oxidizing hydroxyl radicals (HO*) are produced. Their oxidation potential is as high as 2.8V, and they can selectively attack the benzene ring and amide group of CBZ.

3. Physical methods

Physical removal methods separate pharmaceutical residues from wastewater by using physical forces instead of chemical reactions. Common tools are membranes and solid materials such as activated carbon or resins. These methods do not change the drug molecules; they simply move them from water to another phase, so the water becomes cleaner.

a. Removal using Nanofilteration Nanofiltration membranes consistently eliminate over 90 % of pharmaceuticals from water and wastewater by simultaneously acting as a threefunction barrier: their nanometre-scale pores physically exclude larger molecules, their negatively charged surfaces electrostatically repel anionic drugs, and their polymeric matrix adsorbs hydrophobic species. The overall rejection for any given compound is therefore a composite of these effects and varies with the drug's physicochemical attributes (molecular size, charge, hydrophobicity, solubility), the membrane's characteristics (pore size, surface charge, hydrophobicity, permeability), and operating conditions (transmembrane pressure, flux, pH, and feed composition). A clear illustration is the behaviour of sulfamethoxazole and carbadox: as the pH rises above 5.6, both antibiotics deprotonate and acquire a net negative charge, resulting in increased electrostatic repulsion by the negatively charged membrane and a corresponding rise in rejection efficiency from 90 % to 95 %. Figure1 describes aquatic systems

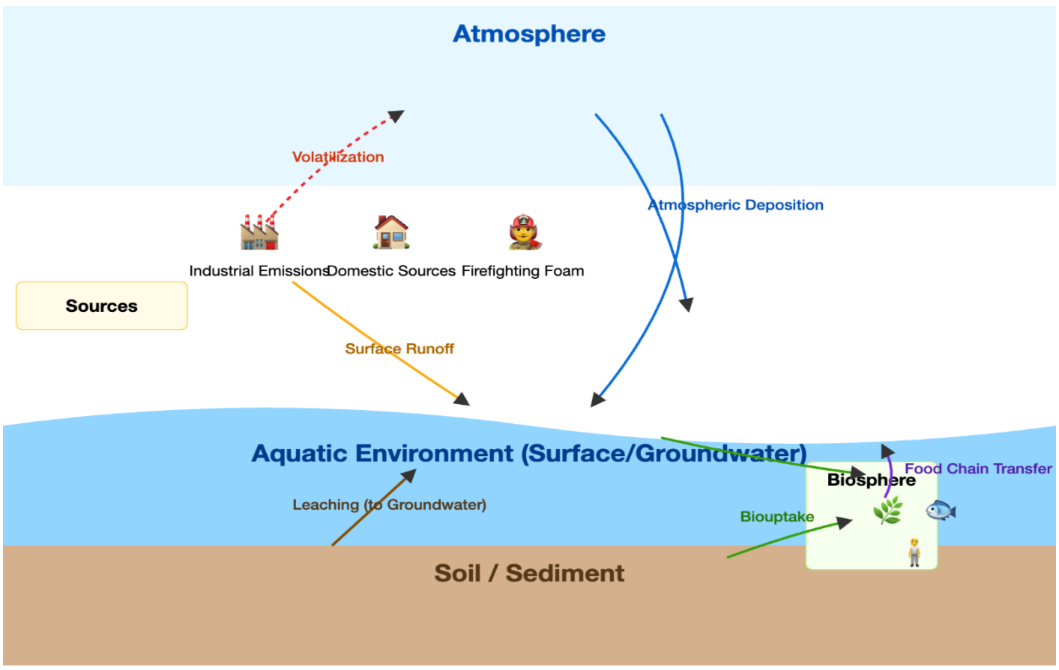

Fig. 1 Two or more references

4. Discussion

4.1. Summary of key findings

Conventional wastewater treatment systems, including primary and secondary processes, are insufficient for the complete removal of pharmaceutical residues. To address this limitation, a range of advanced treatment methods has been investigated. Biological approaches such as microbial biodegradation and constructed wetlands provide environmentally friendly options but are often influenced by natural fluctuations in temperature, pH, and nutrient availability. Chemical methods, including titanium dioxide (TiO_2) photocatalysis and Fenton's oxidation, demonstrate high efficiency in degrading recalcitrant compounds but require specific conditions such as UV irradiation or chemical reagents. Physical methods, particularly nanofiltration, consistently achieve removal rates exceeding 90% through size exclusion and electrostatic interactions. Collectively, these approaches represent promising solutions to enhance the overall efficiency of wastewater treatment and mitigate the ecological risks associated with pharmaceutical contaminants.

4.2. Comparison with previous studies

Earlier approaches such as autoclaving and high-pressure sterilization achieved removal efficiencies above 98% for pharmaceutical and antibiotic residues by subjecting waste to high-temperature and high-pressure conditions. Similarly, supercritical carbon dioxide sterilization demonstrated strong degradation performance. However, these methods require extensive energy input and post-treatment handling, making them impractical for large-scale applications. Their high operational costs and technical complexity limit their feasibility, particularly in developing regions where medical waste generation is substantial [7]. By comparison, advanced methods such as photocatalysis and nanofiltration, although still facing challenges, offer more economically viable and scalable solutions. The key difference lies in balancing treatment efficiency with affordability and operational feasibility, which remains the central challenge for practical implementation.

4.3. Limitations of the study

Although advanced technologies can achieve elimination rates of over 70% for certain pharmaceuticals, significant challenges remain. Biodegradation efficiency varies across seasons and locations due to its dependence on environmental factors such as temperature, pH, and nutrient supply. Photocatalysis, while highly effective against carbamazepine, is hindered by competition with natural organic matter for free radicals and by the requirement of UV irradiation, which is often obstructed by suspended solids and turbidity in real wastewater. Additionally, the process is sensitive to pH, and the simultaneous occurrence of competing reactions complicates control. At present, a robust and scalable system for large-scale demonstration has yet to be developed.

4.4. Suggestions for future research

Future research should prioritize the development of cost-effective yet efficient treatment strategies. Particular emphasis is needed on overcoming the limitations of photocatalysis, such as mitigating the influence of impurities and extending light absorption beyond the ultraviolet range. Field validation of hybrid technologies that integrate biological, chemical, and physical methods will be essential to evaluate their performance under real wastewater conditions. Furthermore, sludge stabilization and environmentally sustainable manufacturing processes should be incorporated to reduce secondary pollution. Policy interventions, including stricter regulations on pharmaceutical disposal and improved monitoring frameworks, are also critical to ensuring the long-term sustainability of water resource management.

5. Conclusion

Pharmaceutical residues represent a growing challenge for aquatic environments due to their persistence, bioaccumulation potential, and resistance to conventional wastewater treatment processes. This review highlights that while biological methods such as microbial biodegradation and constructed wetlands, chemical processes like TiO_2 photocatalysis, and physical techniques including nanofiltration each demonstrate promising removal efficiencies, none are without significant limitations. Environmental variability, high operational costs, and scalability constraints continue to hinder widespread application. Therefore, future efforts must focus on integrating these approaches into hybrid systems that combine efficiency with economic feasibility, while ensuring adaptability to real-world wastewater conditions. In parallel, strengthened regulatory frameworks, public awareness campaigns, and improved pharmaceutical waste management practices are essential to prevent further contamination at the source. Taken together, the development of robust and sustainable solutions is crucial to safeguard aquatic ecosystems and ensure the long-term safety of global water resources.

References

[1] Ternes, Thomas A., et al. "Removal of pharmaceuticals during drinking water treatment." Environmental Science & Technology 36.17 (2002): 3855-3863. 10.1021/es015757k

[2] Patel M, Kumar R, Kishor K, et al. Pharmaceuticals of emerging concern in aquatic systems: chemistry, occurrence, effects, and removal methods [J]. Chemical Reviews, 2019, 119 (6): 3510-3673.

[3] Li, Y.; Zhu, G.; Ng, W. J.; Tan, S. K. A review on removing pharmaceutical contaminants from wastewater by constructed wetlands: design, performance and mechanism. Science of the Total Environment, 2014, 468: 908−932.

[4] Kanakaraju, Devagi, Beverley D. Glass, and Michael Oelgemöller. "Titanium dioxide photocatalysis for pharmaceutical wastewater treatment." Environmental Chemistry Letters 12.1 (2014): 27-47.

[5] Parimal, Al. "Treatment and disposal of pharmaceutical wastewater: toward the sustainable strategy." Separation & Purification Reviews 47.3 (2018): 179-198.

[6] Künnemeyer, J., Terborg, L., Meermann, B., Brauckmann, C., Möller, I., Scheffer, A., and Karst, U. "Speciation analysis of gadolinium chelates in hospital effluents and wastewater treatment plant sewage by a novel HILIC/ICP-MS method." Environmental Science & Technology 43.8 (2009): 2884–2890.

[7] Jean, J., Perrodin, Y., Pivot, C., Trepo, D., Perraud, M., Droguet, J., Tissot-Guerraz, F., and Locher, F. "Identification and prioritization of bioaccumulable pharmaceutical substances discharged in hospital effluents." Journal of Environmental Management 103 (2012): 113-121.

[8] Camacho-Muñoz, D., Martín, J., Santos, J. L., Aparicio, I., and Alonso, E. "Effectiveness of conventional and low-cost wastewater treatments in the removal of pharmaceutically active compounds." Water, Air, & Soil Pollution 223 (2012): 261-121.