Chemosphere 374 (2025) 144153

Contents lists available at ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere

Recent occurrence of pharmaceuticals in freshwater, emerging treatment technologies, and future considerations: A review

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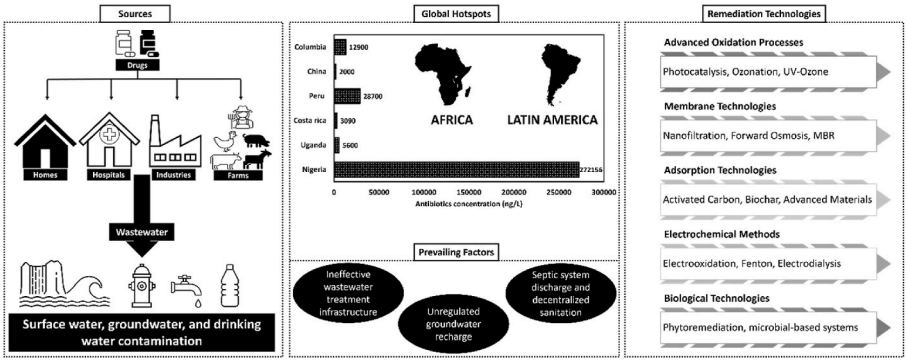
HIGHLIGHTS

- Emerging techs like AOPs, membrane filtration reduce pharmaceuticals in water.
- Population growth predicts rising pharmaceutical pollutants in freshwater.
- Advanced oxidation, nanofiltration effective in treating drug-laden wastewater.
- Antibiotic resistance linked to pharmaceutical contaminants in water.
- Septic systems, landfill leachate contribute to groundwater contamination.

GRAPHICAL ABSTRACT



ARTICLE INFO

Handling Editor: Keith Maruya

Keywords:
Emerging pollutants
Drinking water
Groundwater
Pharmaceutical pollutants
Surface water
Wastewater treatment
Micropollutants

ABSTRACT

Pharmaceuticals represent an emerging class of pollutants raising significant environmental health concerns, with their presence in freshwater systems linked to adverse aquatic ecosystem impacts and acceleration of antibiotic resistance development. This narrative review examines recent (2019–2024) pharmaceutical occurrences in freshwater globally, analyzes contamination pathways, evaluates compound-specific degradability, and assesses treatment technologies.

Analysis revealed significant pharmaceutical contamination in freshwater sources across the six major continents, primarily entering through wastewater treatment plant effluents, groundwater recharge processes, and inadequate sanitation infrastructure/septic systems. Stark geographical disparities were observed, with regions lacking centralized treatment infrastructure showing multiple-fold higher concentrations, particularly in Africa and Latin America (exemplified by amoxicillin levels reaching 272,156 ng/L in Lagos, Nigeria). Pharmaceutical profiles reflected local healthcare patterns, with antimalarials and antiretrovirals prevalent in endemic regions. Globally prevalent compounds included caffeine, acetaminophen, ibuprofen, carbamazepine, sulfamethoxazole, amoxicillin, and diclofenac. While some compounds like caffeine showed relatively good removal in conventional treatment systems, their high usage rates overwhelmed treatment capacity. Others, particularly

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https://doi.org/10.1016/j.chemosphere.2025.144153
Received 13 October 2024; Received in revised form 17 January 2025; Accepted 21 January 2025
Available online 12 February 2025

carbamazepine, demonstrated high recalcitrance to conventional treatment methods. Advanced oxidation processes and membrane technologies showed high removal efficiencies, while biochar-based systems emerged as promising, cost-effective alternatives using locally available resources.

The findings underscore the need for both centralized and decentralized treatment approaches. Point-of-use technologies emerge as crucial immediate interventions for regions with inadequate infrastructure, while advanced technologies show promise for large-scale applications. The review emphasizes that municipalities should conduct systematic screening to identify locally prevalent pharmaceuticals, as treatment requirements vary significantly with local usage patterns, making a one-size-fits-all approach ineffective.

1. Introduction

Pharmaceuticals have become indispensable in modern life, addressing various health challenges for humans, domestic animals, and livestock (Ashiwaju et al., 2023). With a steadily increasing global population, rising life expectancy, and ongoing economic growth, pharmaceutical consumption has surged dramatically (Tannoury and Attieh, 2017; World Health Organization, 2017). This trend is reflected in global prescription drug sales, which were valued at over 800 billion USD in 2018 and are projected to double to 1.6 trillion USD by 2028 (Evaluate Ltd, 2023). Fig. 1 provides an overview of the increasing global drug consumption, reinforcing the urgency of mitigating pharmaceutical pollution in water systems. However, while these advancements signify improved healthcare access, they come with the environmental challenge of pharmaceutical pollutants infiltrating freshwater systems. Improper management of pharmaceutical waste, coupled with inefficient disposal practices, exacerbates this challenge, potentially increasing pollutant concentrations in the environment over time (Wilschnack et al., 2024).

The primary sources of pharmaceutical contaminants in freshwater are untreated or insufficiently treated sewage effluents. These contaminants are introduced through human excretion, which contains active drug compounds or their metabolites, and through improper disposal of unused medications (Meyer et al., 2024; Rehrl et al., 2020). This makes hospitals a significant hotspot for antibiotic release into the environment (Nadeem et al., 2020a; Khan et al., 2022). Veterinary drug use also contributes significantly to pharmaceutical pollution, as these drugs can enter aquatic ecosystems through animal waste or indirectly through human consumption of livestock (Nguyen et al., 2024). These sources, along with others, are summarized in Fig. 2, which highlights the major pathways by which pharmaceutical pollutants reach water systems, including domestic wastewater, livestock effluent, landfill leachates, and agricultural runoff. Unfortunately, most conventional wastewater treatment plants are not equipped to effectively degrade these compounds, leading to their accumulation in surface and groundwater (Kumar et al., 2018). This inefficiency underscores the urgent need to enhance treatment technologies with polishing units (Mazhar et al., 2021) and to explore sustainable alternatives like "green chemistry," which focuses on producing more readily biodegradable drugs (World Health Organization, 2017).

Historically, pharmaceuticals in freshwater systems remained undetected due to a lack of advanced analytical techniques. It was only in recent decades that these emerging contaminants, typically measured in nanograms per litre (ng/L), began to be identified (Wilschnack et al., 2024; Paíga et al., 2024). Unlike conventional pollutants such as heavy metals or salts, which are measured in parts per million (ppm), pharmaceutical pollutants occur in much lower concentrations. While these concentrations are generally not expected to have direct adverse effects on human health, concerns persist about the potential for long-term exposure, aggregation, and the compounding effects of multiple pollutants (World Health Organization, 2012; World Health Organization, 2017; Bexfield et al., 2019). For instance, studies show that the highest concentration of meprobamate in drinking water, measured at 42 ng/L, would require a person to consume over 1.2 million gallons in a day to reach a therapeutic dose (National Association of Clean Water Agencies, 2011). Despite these seemingly low risks, the lack of routine monitoring and limited understanding of the cumulative effects of these pollutants highlight significant knowledge gaps (Ali and Gujiba, 2024; Gasco Cavero et al., 2024).

The potential consequences of pharmaceutical pollution extend beyond human health, particularly through the emergence of antibiotic resistance. Antibiotics in wastewater have been shown to promote the development of antibiotic-resistant bacteria and genes, posing significant public health risks (Manga et al., 2021). Studies conducted in wastewater treatment plants in India revealed the presence of multi-drug-resistant bacteria, including biofilm-producing strains, even

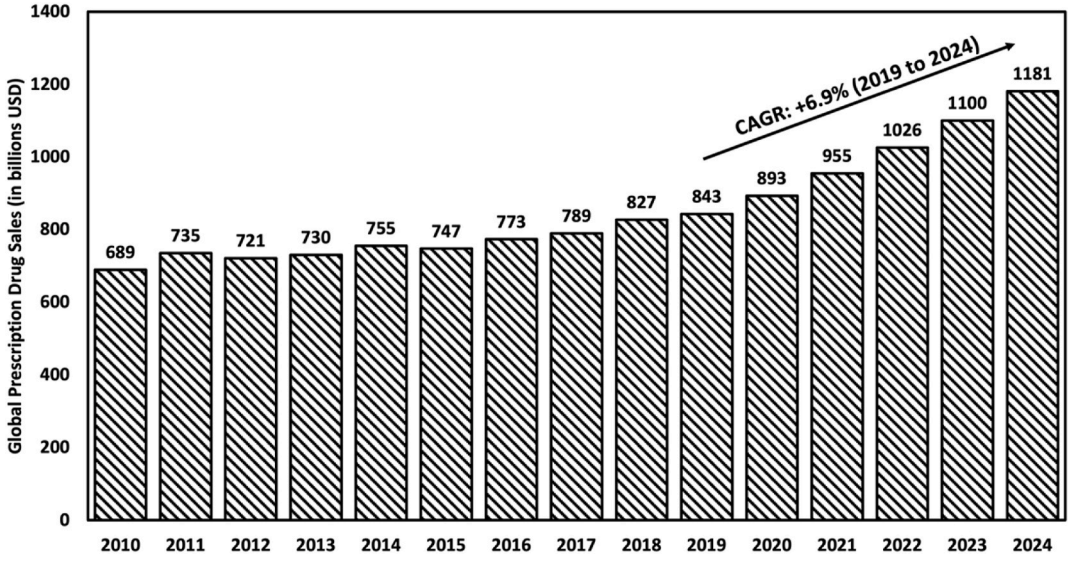


Fig. 1. Global Prescription Drug Sales from 2010 to 2024; Data source (Evaluate Ltd, 2023).

in relatively low pharmaceutical concentrations (Jyoti et al., 2024). Similarly, research in Costa Rica identified antibiotics in nearly half of the water samples tested and antibiotic-resistant genes in all samples, despite pharmaceutical concentrations being below 10 ng/L (Vargas-Villalobos et al., 2024). Beyond antibiotic resistance, pharmaceuticals in water have been linked to sterility, tumours, and hormonal imbalances in humans and wildlife (Munzhelele et al., 2024). Aquatic ecosystems, in particular, are highly vulnerable to pharmaceutical contamination, with documented cases of reproductive abnormalities, morphological changes, and metabolic disruptions in aquatic organisms (Arnold et al., 2014; Brezina et al., 2017). For instance, fish (*Oryzias latipes*) exposed to estrogen in polluted water exhibited induced vitellogenesis, which significantly increased mortality rates (Jukosky et al., 2008). Vitellogenesis was significantly induced at estradiol concentrations as low as 56.27 ± 11.45 ng/L, while mortality effects were observed at higher concentrations (2528.34 ± 760.73 ng/L), with more than 50% mortality in high estrogenicity treatments.

Groundwater systems are particularly at risk due to their long residence times, which allow pharmaceutical pollutants to persist for decades if not properly managed (Lapworth et al., 2017). Pharmaceuticals that settle at the bottom of water bodies also exhibit higher persistence, as limited sunlight penetration reduces photodegradation rates (Konappan et al., 2024; Vaudreuil et al., 2024). Moreover, regions lacking centralized sewage systems, such as parts of Africa and Latin America, face higher concentrations of pharmaceutical pollutants due to the reliance on septic systems and open defecation, which exacerbate contamination levels. These factors, coupled with the global increase in pharmaceutical consumption, indicate that the concentration of these pollutants is likely to rise without immediate intervention.

In light of the growing global concern surrounding pharmaceutical pollutants in freshwater, this review was designed to address critical gaps in understanding their prevalence, treatment technologies, and future implications. Existing reviews have largely focused on either the environmental fate of these pollutants or isolated aspects of their mitigation, often with limited geographical representation. This review differentiates itself by providing a comprehensive global analysis, incorporating data from six continents, including underrepresented regions like Africa and Latin America while acknowledging limitations in Australian studies due to fewer publications in the specified time frame (2019–2024). This review adopts a dual approach to literature analysis: first, examining recent occurrence patterns (2019–2024) through 58 carefully selected papers from Science Direct, ACS publications, and Scopus databases, using keywords 'Pharmaceuticals and Freshwater', 'Pharmaceuticals in Groundwater', 'Pharmaceuticals in Surface water', and 'Pharmaceuticals in Drinking water'. This focused analysis of recent data revealed significant geographical disparities, particularly highlighting elevated concentrations in regions with limited treatment infrastructure. Second, drawing from a broader literature base of over 100 references, we comprehensively examine contamination pathways and evaluate treatment technologies, from advanced centralized systems to point-of-use solutions. This integrated approach enables us to propose contextually appropriate solutions while identifying critical knowledge gaps. Future research should address data limitations in underrepresented regions, explore long-term ecological and human health impacts

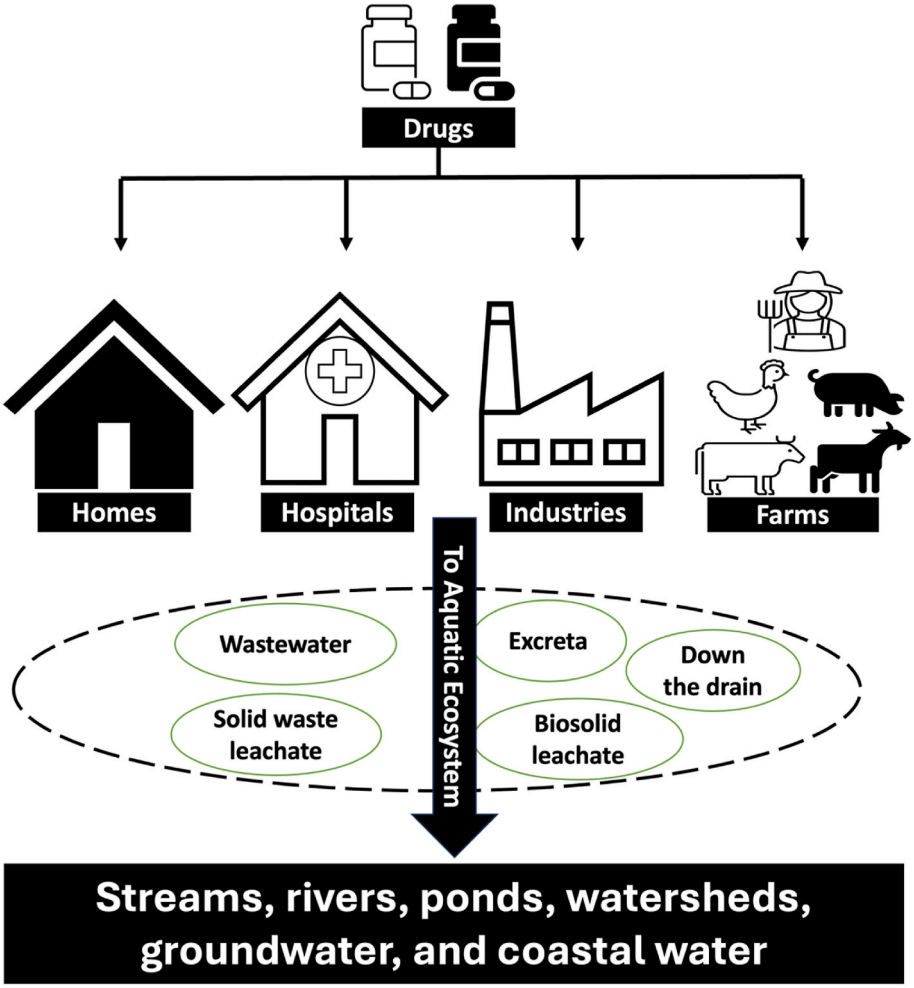


Fig. 2. Prevalent sources of pharmaceutical pollutants in aquatic ecosystem.

of chronic exposure, and develop standardized monitoring protocols. Additionally, location-specific studies are needed to optimize treatment approaches based on local pharmaceutical profiles and infrastructure capabilities.

2. Occurrence of pharmaceutical pollutants in freshwater

The 58 studies reviewed were conducted across 6 continents- Europe (16), South America (11), North America (10), Africa (10), Asia (8), and Australia (3). Around 70% of the studies sampled surface water sources consisting of canals, lakes, and rivers, while the remainder sampled groundwater sources. Over 30 different pharmaceutically active ingredients were detected in the freshwater sources. Table 1 provides detailed information about the individual surveys.

The studies with the two highest maximum concentrations of pharmaceutical pollutants in groundwater, 7900 ng/L (caffeine) and 6490 ng/L (amoxicillin), were conducted in Barbados and Nigeria, respectively (Edwards et al., 2019; Ebele et al., 2020). Results from both surveys posited that domestic wastewater was a major contributor to groundwater pharmaceutical pollutants. The groundwater situation in Barbados is more peculiar because it predominantly consists of a karst aquifer, which is known to be more susceptible to contamination (Edwards et al., 2019; Kim and Lee, 2020). Furthermore, a common factor in the two study locations is the paucity of centralized sewage treatment plants. Less than 15% of Barbados' sewage is treated by a sewage treatment plant, while over 90% of Nigerian States lack centralized sewage systems, leaving the vast majority of domestic waste to be managed at the household level via septic systems, latrines and the like (Nurse et al., 2012; Edwards et al., 2019; Ebele et al., 2020).

In the studies reviewed, caffeine was not only the pollutant detected in the highest concentration, reaching 7900 ng/L in Barbados, but also the most prevalent pollutant. It was the contaminant with the highest concentration in 37.5% of the studies. For example, in a low-density region of Poland, a comparatively high concentration of caffeine (1528.2 ng/L) was detected (Szymczycha et al., 2020). This prevalence likely reflects the widespread consumption of coffee, which is considered a daily staple in many regions globally (Freitas et al., 2024). In fact, globally, coffee consumption is constantly on the rise, with about 166, 340 million 60 kg bags consumed in 2021 (International Coffee Organization, 2021; Freitas et al., 2024). The frequent detection of caffeine in groundwater across various continents underscores its status as one of the most consumed psychoactive substances globally, as well as its pervasive use and the potential for it to enter water systems through various pathways (Brower and Swatek, 2024). Additionally, caffeine's presence in over-the-counter medications, such as cough syrups, tea, and soft drinks (Lavhale et al., 2023; Li et al., 2023), can contribute to its prevalence in groundwater, further indicating multiple sources of contamination. Even though the benefits of caffeine consumption are widely proclaimed (e.g. reduced risk of cardiovascular disease, type 2 diabetes, and certain cancer types) (Di Maso et al., 2021; Li et al., 2024), a few studies have also associated chronic exposure to coffee with increased risk of fracture, open-angle glaucoma, anxiety, stress, and depression (Bae et al., 2020; Magalhães et al., 2021; Li et al., 2023; Qin et al., 2023).

Moreover, the detection of the antibiotic amoxicillin, with a concentration of 6490 ng/L in groundwater in Lagos, Nigeria, was particularly concerning. The presence of antibiotics in drinking water sources could lead to the unintentional exposure of populations to these drugs, thereby increasing the risk of developing antibiotic-resistant bacteria (Vargas-Villalobos et al., 2024). This is a critical public health issue that warrants immediate attention. In Nigeria, amoxicillin is frequently cited as one of the most abused antibiotics because it can be purchased over the counter without a prescription (Nwangwu et al., 2022; Güney and Dokgöz, 2023). It is also one of the first-choice antibiotics prescribed in hospitals due to its broad-spectrum efficacy (Manga et al., 2021; Sekoni et al., 2022). This is probably why it is unsurprising that in the Nigerian survey, all groundwater and drinking water samples contained certain concentrations of antibiotics (Ebele et al., 2020). In addition to amoxicillin, other antibiotics were detected in various locations, indicating a widespread issue. For example, sulfadiazine was found in groundwater in Spain at a concentration of 208 ng/L (Jurado et al., 2020), while sulfamethoxazole was detected in Kenya, Cameroon, and Tanzania at concentrations of 258.2 ng/L, 73 ng/L, 94 ng/L (Branchet et al., 2019; Karimi et al., 2023; Kundu et al., 2024), respectively. Furthermore, fleroxacin was found in China at a concentration of 26.6 ng/L (Gu et al., 2019). The widespread detection of these antibiotics suggests extensive use and potential misuse or overuse of these medications in the respective regions, contributing to their presence in groundwater sources. Beyond antibiotics, other pharmaceuticals, such as nonsteroidal anti-inflammatory drugs (NSAIDs), were also detected in significant concentrations. Acetaminophen, for instance, was found at 122.7 ng/L in the UK (Kibuye et al., 2019), and mefenamic acid was detected at 1848 ng/L in Canada (Husk et al., 2019). These findings reflect the common use and possible overuse of these drugs, further highlighting the need for better management and disposal practices to prevent contamination of water resources. These results affirm that the contamination of groundwater with pharmaceutical pollutants is widespread across the globe. With groundwater being a reliable source of drinking water across the world (Lapworth et al., 2017; Edwards et al., 2019), the results indicate that the need for effective monitoring schemes cannot be underestimated, as there is still a current paucity of standardized monitoring strategy for pharmaceuticals in water (Houtman, 2010; Szymczycha et al., 2020). Fig. 3 provides a summary chart of the maximum concentration of pharmaceutical pollutants in groundwater across the various study locations.

Furthermore, the results from surface water studies reveal that they are more susceptible to pharmaceutical pollution than groundwater. Over 45% of the studies reviewed reported concentrations (ng/L) of pharmaceutical contaminants in their thousands (Table 1). The higher contaminant concentration levels in surface water are anticipated due to the extensive discharge of effluents from point sources into water bodies globally (Hamdhani et al., 2020). However, this was not the case for a survey in Spain, where the groundwater recorded a higher range of contamination (Jurado et al., 2020). This could be due to spatial differences and/or more rapid degradation of the drug residues in surface water due to increased exposure to sunlight, resulting in photodegradation (Lyu et al., 2022). The contamination of surface water with pharmaceutical pollutants in different regions across the world is also quite bothersome. This is not only because these contaminants have been reported to adversely affect aquatic life but also because a significant portion of people across the world rely on surface water as their drinking source (Bwire et al., 2020; Rehrl et al., 2020).

The profile of contaminants present in the surface water was similar to those in the groundwater, implying pollution is from similar point sources. Just as reported with the groundwater studies, the stimulant caffeine was also the highest concentration of contaminant detected in the majority of the studies (31.4%), affirming its widespread consumption and production in goods like coffee, tea, soft drinks, and cough syrup (Brower and Swatek, 2024). Additionally, antibiotics were the class of contaminants with the highest concentrations in 22.9% of the studies reviewed. The high-concentration antibiotics detected varied based on the location reported, where amoxicillin was highest in Nigeria- 272,156 ng/L (Ebele et al., 2020), Sulfamethoxazole highest in Peru- 28,700 ng/L and Uganda- 5600 ng/L (Nantaba et al., 2020; Nieto-Juárez et al., 2021), Cephalexin in Columbia- 12,930 ng/L (Cerón-Vivas and Peñuela Mesa, 2024), Oxacillin in Costa Rica- 3090 (Rodríguez-Rodríguez et al., 2024), Norfloxacin in China- 2000 ng/L (Chen et al., 2024), and Azithromycin in Mexico- 63.5 ng/L (Durán-Álvarez et al., 2023), which could also be indicative of extensive use in these areas. These antibiotics are commonly prescribed and consumed across the world and are reported to have some of the highest antibiotic resistance (Nayiga et al., 2020; Ávila et al., 2021;

Table 1
Pharmaceuticals in freshwater sources in recent times.

Location	Pharmaceuticals	Concentration	Reference
Groundwater, Gdańsk, Poland	16 pharmaceuticals were detected including Caffeine, sulfapyridine, sulfamethoxazole, ketoprofen and diclofenac	0–1528.2 ng/ L (Caffeine highest, then diclofenac 606.1 ng/L)	Szymczycha et al. (2020)
Lake Mälaren Drinking water reservoir, Sweden	76 pharmaceuticals were detected including Carbamazepine, metoprolol, oxazepam, cetirizine, fexofenadine, lidocaine, tramadol, caffeine, lamotrigine, bicalutamide	0–140 ng/L (Lamotrigine highest, then caffeine 80 ng/L)	Rehrl et al. (2020)
Groundwater, Lagos Nigeria	28 pharmaceuticals were detected including Amoxicillin, acetaminophen, nicotine, diclofenac, ibuprofen, caffeine, naproxen, tramadol, metformin, gabapentin, sulfamethoxazole, trimethoprim, metoprolol, carbamazepine, oxazepam, mefloquine HCl, valsartan, glyburide, clotrimazole, gemfibrozil, meclofenamic and codeine	0–6490 ng/L (highest amoxicillin, then nicotine- 3530 ng/L)	Ebele et al. (2020)
Surface water, Lagos, Nigeria	28 pharmaceuticals were detected including: Amoxicillin, acetaminophen, nicotine, diclofenac, ibuprofen, caffeine, naproxen, tramadol, metformin, gabapentin, sulfamethoxazole, trimethoprim, metoprolol, carbamazepine, oxazepam, mefloquine HCl, valsartan, glyburide, clotrimazole, gemfibrozil, meclofenamic and codeine	0 to 272,156 ng/L (highest amoxicillin, then acetaminophen 12430 ng/L)	Ebele et al. (2020)
Lake Victoria, Uganda	The survey includes 24 pharmaceuticals including: Sulfamethoxazole, trimethoprim, ibuprofen, tetracycline, sufacetamide, carbamazepine, sulfamethazine, erythromycin, atenolol, enoxacin, norfloxacin, levofloxacin, norfloxacin, ciprofloxacin, metoprolol, oxyteracycline, azithromycine and diclofenac	0–5600 ng/L (Sulfamethoxazole highest, then ibuprofen- 780 ng/L)	Nantaba et al. (2020)
Groundwater (agricultural/ non-agricultural), Korea	33 pharmaceuticals were detected including Ciprofloxacin, difloxacine, enrofloxacin, flumequine, norfloxacin, ofloxacin, pefloxacine, sulfamethoxine, sulfamerazine, sulfamethoxazole, sulfathiazole, sulfamonomethoxine, lincomycin, spiramycine, trimethoprim, fenbendazole, flubendazole, oxfendazole, atenolol, propranol, acetaminophen, caffeine, carbamazepine, crotamiton	Agricultural- 0 to 45.5 ng/L (anthelmintics) Non-agricultural- 0.085 to 5.74 ng/L (caffeine highest)	Lee et al. (2019)
Groundwater, Barbados, West Indies	5 pharmaceuticals were detected including Carbamazepine, trimethoprim, ibuprofen, and caffeine	0–3.5 ng/L – other drugs 36 ± 4 to 7900 ± 150 ng/l- caffeine	Edwards et al. (2019)
St. Lawrence River, Canada	27 pharmaceuticals were detected including Caffeine, carbamazepine, diclofenac, acebutolol, norfluoxetine, venlafaxine, testosterone, progesterone, estriol, estrone, amoxicillin, clarithromycin ibuprofen, hydroxyibuprofen, and venlafaxine	0 to 7200 ng/L (caffeine highest)	Vaudreuil et al. (2024)
Tributary Rivers, Ottawa & Quebec	27 pharmaceuticals were detected including Caffeine, carbamazepine, diclofenac, acebutolol, norfluoxetine, venlafaxine, testosterone, progesterone, estriol, estrone, amoxicillin, clarithromycin ibuprofen, hydroxyibuprofen, and venlafaxine	0–720 ng/L (caffeine highest)	Vaudreuil et al. (2024)
Ganges River, India	15 pharmaceuticals were detected including Caffein, ketoprofen, ibuprofen, carbamazepine, ciprofloxacin, triclosan, acetaminophen, atenolol, sulfamethoxazole, diclofenac, hydrochlorothiazide, ketoprofen, naproxen, triclocarbon	0–743 ng/L (caffeine highest, then ketoprofen 107 ng/L)	Sharma et al. (2019)
Groundwater in Ganges River area, India	15 pharmaceuticals were detected including Caffein, ketoprofen, ibuprofen, carbamazepine, ciprofloxacin, triclosan, acetaminophen, diclofenac, sulfamethoxazole, hydrochlorothiazide, ketoprofen, naproxen, triclocarbon	0–262 ng/L (caffein highest, then ibuprofen- 49.4 ng/L)	Sharma et al. (2019)
Groundwater, Barcelona, Spain	Sulfadiazine, sulfadimethoxine, sulfamethazine, sulfamethizole, sulfamethoxazole, sulfamethoxypyrisazine, sulfapyridine, sulfaquinoxaline, sulfathiazole, N-acetyl-sulfamethoxazole	0–208 ng/L (Sulfadiazine highest)	Jurado et al. (2020)
River, Barcelona Spain	Sulfadiazine, sulfadimethoxine, sulfamethoxazole, sulfamethoxypyrisazine, sulfapyridine, N-acetyl-sulfamethoxazole, N-acetyl-sulfapyridine	0–30.5 ng/L (Sulfamethoxazole highest highest)	Jurado et al. (2020)
Mijares River, Spain	69 pharmaceutical contaminants were detected including acetaminophen, gabapentin, tramadol, venlafaxine, valsartan, ciprofloxacin, and diclofenac	0–1949 ng/L (tramadol highest)	Fonseca et al. (2020)
Groundwater Patna, India	73 emerging organic contaminants were detected including Sulfamethaxole, sulfanilamide, sulfamethazine, sulfathiazole, sulfonamides, dapson, fluconazole, carbamazepine, lidocaine, tramadol, climbazole, methylprednisolone, cetirizine, lamotrigine, and others	0–360 ng/L	Richards et al. (2021)
Drinking water taps (DWTP), Brazilian Federal District, Brazil	35 micropollutants of emerging concern were studied including diclofenac, Ibuprofen, Mefenamic acid, Atenolol, Sulfamethoxazole, Triclosan, Carbamazepine, Clofibric acid, Gemfibrozil, Caffeine, Paraxanthine, Nicotine, and others	0–7.8 ng/L (caffeine highest)	Sodré and Sampaio (2020)
Surface water, Peri-urban area, Mfoundi watershed Yaoundé Cameroon	15 pharmaceuticals were detected including carbamazepine, Codeine, Ibuprofen, diclofenac, Acetaminophen, sulfamethoxazole, atenolol	0–74 ng/L (Ibuprofen highest)	Branchet et al. (2019)
Surface water, Urban area Mfoundi watershed, Yaoundé Cameroon	15 pharmaceuticals were detected including carbamazepine, Codeine, Ibuprofen, diclofenac, Acetaminophen, sulfamethoxazole, atenolol, Ofloxacin	0–5660 ng/L (Acetaminophen highest)	Branchet et al. (2019)
Ground water, Urban area Mfoundi watershed, Yaoundé Cameroon	15 pharmaceuticals were detected including carbamazepine, Ibuprofen, diclofenac, Acetaminophen, sulfamethoxazole	0–73 ng/L (Sulfamethoxazole highest)	Branchet et al. (2019)
Groundwater, Kisumu, Kenya	Sulfamethoxazole (detected in 14.3% of groundwater sources)	0–258.2 ng/L	Karimi et al. (2023)
Lake Balaton, Hungary	46 pharmacologically active compounds were detected including caffeine, tramadol, diclofenac, lidocaine, verapamil, bisoprolol, alprazolam,	0–2675.1 ng/L (Caffeine highest)	Molnar et al. (2020)

(*continued on next page*)

Table 1 (*continued*)

Location	Pharmaceuticals	Concentration	Reference
	tiapride, mirtazapine, clozapine, lamotrigine, carbamazepine and others (less than 10 ng/L)		
Groundwater systems across the United States	103 pharmaceuticals were detected including 1,2-dimethylxanthine, acetaminophen, carbamazepine, sulfamethoxazole, and others (detection frequency less than 0.3%)	0–677 ng/L (Caffeine highest)	Bexfield et al. (2019)
Groundwater, Pennsylvania, United States	7 pharmaceuticals were detected including Acetaminophen, ampicillin, trimethoprim, naproxen, sulfamethoxazole, ofloxacin and caffeine	0–122.7 ng/L (Ofloxacin highest)	Kibuye et al. (2019)
Surface water (Close to WWTP), Iowa United States	109 pharmaceuticals were detected including metformin, carbamazepine, citalopram, fluconazole, caffeine, venlafaxine, atenolol, lidocaine, sulfamethoxazole, tramadol, methocarbamol, venlafaxine, fexofenadine, 1H-benzotriazole (accounted for 77%) and others	0.28–13500 ng/L (metformin highest)	Zhi et al. (2020)
Groundwater, Poland	Estrone, EE2, propranol, diclofenac, ibuprofen, ketoprofen, naproxen, paracetamol, flurbiprofen, caffeine, carbamazepine, sulfadiazine, sulfamethoxine, sulfamerazine, sulfamethoxazole, sulfapyridine and others less than 10 ng.L	0–869 ng/L (Carbamazepine highest, then caffeine 641 ng/L)	Kuczyńska (2019)
Groundwater/surface rural drinking water, Québec Canada	9 pharmaceuticals were detected including caffeine, naproxen, ofloxacin, acetaminophen, cyclophosphamide, ibuprofen, mefenmic acid, carbamazepine, and bezafibrate	0 to 1848 ng/L (mefenamic acid was highest, then cyclophosphamide- 1233 ng/L)	Husk et al. (2019)
Warta river, Poznan city, Poland	75 pharmaceutical compounds were detected including iomeprol, iopromide, metoprolol, metformin, 1H-Benzotriazole, iohexol, carbamazepine, sulfamethoxazole, diclofenac, naproxen and others.	0–485 ng/L (iohexol highest)	Kruć et al. (2019)
Groundwater, Poznan city, Poland	75 pharmaceutical compounds were detected including carbamazepine, sulfamethoxazole, diclofenac, naproxen, iohexol	0–184 ng/L (iohexol highest)	Kruć et al. (2019)
Groundwater, Xuzhou, China	Sulfacetamide, sulfamethoxypyridazine, sulfamethizole, sulfadimethoxine, sulfapyridine, fleroxacin, cinoxacin, ofloxacin, difloxacin, lomefloxacin, sparfloxacin, nalidixic acid, tilmicosin, josamycin, azitromycin	0–26.61 ng/L (Fleroxacin highest)	Gu et al. (2019)
Estuarine waters, Sao Paulo, Brazil	11 pharmaceutical compounds were detected including caffeine, acetaminophen, benzoylecgonine, atenolol, losartan, diclofenac, cocaine, furosemide, carbamazepine and orphenadrine	0–560 ng/L (caffeine highest, then acetaminophen0 22.24 ng/L)	Roveri et al. (2022)
Surface water, Costa Rica, Latin America	9 pharmaceuticals were detected including caffeine, gemfibrozil, acetaminophen, 1,7-dimethylxanthine, ibuprofen, salicylic acid, doxycycline, ketoprofen, and cephalexin, doxycycline, oxacillin, norfloxacin, ciprofloxacin and azithromycin, lincomycin, carbamazepine, clindamycin and sulfadimethoxine	0–3090 ng/L (oxacillin highest)	Rodríguez-Rodríguez et al. (2024)
Confluence Rivers: Torococha and Coata in Peru	23 pharmaceuticals detected including: acetaminophen, trimethoprim, sulfamethoxazole, flumequine, furaltadone, oxolinic acid, and norfloxacin	0 to 28,700 (acetaminophen highest, followed by sulfamethoxazole- 4360 ng/L)	Nieto-Juárez et al. (2021)
Lake Nahuel Huapi, Argentina	38 target pharmaceuticals were detected including ciprofloxacin, ciprofloxacin, paracetamol, and caffeine	0–110.6 ng/L (caffeine highest)	Beamud et al. (2024)
Drinking waters of Ecuador	Caffeine, sodium diclofenac, acetaminophen, sulfamethoxazole, trimethoprim	1.4–201 ng/L (Caffeine highest)	Jara-Negrete et al. (2023)
Coastal waters in Cape Town, South Africa	58 pharmaceutically active compounds were detected including salicylic acid, acetaminophen, atenolol, bezafibrate, codeine, ofloxacin, sulfamethoxazole, trimethoprim, and valsartan	0 to 5800 ng/L (winter) and 0 to 12,100 ng/L (summer) (Acetaminophen highest)	Newman et al. (2024)
Chinese surface waters	42 pharmaceuticals were detected including norfloxacin, caffeine, erythromycin azithromycin, cimetidine, clarithromycin, erythromycin, ibuprofen, trimethoprim, and sulfamethoxazole	0 to <2000 ng/L (norfloxacin highest)	Chen et al. (2024)
Rivers, western Kenya	785 pharmaceuticals were detected including at least 6 compounds >500 ng/L (Dehydroabietic acid, oxypurinol, metformin, emtricitabine, Guanylurea, and ibuprofen)	0 to 7500 ng/L (metformin highest)	(Chen et al., 2020)
Yarrowee/Leigh/Barwon River system, southeastern Australia	5 pharmaceuticals were detected including carbamazepine, primidone, propranolol, tramadol, and venlafaxine	0 to >500 ng/L (tramadol highest)	Harriage et al. (2024)
Dinaric karst catchment, Jadro and Žrnovnica springs in Croatia	1H-benzotriazole, gabapentin, and ketoprofen	0–5000 ng/L (1H-benzotriazole highest)	Selvaraj et al. (2018)
Surface water in Las Vegas, USA	7 pharmaceuticals were studied including benzoylecgonine, ketamine, 3,4-methylenedioxymethamphetamine (MDMA), and methamphetamine	8–194 ng/L (methamphetamine highest)	Sims et al. (2024)
Oro River Sub-basin (Colombia)	6 pharmaceuticals were studied including Ibuprofen, Cephalexin and Carbamazepine	0.5–12930 ng/L (Cephalexin highest)	Cerón-Vivas and Peñuela Mesa (2024)
Lipu River, China	30 pharmaceuticals were studied including Caffeine, flumequine, nifedipine, and lomefloxacin	33.30 ng/L to 99.60 ng/L (Caffeine highest)	Zhang et al. (2008)
Rivers in Arusha City, Tanzania	11 pharmaceutical compounds were detected including Paracetamol, ciprofloxacin, metronidazole, sulfamethoxazole, carbamazepine, caffeine, trimethoprim, amoxicillin, cetirizine, Ibuprofen, doxycycline.	0–520 ng/L (caffeine highest, followed by ciprofloxacin- 486 ng/L)	Kundu et al. (2024)
Groundwater in Arusha City, Tanzania	11 pharmaceutical compounds were detected including Paracetamol, ciprofloxacin, metronidazole, sulfamethoxazole, carbamazepine, caffeine, trimethoprim, amoxicillin, cetirizine, Ibuprofen, and doxycycline	0–94 ng/L (sulfamethoxazole highest, followed by caffeine- 91 ng/L and ciprofloxacin- 90 ng/L	Kundu et al. (2024)
Káraný waterworks, Czech Republic	38 pharmaceutical compounds were detected including Ibuprofen, gabapentin, acesulfame, oxypurinol, lamotrigine, primidone, carbamazepine, sulfamethoxazole among others	0–379 ng/L (Oxypurinol highest)	Hrkal et al. (2024)
East London Coastline, United Kingdom	5 targeted pharmaceutical compounds were detected including Trimethoprim, sulfamethoxazole, naproxen, ibuprofen, efavirenz	0–572 ng/L (efavirenz highest)	Netshithothole and Madikizela (2024)

(*continued on next page*)

Table 1 (*continued*)

Location	Pharmaceuticals	Concentration	Reference
Tagus River Basin in Spain	23 pharmaceutical compounds were detected including Acetaminophen, carbamazepine, gemfibrozil, ibuprofen, irbesartan, ketoprofen, venlafaxine among others	0–648 ng/L (irbesartan highest)	Royano et al. (2023)
L'Albufera Natural Park (Valencia, Spain)	20 pharmaceutical compounds were detected including fenamiphos, propyzamide, difenoconazole, propiconazole, metsulfuron methyl, sodium bis (perfluorohexyl) phosphinate (6:6 PFPiA), 6:2 fluorotelomer sulfonamide alkylbetaine (6:2 FTAB), 6:2 fluorotelomersulfonate (6:2 FTS), citalopram desmethyl and citalopram	153 ng/L (tebuconazole highest)	Soriano et al. (2024)
Potomac River in metropolitan Washington, DC	85 PPCP detected (caffeine, fexofenadine, nicotine, sulfamethoxazole, hydrochlorothiazide, MDA, desvenlafaxine, and metoprolol)	10–360 ng/L (highest not specified)	Foster et al., (2022)
Yellow River, China	30 PPCP detected, including 8 sulfonamides, 4 tetracyclines, 5 fluoroquinolones, 6 macrolides, and 7 other pharmaceuticals	82.13–115.82 ng/L (Caffeine highest)	Wang et al. (2022)
Wuliangsuhai Lake, China	30 PPCP detected, including 8 sulfonamides, 4 tetracyclines, 5 fluoroquinolones, 6 macrolides, and 7 other pharmaceuticals	111.04–192.26 ng/L – August 40.53–73.90 ng/L- November (Caffeine highest)	Wang et al. (2022)
Saskatchewan River, Canada	7 detected (amitriptyline, bupropion, carbamazepine, clozapine, fluoxetine, lamotrigine, and venlafaxine)	1.79 ng/L to 92.48 ng/L (lamotrigine highest)	Perez et al. (2022)
Wascana Creek, Canada	7 detected (amitriptyline, bupropion, carbamazepine, clozapine, fluoxetine, lamotrigine, and venlafaxine)	2.07 ng/L to 1118.64 ng/L (amitriptyline highest)	Perez et al. (2022)
Cerro Colorado spring, Mexico	Five pharmaceutically active compounds (PhACs), First two detected over quantification limit (azithromycin, ivermectin, famotidine, indomethacin, and dexamethasone)	0–63.5 ng/L (azithromycin, and ivermectin highest)	Durán-Álvarez et al. (2023)
Elbe River, Dresden, Germany	21 frequently detected including oxypurinol, carbamazepine, diclofenac, lamotrigine, valsartan, iomeprol and venlafaxine	0–1270 ng/L (oxypurinol highest)	Adomat and Grischek (2024)
Groundwater, Grombalia Plain, Tunisia	Pharmaceuticals including caffeine, ibuprofen, valsartan, irbesartan mefenamic acid, irgasan and acetaminophen	0–1482 ng/L	Khezami et al. (2024)
River Nile, Egypt	Caffeine	5730 to 53,850 ng/L	Tawfik et al. (2024)
North Canal Basin, Beijing, China	28 detected including ofloxacin, teracycline, ciprofloxacin, erythromycin, carbamazepine, sulfamethoxazole, and ciprofloxacin.	0–193 ng/L (norfloxacin highest)	Huangfu et al. (2024)
Almendares and San Juan River, Cuba	24 detected including acetaminophen, caffeine, cotinine, enalapril. Ibuprofen, naproxen, nicotine and sulfamethoxazole	0 to 40,000 ng/L (acetaminophen highest)	Larrea Murrell et al. (2024)
Lake Hawassa, Ethiopia	16 active pharmaceutical ingredients including ciprofloxacin, artesunate, mefloquine, fluconazole, and tramadol	0–764 ng/L	WM-Bekele et al. (2024)
Creeks and Campaspe River in Victoria, Australia	12 detected including venlafaxine, metoprolol, propranolol, carbamazepine, caffeine and sulfamethoxazole	<20–970 ng/L (venlafaxine highest)	Saaristo et al. (2024)
Yarra and Brisbane Rivers, Australia	16 pharmaceuticals including carbamazepine, nicotine, cotinine, gabapentin, venlafaxine, iopromide, codeine, and paraxanthine	0–118 ng/L (gabapentin highest)	Anim et al. (2020)
River Aconcagua and Maipo basins, Chile	Pharmaceuticals including methenamine, carbamazepine, and metformin	0 to 5600 ng/L (methenamine highest)	Soriano et al. (2024)
Rivers close to WWTPs in Basque County, Spain	110 detected including norfloxacin, crotamiton, amoxicillin, valsartan, tramadol, caffeine, azithromycin, and pefloxacin	0 to 8296 (norfloxaxin highest)	Beltrán de Heredia et al. (2024)
Municipal drinking water facilities in Ohio, USA	11 detected including caffeine, 17-beta-estradiol, naproxen, butalbital, cotinine, sulfamethoxazole, and ibuprofen	Source water: 0–37 ng/L (Cotinine highest) Finished water: 0–23 ng/L (Cotinine highest)	Dutta et al. (2024)
Monjolinho River Basin, Brazil	Acetaminophen, naproxen, and methylparaben	<200–576 ng/L (Acetaminophen highest)	Oliveira et al. (2024)
Chalk streams in Hampshie, UK	PhACs including caffeine, 2-hydroxy-terbuthylazine, atorvastatin, atenolol, sulfamethoxazole, alprazolam, azithromycin, carbamazepine, diclofenac and imidacloprid	0–517 ng/L (carbamazepine highest)	Robinson et al. (2024)
Mondego River, Portugal	PhACs including isopromide, sulfamethoxazole, carbamazepine, diclofenac, and bezafibrate	0–2810 ng/L (Isopromide highest)	Kötke et al. (2024)
Groundwater in La Palma and El Hierro, Canary Island	PhACs including caffeine, acetaminophen, carbamazepine, diclofenac, erythromycin, naproxen, mefenamic acid, gemfibrozil, and salicylic acid	0 to 235,004 ng/L (Caffeine highest)	Gasco Cavero et al. (2024)
Olt and Siret River, Romania	9 pharmaceuticals including omeprazole, lansoprazole, pantoprazole, nizatidine, cimetidine and famotidine,	0–20 ng/L (Nizatidine highest)	Chiriac et al. (2024)
Day River, Vietnam	14 pharmaceuticals including, azithromycin, carbamazepine, cefotaxime, cephalexin, ciprofloxacin, clarithromycin, erythromycin, levofloxacin, norfloxacin, roxithromycin, sotalol, sulfamethoxazole, and trimethoprim	1–24 ng/L (sulfamethoxazole highst)	Nguyen et al. (2024)

Contreras-Omaña et al., 2021; Murungi et al., 2023). Sulfamethoxazole is commonly administered in combination with trimethoprim (Ávila et al., 2021). However, trimethoprim is not as persistent in water due to its high distribution coefficient and water mobility and solubility (Karimi et al., 2023). This was the case of a study that examined the presence of sulfamethoxazole and trimethoprim in 49 water sources in Kenya (Karimi et al., 2023). Only sulfamethoxazole was detected. Finally, NSAIDs like acetaminophen and ibuprofen were the peak surface water contaminants detected in 11.4% of the studies reviewed. This was most prevalent in samples from Peru, Cameroon, and South Africa, with 28,700 ng/L, 5660 and 5800 ng/L acetaminophen (Branchet et al., 2019; Nieto-Juárez et al., 2021; Munzhelele et al., 2024).

The results also reveal that surface waters in African and Latin American countries exhibit comparatively higher concentrations of pharmaceutical pollutants. The most striking instance was recorded in Lagos, Nigeria, where amoxicillin was found at a concentration of 272,156 ng/L and acetaminophen at 12,430 ng/L (Ebele et al., 2020). Other notable findings (>5000 ng/L) in Africa include maximum concentrations in the coastal waters of Cape Town, South Africa (12,100 ng/L for acetaminophen), Lake Victoria in Uganda (5660 ng/L for sulfamethoxazole), and an urban stream in Yaoundé, Cameroon 5660 ng/L for acetaminophen) (Branchet et al., 2019; Nantaba et al., 2020;

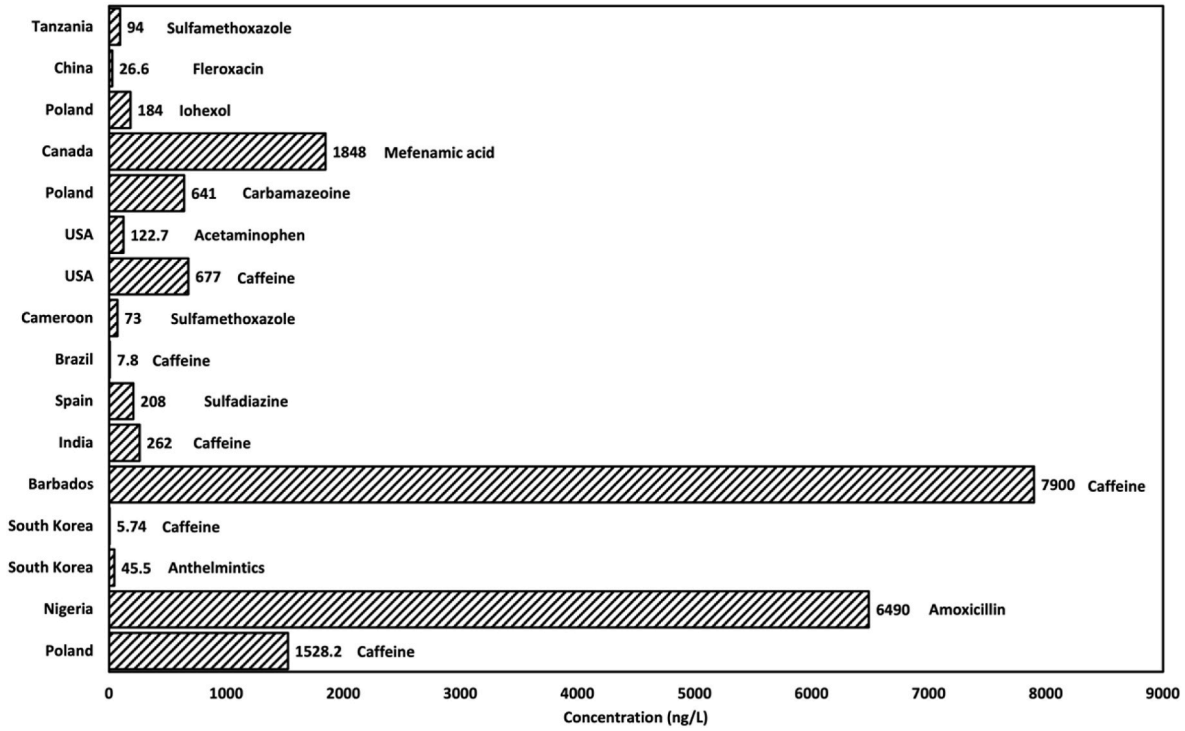


Fig. 3. Maximum pharmaceutical contaminant concentration detected in groundwater sources.

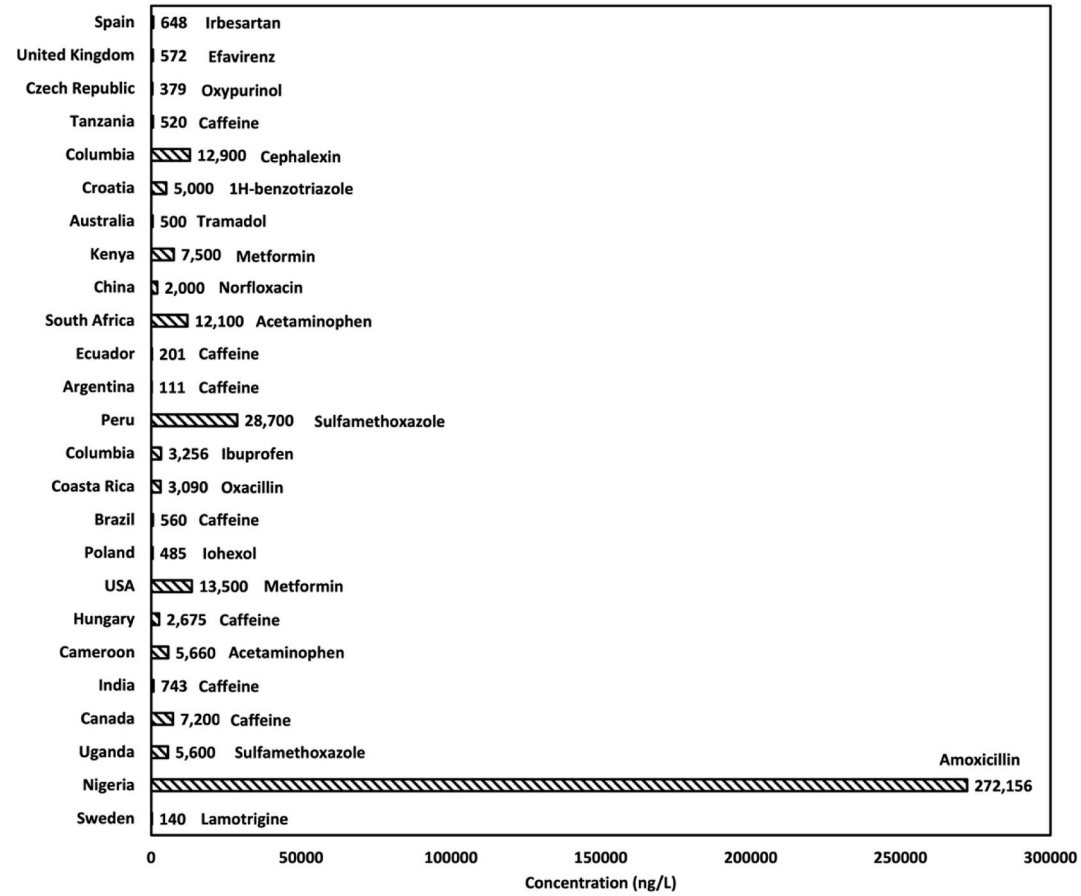


Fig. 4. Maximum concentrations of pharmaceutical pollutants in surface water.

Newman et al., 2024). Additionally, Latin American countries such as Peru (28,700 ng/L-sulfamethoxazole) and Colombia (12,900 ng/L-Cephalexin) also showed significantly high levels of pharmaceutical contaminants (Nieto-Juárez et al., 2021; Cerón-Vivas and Peñuela Mesa, 2024). All other studies reported peak concentrations of 5000 ng/L or less. A unifying characteristic of these regions is the sparse presence of centralized sewage systems and limited wastewater treatment facilities. Less than a third of the sewage generated in both African and Latin American countries undergoes any form of treatment (Diego, 2017; Ali and Gujiba, 2024). Moreover, a UN report highlighted that only 8% of domestic and industrial wastewater in Africa is treated to meet basic effluent quality standards (UNESCO, 2017). This stark reality underscores the immense challenges these regions face, especially when compared to developed countries, which are now focusing on retrofitting existing wastewater treatment plants to address emerging pollutants (Tian et al., 2020). Fig. 4 provides a summary chart of the maximum concentration of pharmaceutical pollutants in surface water across the study locations.

3. Factors associated with the occurrence of pharmaceuticals in freshwater

Pharmaceuticals in freshwater systems stem from multiple interconnected pathways, with wastewater treatment plant effluents, groundwater recharge processes, and inadequate sanitation infrastructure emerging as primary contributors (Fig. 5). While wastewater treatment facilities serve as point sources introducing pharmaceutical loads through treated effluents, groundwater recharge mechanisms facilitate contaminant transport through soil matrices and aquifer systems. In regions lacking adequate infrastructure, septic systems and informal sanitation facilities create diffuse pollution sources, often directly contaminating water resources. Understanding these pathways is crucial for developing effective mitigation strategies and protecting water quality across diverse geographical and socioeconomic contexts. This section provides insights into each of these primary point sources and ends with a table (Table 2) highlighting characteristics of some of the most prevalent pharmaceuticals in freshwater and potential means of remediation.

3.1. Wastewater effluent

Municipal and industrial wastewater treatment plants represent a critical pathway for pharmaceutical entry into water systems, with their effluents showing distinct regional characteristics that reflect local healthcare patterns and treatment capabilities. Treatment efficiency varies significantly across facilities and compounds, often resulting in substantial pharmaceutical loads entering receiving waters. Treatment performance studies reveal concerning removal inefficiencies.

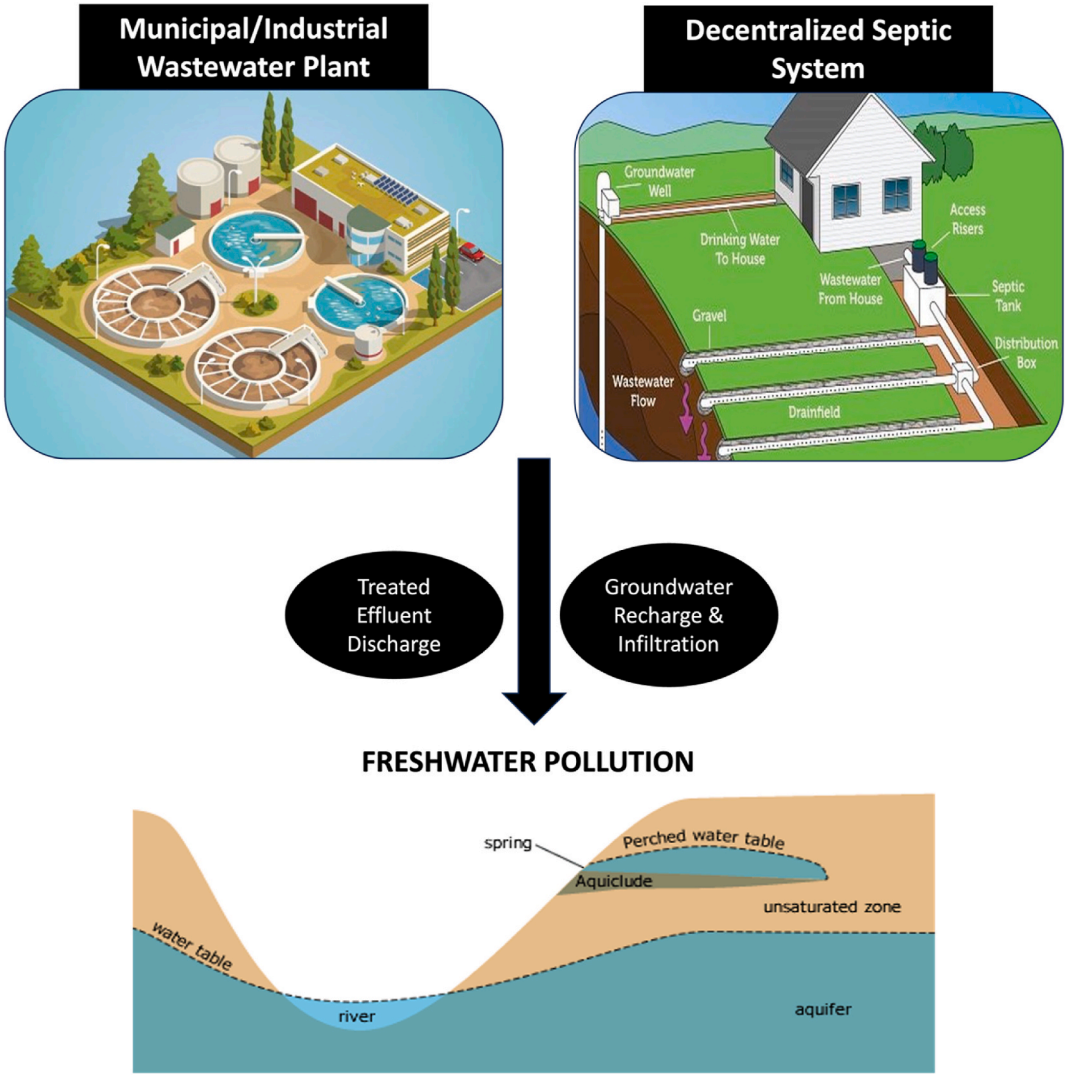


Fig. 5. Point sources of pharmaceutical pollution in freshwater.

Table 2
Characteristics of some of the most prevalent pharmaceuticals in freshwater and recommended remediation methods.

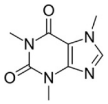
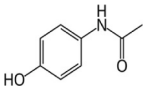
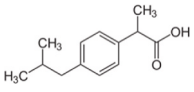
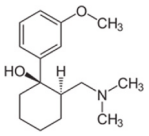
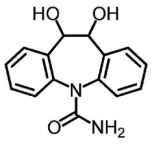
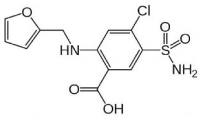
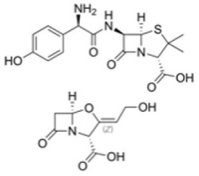
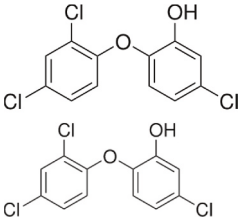
Pharmaceutical Class	Name	Molecular Structure	Chemical Properties	Degradability and recommended treatments	References
Stimulant	Caffeine		MW: 194.19 g/mol Solubility: 2 g/100 mL (20 °C) pKa: 0.7	Highly degradable in conventional systems but present in exceptionally high influent concentrations. Efficient treatment achieved via nanoparticle aided photocatalysis	(Muthukumar et al., 2020; National Center for Biotechnology Informatio, 2024; Tawfik et al., 2024)
Analgesic	Acetaminophen		MW: 151.16 g/mol Solubility: 1.4 g/ 100 mL (20 °C) pKa: 9.4	Moderately degradable in conventional systems due to solubility in water. Photocatalysis, bimetallic metal-organic framework adsorption, and Fenton-based processes reportedly efficient	(Pacheco-Álvarez et al., 2022; Mohsentabar et al., 2023; Alrefaee et al., 2024; National Center for Biotechnology Information, 2024a)
	Ibuprofen		MW: 206.29 g/mol Solubility: 5g/100 mL (20 °C) pKa: 4.9	Highly degradable in conventional systems via aerobic biodegradation. However, it is present in significant concentrations due to extensive use and can transform to harmful metabolites like 4-isobutylacetophenone. Tertiary treatment such as advanced oxidation processes recommended.	(Smook et al., 2008; Minella et al., 2019; National Center for Biotechnology Information, 2024b)
	Tramadol		MW: 206.29 g/mol Solubility: <20 mg/ mL (20 °C) pKa: 9.4	Moderately degradable in conventional systems. Due to relatively high solubility, it mostly persists in water instead of accumulating in sludge/ sediments. Efficient treatments recently reported with electro-Fenton and gamma irradiation-nanofiltration	(Smyj et al., 2013; Ghazouani et al., 2022; Benkayba et al., 2023)
Anticonvulsant	Carbamazepine		MW: 236.27 g/mol Solubility: 17.7 mg L^{-1} (25 °C) pKa: neutral	Poor biodegradability due to molecular stability. Exhibits extremely low water-sludge distribution coefficient (Kd), preventing significant sorption onto activated sludge. Low Henry coefficient ($1.09 \times 10{-}5$) limits removal via air stripping, resulting in persistence in aqueous phase. Efficient tertiary treatment methods include electrochemical methods, photocatalytic, and AOPs.	(Zhang et al., 2008; García-Espinoza et al., 2018; Feijoo et al., 2023)
Antibiotics	Sulfamethoxazole		MW: 253.28 g/mol Solubility: 0.46 g/L (20 °C) pKa: 6.16 to 1.97	Moderate biodegradation in conventional biological treatment systems due to antimicrobial properties and complex molecular structures. High water solubility and low sorption affinity to activated sludge/biological granules facilitates mobility through treatment systems and subsequent infiltration into groundwater aquifers. Efficient treatment reported via electrochemical and AOP systems.	(Hassan et al., 2021; Soares et al., 2022; Tulková et al., 2023)
	Amoxicillin		MW: 289.54 g/mol Solubility: 10 mg L^{-1} (20 °C) pKa: 2.68 (carboxyl group); 7.49 (amine group); 9.63 (phenol group)	Moderately biodegradable but present in high concentrations due to extensive use and low metabolic rate (10–30%) in humans. Tertiary treatment such as nanophotocatalysis and other advanced oxidation methods recommended.	(Olama et al., 2018; Silva et al., 2022; Verma et al., 2022)
	Triclosan		MW: 289.54 g/mol Solubility: 10 mg L^{-1} (20 °C) Solubility: 10 mg L^{-1} (20 °C) pKa: 7.9	Moderately degradable during aerobic biodegradation (t1/2 ≈ 8 days) but shows poor removal under anoxic conditions (t1/2 ≈ 53 days). Removal efficiency decreases at higher concentrations. Strong sorption onto soil particles through hydrophobic interactions and π–π bonding with organic matter. Efficiently removed via photolysis (100% in 60 min) and aerobic composting of sewage sludge.	(Durán-Álvarez et al., 2015; González-Fernández et al., 2024; National Center for Biotechnology Information, 2024c; Wang et al., 2024)

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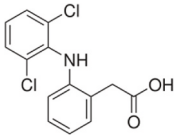
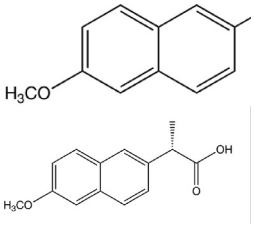
Table 2 (*continued*)

Pharmaceutical Class	Name	Molecular Structure	Chemical Properties	Degradability and recommended treatments	References
Non-steroidal anti-inflammatory drug	Diclofenac		MW: 296.16 g/mol Solubility: 23.73 mg L^{-1} (25 °C) pKa: 4.15	Poor biodegradability and structural stability over extended periods. Low water-sludge distribution coefficient limits sorption onto activated sludge, while minimal air stripping occurs due to very low Henry coefficient (4.79 × 10−7). Efficient degradation reported using integrated photocatalysis process and advanced oxidation.	(Zhang et al., 2008; Tra et al., 2023)
	Naproxen		MW: 230.29 g/mol Solubility: 15.9 mg L^{-1} (25 °C) pKa: 4.15	Moderately biodegradable under aerobic conditions (t1/2 ≈ 7 days) but shows significant reduction in removal under anoxic conditions (t1/2 ≈ 74 days) and at higher concentrations (t1/2 increases to 15 days). Low soil retention indicates high mobility in the environment. Effectively removed through photolysis (92% in 2 h) and advanced oxidation processes.	(Durán-Álvarez et al., 2015; Moreno Ríos et al., 2022; National Center for Biotechnology Information, 2024d; Schattschneider et al., 2024)

Treatment technology significantly influences removal efficiency.

A comprehensive study of 22 municipal treatment plants revealed varying performance across nine technologies: membrane bioreactors achieved highest removal (99.8%), followed by oxidation ditches (99.0%) and aerated/facultative lagoons (~98%), while primary treatment showed minimal effectiveness (3.0%). Longer hydraulic retention times in lagoon systems contributed to enhanced pharmaceutical degradation, though compounds like venlafaxine, metoprolol, and metformin showed persistent resistance to removal (Greenham et al., 2019). In Patagonia, a conventional treatment plant employing mechanical pretreatment and biological activated sludge processes demonstrated highly variable removal rates: while achieving 66% removal for ciprofloxacin, it showed complete ineffectiveness (0% removal) for carbamazepine. Even with three-stage treatment including chlorination, high concentrations persisted in effluents, with caffeine detected at 41,728 ng/L in influent waters (Beamud et al., 2024). The impact of treatment type on pharmaceutical removal is further evidenced in waste stabilization ponds, where removal efficiencies exceed 95% for compounds like chloramphenicol and paracetamol, but remain low for carbamazepine (32%) and nevirapine (11–49%) (K'oreje et al., 2016).

The impact of WWTP effluents extends significantly into receiving waters. In La Palma island, despite conventional primary and secondary treatment with chlorination, effluents contained elevated levels of multiple pharmaceuticals: acetaminophen (42,458 ng/L), caffeine (235,044 ng/L), and salicylic acid (78,353 ng/L) (Gasco Cavero et al., 2024). More concerning, these compounds persisted in receiving water bodies, with similar detection rates observed in downstream water springs and galleries, suggesting ineffective removal and extensive environmental persistence (Gasco Cavero et al., 2024). Long-term monitoring demonstrates the persistent impact of WWTP effluents on receiving waters. A five-year study of the St. Lawrence watershed revealed significant pharmaceutical contamination extending 70 km downstream from municipal effluents, with high concentrations of ibuprofen (860 ng/L), hydroxyibuprofen (1800 ng/L), and caffeine (7200 ng/L). Risk assessment identified chronic exposure risks to aquatic organisms from caffeine, carbamazepine, diclofenac, and ibuprofen, despite substantial river dilution (Vaudreuil et al., 2024).

Regional pharmaceutical profiles in wastewater reflect local disease burdens and healthcare practices. In Ethiopia, high concentrations of antimalarial drugs (artesunate, mefloquine) dominate the pharmaceutical profile due to endemic malaria (WM-Bekele et al., 2024), while Ugandan wastewaters show elevated levels of sulfamethoxazole and trimethoprim, reflecting their widespread use in HIV treatment protocols (Nantaba et al., 2020). This geographic variation is further exemplified in a comparative study across Brazil, Cameroon, and Madagascar, where hospital wastewaters showed distinct pharmaceutical signatures: chlorhexidine dominated in Brazil (up to 89,280 ng/L), azithromycin in Cameroon (1140–1210 ng/L), and ceftriaxone in Madagascar (680-11,530 ng/L) (Scaccia et al., 2024).

3.2. Groundwater recharge

Groundwater recharge, both natural and artificial, represents a significant pathway for pharmaceutical contamination of aquifers. research reveals more complex transport and attenuation mechanisms during recharge processes. A nationwide survey assessing micro-pollutants in groundwater across the United States revealed that the pollutants were more commonly detected in recently recharged shallow wells. (Bexfield et al., 2019). Another survey examining the effect of bank infiltration on pharmaceutical contamination revealed that farther wells are located from the riverbanks, the lower the levels of pharmaceutical pollutants detected. A safe gap of 60 m was suggested to reduce infiltration of contaminants to groundwater sources located near polluted surface water (Kruć et al., 2019). Recent research reveals more complex transport and attenuation mechanisms during recharge processes. In managed aquifer recharge systems using treated wastewater, pharmaceutical behavior varies significantly by compound.

Detailed analysis of natural bank filtration systems reveals compound-specific removal patterns. In the Jizera River system, monitoring over 180 m of fluvial Quaternary sediments showed varying attenuation rates: while iohexol, iopromide, metoprolol, cetirizine, valsartan, and clarithromycin were removed within 60 m, other compounds like sulfamethoxazole showed minimal attenuation (9%). Notably, some compounds (benzotriazole, propylparaben, bisphenol S, hydrochlorothiazide, ibuprofen-2-hydroxy) passed through the quaternary fluvial aquifer virtually unchanged, indicating the limitations of natural filtration processes (Hrkal et al., 2024). Column experiments demonstrate diverse attenuation mechanisms: while carbamazepine primarily attenuates through sorption, compounds like naproxen show progressive degradation with depth, achieving >90% removal. Diclofenac demonstrates condition-dependent behavior, with approximately 50% degradation during wetting-drying cycles but minimal degradation under continuous infiltration (Silver et al., 2018). Long-term monitoring of managed recharge systems reveals that atenolol, propranolol, and trimethoprim achieve high removal rates (>80%), while compounds like carbamazepine, primidone, and certain sulfonamides persist, showing removal rates below 20% (Park and Lee, 2018).

The scale of contamination is particularly evident in nationwide surveys. In China, a comprehensive analysis of 15 recharge sites

revealed antibiotics at concentrations ranging from 212-4035 ng/L in reclaimed water and 19-1270 ng/L in groundwater, with fluoroquinolones dominating in northern regions and sulfonamides in the south (Ma et al., 2015). Another study in China analysing 151 organic compounds identified nonylphenol (947.79 ng/L), erythromycin, and ibuprofen as the highest-priority contaminants, with pharmaceuticals and endocrine-disrupting compounds comprising the majority of high-priority compounds regardless of recharge method (Li et al., 2014). Similar patterns emerge in detrital aquifers receiving treated wastewater, where monitoring within a 1-km radius of injection wells showed the persistence of multiple pharmaceuticals above 100 ng/L, with changes in water chemistry suggesting complex interactions between recharge processes and pharmaceutical transport (Candela et al., 2016).

The influence of surface water-groundwater interactions is particularly evident in areas receiving wastewater treatment plant effluents. In Barcelona, Spain, groundwater monitoring revealed 72 pharmaceuticals and 23 transformation products, with antibiotics being the most frequently detected compounds at concentrations up to 1000 ng/L. Natural bank filtration from rivers receiving wastewater effluents proved to be the dominant contamination source, resulting in groundwater concentrations sometimes exceeding those in the source river (López-Serna et al., 2013). Studies in Tunisia demonstrate that groundwater zones near Wadis receiving wastewater treatment plant effluents show the highest concentrations (>2000 ng/L) and the largest number of detected compounds. The detection of typically soil-retained compounds like metoprolol and tramadol suggests direct aquifer contamination without soil filtration in some cases (Khezami et al., 2024).

Recent research has expanded to include submarine groundwater discharge as a pathway for pharmaceutical transport to coastal waters. In Sydney Harbour, Australia, groundwater discharge explains over 80% of observed coastal inventories for several compounds, including caffeine, carbamazepine, and sulfamethoxazole, with some compounds reaching concentrations posing high ecological risk (McKenzie et al., 2020). This emerging understanding of groundwater-surface water interactions highlights the need for comprehensive management strategies addressing both recharge quality and discharge impacts (Jurado et al., 2020).

3.3. Inadequate sanitation infrastructure and septic system discharge

Sanitation infrastructure varies significantly in effectiveness, with centralized wastewater collection systems connected to properly maintained treatment plants offering the best protection against pharmaceutical contamination. While septic tanks and French drains, common in suburban and rural areas, show higher leakage incidence, they still outperform pit latrines and direct emissions in preventing pharmaceutical seepage into the environment (Burri et al., 2019). This infrastructure gap is particularly critical in developing countries, where rapid population growth, inadequate sanitation facilities, open defecation, and water scarcity challenge the implementation of effective sanitation solutions (Burri et al., 2019; Wada et al., 2020, 2022).

The relationship between inadequate sanitation infrastructure and pharmaceutical contamination of water resources represents a significant global challenge, with particularly severe implications in developing regions and rural areas. Septic systems and decentralized treatment facilities serve as major pathways for pharmaceutical contamination, especially when poorly designed, maintained, or operated beyond their intended lifespan (Kibuye et al., 2019). In developed nations, the challenge persists even with better infrastructure. For instance, in the United States, approximately 25% of the population relies on septic systems for wastewater treatment, while 13% source drinking water from private wells, creating potential contamination pathways where soil conditions are unsuitable for proper filtration (Collins, 2023). A nationwide study in Poland found pharmaceutical contamination in over 50% of groundwater samples, with notably higher concentrations in rural areas dependent on septic systems (Kuczyńska, 2019).

The situation is more critical in developing regions where sewerage connectivity is severely limited. In Nigeria, the absence of comprehensive sewage systems in most urban communities has resulted in extreme contamination levels, with amoxicillin detected at concentrations up to 272,150 ng/L in surface waters (Ebele et al., 2020). Similarly, in Kenya's peri-urban areas, poor sewage connectivity and inadequately designed decentralized systems result in the direct release of pharmaceuticals into open drains, with extremely high concentrations reported: Lamivudine (48,700 ng/L), Sulfamethoxazole (108,000 ng/L), and Ciprofloxacin (532,000 ng/L) (Muriuki et al., 2020). In Sri Lanka, insufficient on-site sanitation systems led to significant pharmaceutical contamination in surface drainage systems, with acetaminophen dominating hospital discharge (70,200–123,600 ng/L) and caffeine prevalent in surface drainage (950-21,730 ng/L) (Quyen et al., 2021). In Kenya, nevirapine, the antiretroviral drug was detected in concentrations up to 2000 ng/L in shallow wells located in close proximity to pit latrines, indicating the vulnerability of individuals living in such underdeveloped societies (K'oreje et al., 2016).

The disparity between high and low-income countries is particularly stark in terms of contamination pathways. While high-income countries primarily deal with point-source contamination due to high sewer connectivity, low and middle-income countries face diffuse-source impacts from leaking septic systems and raw sewage disposal (Kookana et al., 2014). This is exemplified in cities like Yaoundé, where limited sanitation infrastructure has made pharmaceuticals like carbamazepine reliable anthropogenic tracers in surface waters (Branchet et al., 2019). Most of the pharmaceuticals detected in the urban streams in the Cameroon capital city were associated with wide use of pit latrines and landfills in the rapidly urbanizing city (Branchet et al., 2019). Even in developed rural settings, the challenges persist. A UK study of rural hospital discharge and wastewater treatment revealed pharmaceutical concentrations ranging from 3 ng/L (carbamazepine) to 105,910 ng/L (paracetamol) in hospital discharge, with varying removal efficiencies in treatment plants. Some compounds, like carbamazepine and clarithromycin, showed negligible removal, highlighting the persistence of these contaminants even in advanced treatment systems (Niemi et al., 2020). Further evidence of septic system impacts comes from a comprehensive Scottish study of community septic tanks serving populations of 217–475 people. The study detected all 68 investigated emerging contaminants in septic tank effluent, with concentrations ranging from 0.016 ng/L to 2,605,000 ng/L. Notably, pharmaceuticals used for acute conditions, such as antibiotics and antifungals, showed high monthly variability and sometimes exceeded concentrations found in centralized wastewater treatment works. The study revealed minimal to no removal of pharmaceuticals in septic tanks, with downstream river concentrations increasing by up to 95% at discharge points. While dilution generally maintained low environmental risk quotients, compounds like ibuprofen, diclofenac, and ciprofloxacin occasionally exceeded risk thresholds, particularly in areas with low dilution factors (Wilschnack et al., 2024).

4. Existing and emerging technologies for treating pharmaceutical pollutants in water

The presence of pharmaceutical pollutants in wastewater is an escalating environmental challenge, prompting the development of innovative treatment technologies (Chai et al., 2021; Samantaray et al., 2021). The escalating presence of pharmaceutical pollutants in water systems necessitates both centralized and decentralized treatment approaches to ensure comprehensive mitigation. While centralized wastewater treatment plants employ sophisticated technologies for large-scale removal, decentralized point-of-use systems offer crucial solutions, particularly in regions lacking adequate infrastructure or where additional treatment is desired. This dual approach enables a

more robust strategy for addressing pharmaceutical contamination across diverse geographical and socioeconomic contexts. This section examines technologies for both centralized and decentralized systems. Fig. 6 broadly categorizes available and emerging technologies, while Table 3 highlights some specific technologies for the degradation of some of the most prevalent pharmaceutical pollutants in wastewater treatment facilities and their respective treatment efficiencies.

4.1. Advanced oxidation processes

Advanced Oxidation Processes (AOPs) are a highly effective method for degrading pharmaceuticals in freshwater ecosystems, offering a promising solution to mitigate pharmaceutical pollution (Kanakaraju et al., 2018). These processes are characterized by the production of highly reactive species, primarily hydroxyl radicals (•OH), which exhibit non-selective and potent oxidative properties. The versatility of AOPs lies in their ability to break down organic contaminants into harmless by-products, such as carbon dioxide and water, making them an attractive option for advanced water treatment systems (Kamath et al., 2018; Pandis et al., 2022).

4.1.1. Hydroxyl radical formation

Hydroxyl radicals, the cornerstone of AOP efficiency, are generated through various mechanisms. These include ultraviolet (UV) irradiation, the decomposition of ozone, and reactions with hydrogen peroxide. For instance, UV irradiation can directly split hydrogen peroxide molecules, while ozone decomposition in water generates radicals through catalytic processes. Similarly, persulfate activation by UV leads to the formation of sulfate radicals (Biard et al., 2018; Wang et al., 2020; Maier et al., 2019). These radicals are highly reactive and capable of oxidizing a wide range of organic pollutants. Key reactions include:

$$H_2O_2 + h\nu \rightarrow 2{\cdot}OH$$

$$O_3 + H_2O \rightarrow 2 \cdot OH + O_2$$

$$S_2O_8^{2-} + UV \rightarrow 2{\cdot}SO_4^{-}\ (\text{persulfate})$$

4.1.2. Direct and indirect oxidation pathways

AOPs function through two primary oxidation pathways. Direct oxidation involves pollutants directly interacting with hydroxyl radicals, leading to the breakdown of the contaminant (Chen et al., 2020). Indirect oxidation, on the other hand, occurs when intermediate species such as superoxide anions ($\cdot O_2^-$) participate in secondary reactions, enhancing the overall degradation process (Kato et al., 2022). This combination of direct and indirect pathways ensures a robust pollutant removal mechanism.

The chemical processes underlying AOPs are diverse and effective in generating reactive radicals. Examples include the catalytic decomposition of ozone to form hydroxyl radicals, as well as the electron-hole generation in photocatalysis, exemplified by:

$$O_3 \rightarrow \cdot OH\ via\ catalytic\ decomposition$$

$$TiO_2 + h\nu \rightarrow e^- + h^+\ (electron - hole\ generation\ for\ photocatalysis)$$

4.1.3. Photocatalysis

Photocatalysis, an extensively researched advanced oxidation process, utilizes semiconductor materials such as titanium dioxide (TiO_2), which are activated by UV or visible light to produce reactive radicals that decompose pharmaceuticals on the catalyst surface (Nasr et al., 2018a,b). Recent breakthroughs encompass the creation of doped TiO_2 for improved light absorption for instance 3D nanostructured N-doped

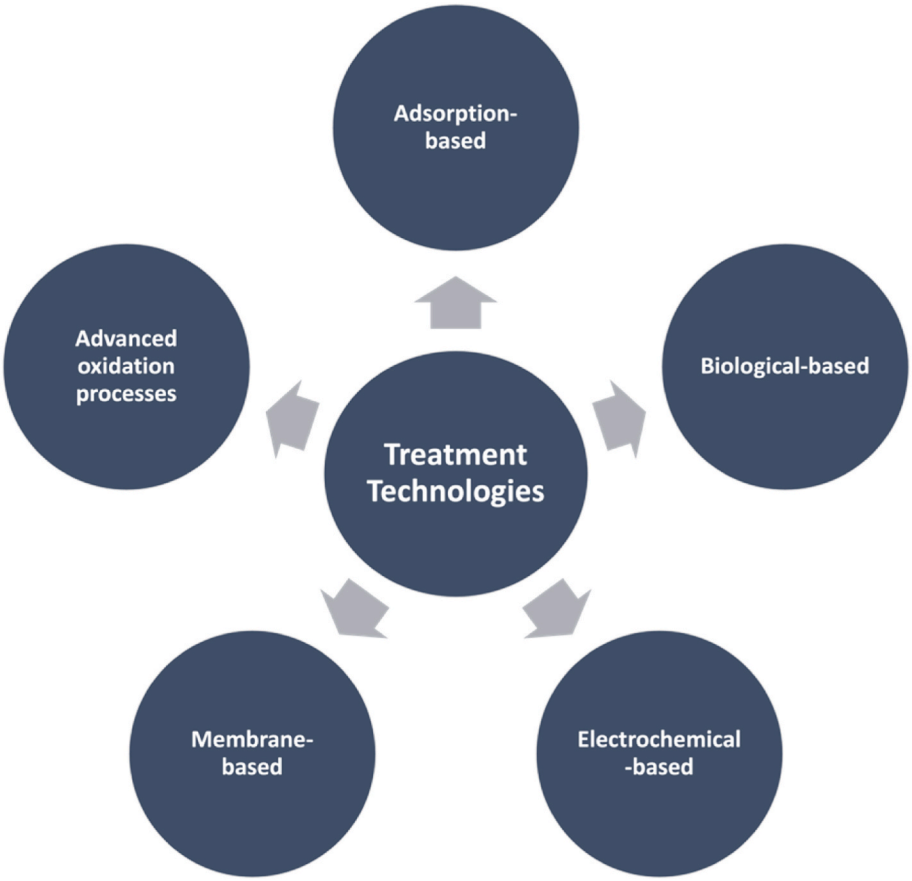


Fig. 6. Major technologies available for the treatment of pharmaceutical pollutants in water.

Table 3
Technologies for treating pharmaceutical pollutants in wastewater.

Technology	Pharmaceuticals	Treatment Efficiency	Reference
Photocatalysis	Carbamazepine, diclofenac, ciprofloxacin, and sulfamethoxazole	High	(Antoniadou et al., 2021; Mestre and Carvalho, 2019; Mahmood et al., 2024)
Ozonation	Ibuprofen, carbamazepine, frusemide and ofloxacin	High (100%)	(Khan et al., 2020; Nadeem et al., 2020b)
Forward Osmosis	Trimethoprim and sulfamethoxazole	High (98%)	(Dong and Ge, 2019)
Nanofiltration	Diclofenac, ibuprofen, and paracetamol	High [diclofenac (99.7%) > ibuprofen (81.2%) > paracetamol (49%)]	(Martínez-Huitle and Panizza, 2018)
Constructed Wetlands	Anthrazine	High (90%)	(Chen et al., 2020)
Bioaugmentation	Ibuprofen, naproxen, diclofenac and paracetamol	Moderate	(Żur et al., 2020)
Electro-Fenton Process	gabapentin, ibuprofen, naproxen, pentoxifylline, and venlafaxine.	Moderate (24.2%–56%)	(Jiménez et al., 2019)
Electrocoagulation	Amoxicillin, carbamazepine, and diclofenac	Moderate (42%–46%)	(Ensano et al., 2019)
Adsorption	Acetaminophen	High (97%)	(Negarestani et al., 2024)
Fixed-bed membrane bioreactors	Naproxen, ibuprofen, and ofloxacin	High (>90%)	(Mokhtariazar et al., 2024; Husain et al., 2020)
Green polymeric membrane	Sodium diclofenac	High (80%)	(Suliani Raota et al., 2024)
Sponged-based biofilm reactor	Ibuprofen	High (92.7%)	(Chai et al., 2021)
Fenton and adsorption (simultaneous process)	Paracetamol and atenolol	High (98–99%)	(Jurado et al., 2020)
Nanocomposite beads	Diclofenac and tetracycline	High (660% and 747%, respectively)	(Abioye et al., 2025)
Hydrodynamic cavitation and cold plasma	Furosemide	High (100%, 10 min)	(Verma et al., 2022)
Catalytic ozonation	Ibuprofen	High (85%)	Huangfu et al. (2024)

TiO_2 photocatalysts with enhanced visible light absorption show 33% enhanced photocatalytic performance compared to pure 3D TiO_2 under sunlight (Cho et al., 2018), and graphene-based composites for augmented surface area - Adding graphene to CdS/graphene composites improves specific surface area and catalytic activity, leading to efficient treatment of organic pollutants and electron mobility (Chen et al., 2020), and metal-organic frameworks (MOFs) for customized catalytic characteristics - MOFs-based heterogeneous photocatalysts provide enhanced photocatalytic performance for hydrogen production, CO_2 reduction, and photodegradation of organic dyes (Reddy et al., 2020). These developments seek to enhance the efficacy and application of photocatalysis in the remediation of pharmaceutical pollutants in water.

4.1.4. Ozonation

Ozonation is a potent advanced oxidation process wherein ozone decomposes in water to produce reactive radicals that can degrade medicines for example antineoplastic drug formulations like gemcitabine and irinotecan (Kato et al., 2022). The efficacy of this process can be markedly improved through the utilization of catalysts such activated carbon, which amplifies radical generation, or metal oxides, which facilitate selective oxidation routes for instance, Ozone treatment with O_3 and activated carbon can reduce phenol concentration in pharmaceutical wastewater from 11.2 to 1.2 ppm (Ratnawati et al., 2020). These catalytic improvements render ozonation a versatile and efficacious method for addressing pharmaceutical pollutants in aquatic systems. Example: $O_3 \rightarrow O_2 + \cdot OH$.

4.1.5. Advanced oxidation processes for pharmaceutical degradation in water systems

UV/Ozone Combined Systems represent an advanced hybrid approach that combines UV light and ozone to enhance hydroxyl radical formation. This method significantly improves pharmaceutical degradation and facilitates the removal of total organic carbon from water systems (Rivas et al., 2012). Its effectiveness is particularly notable in treating micropollutants present at low concentrations, offering a viable solution for addressing emerging contaminants in water treatment processes (Granzoto et al., 2021). Persulfate-based systems involve the activation of persulfate ions $\left(S_2O_8^{2-}\right)$ using ultraviolet light, thermal energy, or transition metals. The process generates sulfate radicals $\left(\cdot SO_4^-\right)$, which exhibit high reactivity and selectivity, making them effective for degrading pharmaceuticals in high ionic-strength water matrices (Karim et al., 2021; Xu et al., 2023). This selectivity allows persulfate systems to operate efficiently under challenging water conditions, further demonstrating their adaptability in water treatment applications.

AOPs achieve significant removal efficiencies for a range of pharmaceuticals, including antibiotics, analgesics, and hormones (Wang and Zhuan, 2020). However, their performance is strongly influenced by the composition of the water matrix and the specific properties of the contaminants. Constituents of the water matrix, such as natural organic matter (NOM), bicarbonates, and chloride ions, can affect radical availability. For example, the interaction between chloride ions and hydroxyl ($Cl^- + \cdot OH \rightarrow \cdot ClOH^-$) results in less reactive intermediates, potentially reducing process efficacy (Lado Ribeiro et al., 2019). Operational parameters, such as pH, temperature, and oxidant concentration, also play a critical role in determining the efficiency of AOPs. Ozone systems, for instance, perform optimally at a pH of 7–8. This underscores the importance of carefully managing these variables to maximize pollutant degradation. Although AOPs effectively degrade parent pharmaceutical compounds, they may produce intermediate transformation products that require additional treatment. For example, the oxidation of diclofenac can lead to chlorinated by-products, which may pose environmental risks if not adequately removed (Zilberman et al., 2023). Therefore, the formation of these by-products necessitates further research and refinement of treatment processes to ensure comprehensive pollutant removal.

4.1.6. Limitations

AOPs face several limitations, including challenges in achieving complete mineralization of pharmaceuticals. Often, these processes leave behind partially oxidized intermediates in the treated water, which may require additional treatment to ensure environmental and human safety (Ike et al., 2019). Another critical concern is the formation of toxic by-products during the oxidation of pharmaceuticals. For instance, in the presence of halides or nitrogen-containing pharmaceuticals, oxidation can produce harmful substances such as aldehydes, halogenated compounds, or nitrosamines. Photocatalytic oxidation, in particular, has been associated with the generation of toxic by-products, raising significant environmental safety concerns about water treatment technologies (Gomes et al., 2021).

Moreover, AOPs, especially those relying on UV-based systems, are energy-intensive, leading to high operational costs. This necessitates the use of more efficient light sources and process optimization to improve energy efficiency and sustainability (Sgroi et al., 2021). The efficiency of AOPs is further hindered by the effects of the water matrix, where constituents such as organic matter or ions quench reactive radicals, thereby reducing treatment effectiveness. To mitigate this, pretreatment steps like coagulation or filtration are often required to minimize the adverse impacts of these matrix effects on the overall process (X. Yang et al., 2022; Wen et al., 2022).

4.1.7. Recent advancements

Recent advancements in AOPs have significantly improved their efficiency, scalability, and sustainability. The development of novel catalysts, such as graphene-based materials, doped semiconductors, and MOFs, has enhanced the generation of reactive radicals while improving process stability and reusability (Wang et al., 2019). These advanced materials represent a breakthrough in addressing challenges related to catalyst degradation and operational longevity.

Hybrid systems have also emerged as a promising innovation, combining AOPs with biological or membrane technologies to harness synergistic benefits. For example, coupling photocatalysis with membrane reactors achieves higher contaminant removal rates while simultaneously mitigating fouling, a common issue in water treatment systems (Binazadeh et al., 2023). Furthermore, advancements in reactor design, such as the development of flow-through photoreactors and optimized light distribution systems, have made AOPs more efficient and scalable. Computational modelling is increasingly being utilized to tailor operating conditions for specific contaminants, further enhancing the precision and effectiveness of these processes (Giwa et al., 2021; Shetty et al., 2003).

Innovative strategies such as solar-driven photocatalysis and energy recovery systems are employed to address cost concerns. These approaches not only reduce operational costs but also improve the overall sustainability of AOPs. Additionally, the integration of renewable energy sources, including solar and wind power, is being explored to make these technologies more environmentally friendly and economically viable (Goodarzi et al., 2023; Klemeš et al., 2019). These advancements collectively demonstrate the potential of AOPs to meet the growing demand for efficient and sustainable water treatment solutions.

4.2. Membrane technologies

Membrane technologies offer a versatile approach to water treatment, utilizing the selective permeability of membranes to separate contaminants. Based on pore size classification, membranes are categorized into microfiltration (70 nm), ultrafiltration membranes have an MWCO parameter β 10–150 kD, nanofiltration (0.1–1 nm), and reverse osmosis (0.1–1.0 nm) (Potapov et al., 2020a,b; Teow et al., 2021). Microfiltration and ultrafiltration primarily rely on size exclusion, where larger particles and suspended solids are retained, while nanofiltration and reverse osmosis operate on more complex separation mechanisms such as charge interactions and solution diffusion. The material type and properties play a crucial role in determining the membrane's functionality. Polymers like polyethersulfone and ceramics are commonly used, with each offering specific advantages such as chemical resistance or durability (Jahani et al., 2023). Surface modifications, such as hydrophilic coatings, anti-fouling layers, or grafting with antimicrobial agents, enhance performance and longevity by mitigating fouling and improving water flux (Barambu et al., 2019).

4.2.1. Specific technologies

Several membrane technologies cater to different treatment needs. Nanofiltration membranes like the G5/TAC2/PIP membrane have an ultra-high specialization in charge-based separation, efficiently removing mono-/divalent anions and cations along with organic contaminants (Qiu et al., 2021). Ultrafiltration membranes are used for size exclusion, effectively filtering out bacteria, viruses, and macromolecules (Pan et al., 2020). Reverse osmosis, one of the most advanced techniques, employs the solution-diffusion mechanism to achieve high rejection rates for dissolved salts and organic compounds. Forward osmosis, a relatively newer method, leverages osmotic pressure gradients for water recovery, requiring lower energy compared to reverse osmosis. Forward osmosis shows higher solute rejection rates compared to reverse osmosis for both nicotinamide (94.8%) and caffeine (99.9%) due to the presence of salt on the permeate side of the membrane (Sanahuja-Embuena et al., 2021). Membrane bioreactors (MBRs) combine biological degradation processes with membrane filtration, effectively addressing complex wastewater compositions, including pharmaceutical residues (Belafi-Bako and Bakonyi, 2019).

4.2.2. Performance factors

The efficiency of membrane technologies depends on factors like molecular weight cut-off (MWCO), which determines the size of particles retained, and surface charge effects, which influence the rejection of charged contaminants (Fadel et al., 2020). Membrane hydrophobicity impacts fouling tendencies, with negatively charged membranes showing no visible foulant layer, while positively charged membranes experience a 78% rejection efficiency due to foulant accumulation (Guo et al., 2020), and pH dependence affects the stability and performance of certain materials. Fouling mechanisms, including scaling, biofouling, and organic fouling, can hinder performance and necessitate regular cleaning and maintenance to restore operational efficiency (Lin et al., 2020).

4.2.3. Limitations

Despite their effectiveness, membrane technologies face several limitations that hinder their widespread adoption. One of the most significant challenges is fouling in membrane bioreactors, which reduces permeability over time and necessitates frequent cleaning. This not only increases operational costs but also leads to downtime, impacting efficiency (Martí-Calatayud et al., 2018). Additionally, high energy consumption is a notable drawback, particularly in pressure-driven systems like reverse osmosis, which require substantial energy inputs to maintain performance. Environmental concerns also arise from the disposal of concentrated brine or retentate, a by-product of the filtration process that contains high levels of contaminants. Improper disposal can lead to secondary environmental pollution, making it a critical issue to address (Bello et al., 2021). Furthermore, membrane technologies exhibit limited selectivity for certain pharmaceuticals, which can reduce their effectiveness in treating complex wastewater compositions. The high cost of membrane materials adds another layer of complexity, especially in resource-constrained settings, where affordability is a key consideration. These limitations underscore the need for continued innovation and optimization to enhance the feasibility and sustainability of membrane technologies.

4.2.4. Recent developments

Recent advancements in membrane technologies focus on improving performance, reducing fouling, and enhancing sustainability. The development of novel materials, such as graphene oxide and mixed-matrix membranes, has significantly enhanced membrane properties, including selectivity, antifouling, and antibacterial capabilities (Hu et al., 2019). For example, graphene oxide-based mixed-matrix membranes containing 0.6 wt% GO have demonstrated improved hydrophilicity, high water flux, and robust antifouling properties. These membranes achieved a humic acid rejection rate of 95% and a flux recovery ratio of 88%, showcasing their effectiveness in wastewater treatment (Chai et al., 2021).

To address fouling challenges, anti-fouling strategies such as chelation-directed interface mineralization have been developed, enabling dynamic coatings and self-cleaning capabilities on inert

polymeric membranes. These innovations reduce maintenance requirements and extend the operational lifespan of membranes (Yang et al., 2024). Additionally, energy optimization techniques, including integrating renewable energy systems and hybridizing membrane processes with other advanced technologies, have been shown to enhance desalination efficiency while minimizing environmental impacts. For instance, hybrid approaches combining renewable energy with membrane operations offer a promising pathway toward more sustainable and cost-effective water treatment solutions (Azhar et al., 2017).

4.3. Adsorption technologies

Adsorption technologies leverage materials with high surface areas and tunable pore structures to remove contaminants effectively. Adsorption capacity is significantly influenced by the nature of the surface. For instance, high surface area and basic sites resulted in the highest CO_2 adsorption capacity (159.1 mg/gcat) for calcined layered double hydroxides LDH (Gouveia et al., 2020). Adsorbents like activated carbon, biochar, and MOFs possess properties such as high porosity, specific surface chemistry, and tailored functional groups to enhance interaction with pharmaceuticals (He et al., 2022a,b). Biochar and activated carbon adsorbents with larger pore diameters (1.5–2.5 times) favored the adsorption of PPCPs (Zhu et al., 2022). Surface modifications, such as oxidation or amination, improve the adsorption capacity of biochar by affecting the pore structure, oxygen-containing functional groups, and adsorption capacity, and introducing reactive sites that interact specifically with target contaminants (Zhu et al., 2018).

4.3.1. Types

Activated carbon, available in granular (GAC) and powdered (PAC) forms, remains the most widely used adsorbent due to its affordability, ease of synthesis, and high removal performance. Its large specific surface area and porous structure enable it to adsorb a wide range of organic pollutants, making it an effective solution for pharmaceutical removal in water treatment processes (Srivastava et al., 2021). Biochar, a sustainable alternative derived from biomass, offers comparable adsorption capabilities while being environmentally friendly. It provides an eco-conscious option for regions prioritizing waste valorization and low-cost solutions (Kumar and Bhattacharya, 2021). Advanced materials, such as MOFs and carbon nanotubes (CNTs), represent state-of-the-art developments in adsorption technology. These materials exhibit superior adsorption performance due to their high porosity, specific surface area, and chemical stability, making them reusable and efficient in complex water matrices. Emerging nanomaterials, including graphene derivatives, are also under extensive investigation. Porous graphene, for instance, has shown exceptional removal efficiencies exceeding 99% for trace concentrations of pharmaceuticals at a dose of only 100 mg L^{-1}, emphasizing its potential as a high-performance adsorbent (Khalil et al., 2020).

4.3.2. Adsorption mechanisms

Adsorption mechanisms encompass a range of physical and chemical processes. Physical adsorption, driven by van der Waals forces, relies heavily on the adsorbent's surface area and pore structure. This process is reversible, enabling the adsorbent to be regenerated and reused in some cases (Ranea et al., 2019). Chemical adsorption, on the other hand, involves the formation of stable bonds between the adsorbent and the contaminant, providing enhanced retention even in dynamic water systems where fluctuating conditions could otherwise reduce performance (Alaqarbeh et al., 2021; Samantaray et al., 2021). Ion exchange and surface complexation mechanisms are particularly valuable for targeting polar or charged pharmaceutical molecules, offering an additional pathway for contaminant capture. For instance, positively charged contaminants can be effectively removed through ion exchange processes in appropriately functionalized adsorbents (Kocevski et al., 2018; Bompoti et al., 2019).

4.3.3. Performance factors

The efficiency of adsorption systems is largely influenced by isotherms and kinetic parameters. Adsorption isotherms, such as Langmuir and Freundlich models, predict the maximum adsorption capacity and equilibrium concentration, providing critical insights into system optimization (Al-Ghouti and Da'ana, 2020; Wang and Guo, 2020; Musah et al., 2022). The Langmuir model is particularly useful for describing monolayer adsorption, while the Freundlich model applies to heterogeneous surfaces and multilayer adsorption scenarios. Kinetics, describing the rate of adsorption, are equally important in determining the feasibility of real-time applications (Luo et al., 2019). Environmental factors like pH can significantly influence adsorption performance by altering the surface charge of the adsorbent and the ionization state of pharmaceutical contaminants. For example, acidic or basic conditions can either promote or inhibit the adsorption process, depending on the chemistry of the adsorbent and the contaminant. Additionally, the presence of competing compounds in complex wastewater matrices can reduce adsorption efficiency, as these species vie for active adsorption sites on the adsorbent.

4.3.4. Practical aspects

Practical challenges associated with adsorption technologies include regeneration and the management of spent adsorbents. Regeneration methods, such as thermal treatment or solvent washing, are used to restore the adsorbent's capacity for reuse. However, these processes can be energy-intensive and costly, particularly for materials like activated carbon (Dutta et al., 2019; Vakili et al., 2019). The disposal of spent adsorbents is another critical concern, as improper management could lead to secondary contamination. Strategies for recycling or safely disposing of adsorbents are crucial for ensuring the sustainability of adsorption systems (Kumar et al., 2018). Scaling up adsorption processes from laboratory settings to industrial applications presents additional challenges, including maintaining consistent performance and ensuring economic feasibility. For example, large-scale operations may require custom designs for adsorption systems to account for variations in contaminant concentrations and water quality. Innovations in adsorbent materials and process integration are essential for addressing these practical limitations and improving the viability of adsorption technologies for pharmaceutical removal.

4.4. Electrochemical methods

4.4.1. Process types

Electrochemical methods utilize electrical energy to treat contaminants through oxidation, reduction, or separation processes (Martínez-Huitle and Panizza, 2018). Electrochemical advanced oxidation processes (EAOPs) are effective in removing pharmaceutical contaminants from water and wastewater, but challenges remain in treating complex matrices, multi-contaminants, and scaling up (da Silva et al., 2021). Direct oxidation involves degradation at the electrode surface, while indirect oxidation uses oxidants such as chlorine or hydroxyl radicals generated during electrolysis (Fu et al., 2023). Electro-Fenton processes combine electrochemistry and Fenton's reaction to produce powerful oxidants for contaminant removal (Sirés and Brillas, 2021). Electrodialysis separates ions using selective membranes under an electric field, and electrocoagulation aggregates pollutants for removal (Cerrillo-Gonzalez et al., 2024). Selective electrodialysis effectively separates sodium formate and sodium thiosulfate from industrial wastewater, with a purity of 87% and current efficiency of 70% (Selvaraj et al., 2018a,b).

4.4.2. Operating parameters

The effectiveness of electrochemical processes depends on current density, which dictates the reaction rate and energy consumption (Liu et al., 2021). Electrode materials, such as boron-doped diamond, platinum, or graphite, influence stability and efficiency. For instance,

Boron-doped diamond (BDD) electrodes have good stability over time, reduced fouling, and large potential windows, making them suitable for flow-based systems like flow injection analysis, batch injection analysis, and high-performance liquid chromatography (Freitas et al., 2019). Electrolyte composition and pH conditions must be optimized to maximize contaminant degradation while minimizing side reactions. For example, Optimized parameters for ofloxacin degradation include pH = 6.3, ultrasonic power = 54 W, current density = 213 A m-2, and Na_2SO_4 electrolyte dose = 2.0 g/L (Patidar and Srivastava, 2020).

4.4.3. Removal mechanisms

Pharmaceutical contaminant removal in electrochemical systems occurs through two primary mechanisms: direct electron transfer at the electrode surface and indirect oxidation by in situ-generated oxidants, such as chlorine, ozone, or hydroxyl radicals (Shen et al., 2020). Direct electron transfer involves redox reactions where contaminants are directly oxidized or reduced at the electrode surface. Indirect mechanisms leverage oxidants formed during the process to attack and degrade pharmaceutical pollutants. These combined effects, including coagulation and oxidation, enhance the flexibility of electrochemical technologies in treating complex pharmaceutical mixtures, making them suitable for diverse wastewater compositions (Goodarzi et al., 2021).

4.4.4. Efficiency factors

Key factors influencing the efficiency and viability of electrochemical treatment include energy consumption, electrode stability, and operational costs. Energy use is a primary concern, as it directly affects the overall cost-effectiveness of the process. Electrocoagulation (EC), an alternative electrochemical method, has demonstrated advantages in reducing energy consumption compared to other conventional wastewater treatment methods (Shahedi et al., 2020). Electrode stability is another critical factor, as it determines the longevity and reusability of the system. Treatment time must be optimized to balance operational efficiency with the desired removal levels of pharmaceutical contaminants. Additionally, cost analysis plays a vital role, encompassing the expense of electrode materials, energy input, and maintenance, which are key considerations for scaling these technologies from laboratory settings to industrial applications.

4.4.5. Recent advances

Recent advancements in electrochemical treatment technologies have focused on enhancing efficiency and scalability. The development of innovative electrode materials, such as nanostructured surfaces and catalytic coatings, has significantly improved reaction rates and selectivity, enabling the effective degradation of a broader range of pharmaceutical pollutants (Yang et al., 2023). Integration of electrochemical methods with other technologies, such as biological treatment or membrane filtration, has shown synergistic benefits by combining the strengths of multiple treatment processes (Urtiaga et al., 2018). Furthermore, efforts to optimize energy usage, such as employing renewable energy sources or designing more efficient electrode configurations, are paving the way for large-scale adoption of electrochemical methods. These advancements not only improve environmental sustainability but also make these technologies more economically viable for widespread implementation (Ganiyu and Martínez-Huitle, 2020).

4.5. Biological methods

Biological methods offer a sustainable and eco-friendly approach to removing pharmaceutical contaminants from water systems by leveraging natural processes involving plants, microbes, and constructed ecosystems (Adeola et al., 2022). These methods are particularly suited for addressing emerging contaminants, such as pharmaceuticals, which are often not effectively removed by conventional wastewater treatment technologies. The low operational cost, potential for large-scale implementation, and minimal environmental footprint make biological methods highly attractive, especially for resource-limited settings (Adeola et al., 2022). Recent advancements have improved their efficiency, scalability, and integration with other treatment systems, making them a promising solution to the growing problem of pharmaceutical pollution.

4.5.1. Phytoremediation

Phytoremediation employs plants to absorb, transform, and degrade pharmaceutical contaminants from water. The selection of plant species is critical, focusing on their tolerance and ability to metabolize or accumulate pharmaceutical residues. Invasive plant species, with their hardiness and high growth rates, are increasingly being considered for such applications (Prabakaran et al., 2019). The mechanism of phytoremediation primarily involves root absorption, where plants extract contaminants from the water. Once absorbed, these pollutants undergo transformation within the plant tissues, converting them into less toxic or more stable forms through enzymatic and metabolic processes (Z. Yang et al., 2022). Innovative system designs, such as floating treatment wetlands and hydroponic systems, enhance the contact between plant roots and contaminated water, significantly improving the efficiency of pollutant removal (Thakur et al., 2023). Floating wetlands are particularly useful for dynamic water bodies, such as rivers and lakes, as they allow for the remediation of contaminants without disturbing aquatic ecosystems. For example, species like *Eichhornia crassipes* (water hyacinth) have been demonstrated to reduce pharmaceutical concentrations effectively while providing ancillary benefits such as nutrient cycling and habitat support for aquatic organisms.

4.5.2. Microbial systems

Microbial systems rely on the ability of bacteria and fungi to enzymatically degrade pharmaceutical compounds. These microorganisms use contaminants as a carbon or energy source, breaking them down into simpler, less harmful compounds. Specific enzymes, such as laccases, peroxidases, and cytochrome P450 monooxygenases, have been identified as particularly effective in degrading recalcitrant pharmaceuticals, including antibiotics and hormones (Morsi et al., 2020). Laccase-producing fungi, for instance, degrade pharmaceuticals by generating highly oxidative hydroxyl radicals, which attack and break down complex molecular structures (Nancy and Kumari, 2024). Bioaugmentation, a technique that introduces specialized microbial strains into contaminated environments, enhances the degradation process, particularly for pharmaceuticals that are resistant to conventional microbial activity (Ferraro et al., 2021). Advances in microbial systems also involve the use of genetically engineered microorganisms designed to target specific contaminants with higher efficiency and specificity. These systems are ideal for use in combination with other treatment methods, such as constructed wetlands or bioreactors, to maximize contaminant removal.

4.5.3. Constructed wetlands

Constructed wetlands are engineered ecosystems that mimic the natural processes of wetland environments to treat contaminated water. These systems integrate wetland vegetation, soils, and microbial communities to remove pollutants through physical, chemical, and biological processes. Surface-flow wetlands allow water to flow over vegetation and soil, while subsurface-flow wetlands direct water through the root zone, where interactions with plants and microbes are maximized (Badejo et al., 2022). Plants in constructed wetlands provide oxygen to the rhizosphere (root zone), stimulating microbial activity that facilitates the breakdown of pharmaceutical contaminants (Shahid et al., 2020). Research shows that vertical subsurface-flow wetlands can remove approximately 50% of PhACs, outperforming free-water surface wetlands for certain contaminants (He et al., 2018). These systems are particularly valuable for decentralized wastewater treatment in rural or peri-urban areas, where conventional infrastructure may be limited. Constructed wetlands are also highly adaptable and capable of treating a

range of wastewater types, from hospital effluents rich in pharmaceutical pollutants to municipal wastewater with complex contaminant profiles. Their low maintenance and operational costs make them ideal for low-income and resource-constrained settings.

4.5.4. Performance factors

The efficiency of biological methods is influenced by various environmental factors, including temperature, light availability, nutrient levels, and seasonal variations. These factors can impact the metabolic activity of plants and microbes, necessitating adaptive management strategies to ensure consistent performance throughout the year (Tajarudin et al., 2019). For instance, cold temperatures may reduce microbial enzymatic activity, slowing down degradation processes during winter months. Maintenance is another critical factor, as systems like constructed wetlands require periodic replacement of plants and monitoring of microbial communities to maintain optimal functionality. Additionally, the presence of competing contaminants in complex wastewater matrices can interfere with the removal efficiency of target pharmaceuticals. Despite these challenges, the low operational cost and environmental compatibility of biological methods make them an attractive option for sustainable water treatment (Ghernaout, 2019).

4.5.5. Integration strategies

Biological methods are increasingly being integrated with other treatment technologies to overcome their inherent limitations, such as slow degradation rates and incomplete contaminant removal. Hybrid systems that combine biological approaches with adsorption or electrochemical processes have demonstrated improved treatment efficiency and broader contaminant removal capabilities (Mousset et al., 2021). For example, pairing constructed wetlands with AOPs can address pharmaceuticals that are resistant to microbial degradation while ensuring minimal formation of harmful by-products (García et al., 2021). These integrated approaches offer a more comprehensive solution for managing pharmaceutical pollutants, aligning with global efforts to develop sustainable and efficient water treatment technologies. As research advances, the role of biological methods in addressing pharmaceutical pollution is expected to expand, contributing significantly to the preservation of water quality and public health.

4.6. Point-of-use treatment technologies

Point-of-use (POU) treatment systems present a viable solution for pharmaceutical removal in drinking water, particularly crucial in regions lacking centralized treatment infrastructure or where additional purification is desired. Recent comprehensive evaluations demonstrate varying removal efficiencies across different POU technologies, influenced by both system design and pharmaceutical physicochemical properties.

Recent evaluations of pitcher and bottle filters reveal significant variations in pharmaceutical removal efficiency. In a systematic study of twelve pitchers and five bottle filters, removal efficiencies exceeding 80% were achieved by eight filters, with the best-performing systems demonstrating exceptional removal rates: 99% for pharmaceuticals (reducing concentrations from 300 μg/L to 3 μg/L), 98% for pesticides (reduction to 6 μg/L), and 97% for PFAS (reduction to 9 μg/L) (Zarębska et al., 2024). The efficiency strongly correlated with the hydrophobicity of target compounds and filter characteristics, particularly BET surface area and micropore volume. Filter performance varies substantially based on design and target compounds. Under-sink dual-stage and reverse osmosis systems demonstrated near-complete removal of PFASs, while activated carbon-based systems show chain-length dependent removal: 60–70% for long-chain PFASs versus approximately 40% for short-chain variants (Herkert et al., 2020). Notably, whole-house activated carbon systems displayed inconsistent performance, with some systems (4 out of 8 studied) paradoxically increasing PFAS levels in filtered water.

A comprehensive evaluation of residential treatment systems revealed a hierarchy of treatment effectiveness. Activated carbon filters and reverse osmosis systems demonstrated superior performance with 100% removal efficiency for various organic contaminants, including pharmaceuticals and pesticides (Schreiber et al., 2024). Ion exchange (mixed bed resin) and ultraviolet radiation systems showed intermediate removal potential. However, basic membrane filters, including absolute, pleated, polypropylene, and string wound variants, exhibited inadequate removal efficiencies and are not recommended as standalone treatment options for pharmaceutical removal (Schreiber et al., 2024). Notably, degradation-based treatments such as ozonation and UV radiation present additional considerations. While these methods can break down pharmaceutical compounds, they may generate metabolites potentially more toxic than parent compounds (Zilberman et al., 2023). This limitation necessitates coupling these technologies with removal-based methods.

Biochar represents an emerging, cost-effective alternative to traditional activated carbon for pharmaceutical removal. Comprehensive testing of various biochar materials demonstrated remarkable removal capabilities, with activated coconut carbon, bamboo, and southern yellow pine biochar achieving >90% removal efficiency for multiple pharmaceuticals including acetylsalicylic acid, paracetamol, ibuprofen, naproxen, citalopram, carbamazepine, and diclofenac at biochar doses of 40 g/L (Solanki and Boyer, 2017). The removal mechanism involves a complex interplay of adsorption, filtration, biodegradation, ion exchange, and pore entrapment, enhanced by the synergistic interaction between biochar properties and microbial biofilm formation (Muoghalu et al., 2023).

Novel two-stage treatment systems combining woodchip bioreactors with biochar demonstrated promising results for the simultaneous removal of pharmaceuticals and nutrients (Zhou et al., 2024). With optimized hydraulic retention times (12 ± 1.4 h for woodchip bioreactor, 2.1 ± 0.1 h for granular biochar), these systems achieved removal efficiencies of 69.51% for ibuprofen, 73.65% for naproxen, 91.09% for sitagliptin, and 96.96% for estrone (Zhou et al., 2024). The effectiveness of biochar systems extends to various pharmaceutical compounds including tetracycline, doxycycline, diclofenac, triclosan, ciprofloxacin, and sulfamethoxazole, with removal efficiency influenced by biochar characteristics and preparation methods (Ihsanullah et al., 2022).

4.7. Implementation considerations

The selection and implementation of treatment technologies must consider local context and infrastructure availability. In regions with developed centralized systems, POU technologies can serve as complementary safeguards, particularly for vulnerable populations or in response to emerging concerns. However, in areas lacking adequate centralized infrastructure, properly maintained POU systems may serve as primary treatment barriers against pharmaceutical contamination (Wu et al., 2021). A suggested framework for developing localized POU treatment solutions is highlighted in Fig. 7 below.

The long-term effectiveness of POU systems depends critically on proper maintenance and timely replacement of filter media. Studies indicate that some whole-house systems may show variable performance over time, with some cases reporting increased contaminant levels in filtered water (Herkert et al., 2020). Therefore, regular monitoring and maintenance protocols are essential for ensuring consistent treatment efficiency. The selection of appropriate POU technology should consider both target compounds and local water quality parameters. While activated carbon and reverse osmosis systems demonstrate superior overall performance, biochar-based solutions offer a sustainable alternative, particularly in resource-limited settings (Gwenzi et al., 2017). The integration of multiple treatment mechanisms, as demonstrated in dual-stage systems, provides more robust removal across a broader range of pharmaceutical compounds.

The integration of both centralized and decentralized approaches,

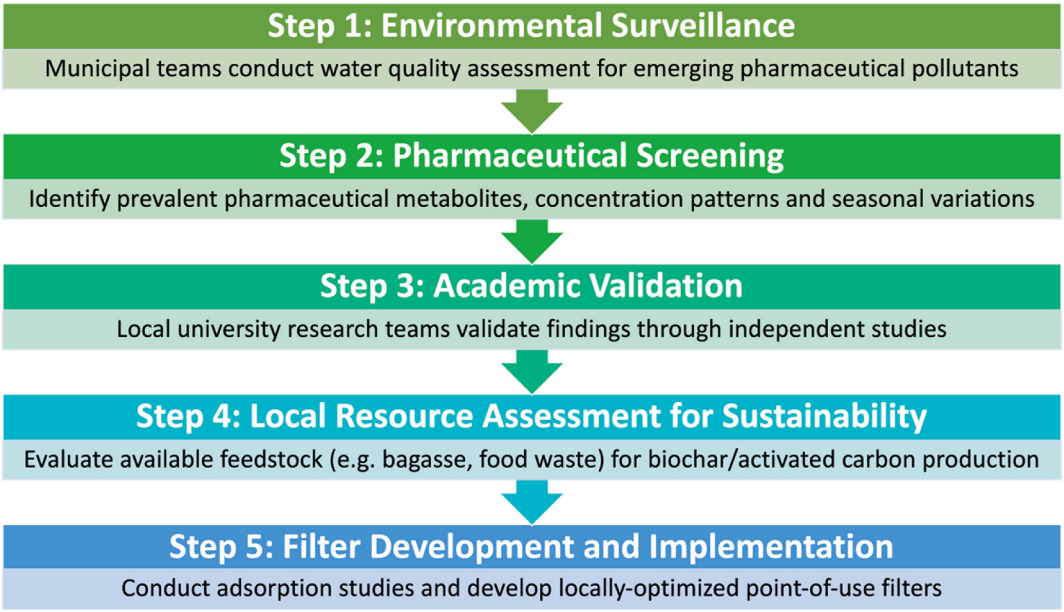


Fig. 7. Framework for developing localized POU treatment solutions.

tailored to local conditions and resources, presents the most comprehensive strategy for addressing pharmaceutical pollution in water systems. Continued advancement in both treatment approaches, coupled with an improved understanding of their complementary roles, will be crucial for protecting public and environmental health against pharmaceutical contamination.

5. Future considerations

While the direct implications of exposure to low doses of pharmaceutical pollutants in humans have not been firmly established, the presence of multiple pharmaceutically active compounds in a single sample suggests a high potential for aggregation and compounding effects, particularly with long-term exposure. This highlights a significant gap in current risk assessments, which are predominantly conducted on single compounds, despite the common occurrence of pharmaceutical pollutants as complex mixtures in water (Molnar et al., 2020). The detection of high levels of carcinogenic compounds, such as cyclophosphamide, in rural communities in Québec underscores the need for systematic and standardized surveys and health assessments to be conducted routinely (Husk et al., 2019). Moreover, the lack of monitoring for priority drinking water parameters in private wells further exacerbates the risk, as these sources are less likely to be assessed for emerging pollutants (Kibuye et al., 2019). To sustainably address these challenges, a holistic and multi-tiered approach is essential.

5.1. Individual level

Individuals should be educated on the proper use and disposal of medications to reduce down-the-drain incidences, self-prescription, and improper disposal in trash bins (Okoro et al., 2023). Public awareness campaigns can play a significant role in mitigating the impact of pharmaceuticals on water systems. If individuals understand that improperly disposed drugs can re-enter their water supply and potentially harm them, they are likely to exercise greater caution in their disposal practices.

5.2. Industry level

Pharmaceutical industries must be encouraged to invest in research and development to identify affordable and effective treatment technologies for their drug classes. Big pharma companies should also be encouraged to focus on developing green pharmaceuticals that are more readily degradable (Puhlmann et al., 2021). Also, industries and hospitals should ensure that their effluents meet the highest environmental standards, minimizing the release of harmful pharmaceuticals into the environment (Khan et al., 2021; Singh et al., 2023).

5.3. Government and international level

Middle- and low-income countries should prioritize the development of centralized sewage systems where feasible to improve wastewater management and reduce environmental contamination (Pasciucco et al., 2022). Additionally, the allocation of funding for comprehensive risk assessments, particularly those that consider the presence of multiple pharmaceuticals in water samples, needs to be prioritized as the majority of available research focuses on single active pharmaceutical ingredients (Duarte et al., 2022).

Furthermore, there is a need for the development of unified water quality standards that address emerging pharmaceutical pollutants, ensuring consistency and safety in water quality management. Also, existing wastewater treatment plants should be retrofitted and upgraded to effectively tackle emerging pollutants, employing advanced treatment technologies such as advanced oxidation processes, membrane filtration, and photocatalysis (Tian et al., 2020). This is especially important for hospitals and other healthcare providers (Khan et al., 2020). Lastly, large-scale surveillance and monitoring programs should be prioritized to track the presence and concentrations of pharmaceutical pollutants in water sources. This data is critical for informed decision-making and the protection of public health.

5.4. Synergistic role and necessity of collaborative efforts

The fight against pharmaceutical pollution demands an integrated and collaborative approach that recognizes the interdependence of individuals, industries, and governments. No single stakeholder can address this multifaceted issue in isolation. Instead, fostering synergy among these entities ensures that collective resources, expertise, and actions are effectively aligned toward a shared goal. Collaborative efforts amplify the impact of individual contributions by bridging gaps in knowledge, technology, and implementation strategies. For instance, governments can provide funding and regulatory frameworks that

incentivize industries to develop greener pharmaceuticals and invest in advanced treatment technologies. A practical example is the introduction of extended producer responsibility (EPR) programs, where pharmaceutical companies are mandated to fund the collection and proper disposal of unused or expired drugs. Such programs have been successfully implemented in countries like Canada and Sweden, demonstrating how government and industry collaboration can drive impactful outcomes (Albrecht, 2012; Chai et al., 2021). Similarly, governments can partner with academic institutions and industries to support research into effective and affordable wastewater treatment technologies, ensuring scalability and accessibility in low- and middle-income countries.

Industries, in turn, can support public education campaigns led by governments or non-governmental organizations to inform individuals about safe disposal methods. An example of this is the pharmaceutical take-back initiatives in the United States, where pharmacies, often funded by pharmaceutical companies, provide drop-off points for unused medications (Craver, 2016; Jaramillo-Stametz et al., 2018). This approach exemplifies how industry and individual efforts can be interconnected through a supportive policy environment. On the community level, individuals can serve as both beneficiaries and agents of change by engaging in local monitoring efforts, such as citizen science projects that track pharmaceutical pollutants in nearby water sources. When supported by government funding and industry-provided tools or data-sharing platforms, these grassroots initiatives can generate valuable data while fostering public accountability. For instance, in the Netherlands, a project called "Medicines and the Environment" unites individuals, healthcare providers, and local authorities to reduce pharmaceutical waste by raising awareness and promoting green prescription practices.

Internationally, partnerships between governments have shown how cross-border collaboration can fund large-scale projects that address pharmaceutical pollution while sharing knowledge across regions. This can inspire further cooperation in developing nations, where governments can seek assistance from more technologically advanced countries or global organizations to implement effective waste management systems. A synergistic framework ensures co-creation of solutions, blending community-driven insights with industrial innovation and regulatory oversight. Such integrated collaboration not only increases efficiency and effectiveness but also builds public trust. By aligning resources and expertise, these partnerships create a robust foundation for addressing the global challenge of pharmaceutical pollution, fostering a cleaner and healthier environment for all.

5.5. Future research

Future research should focus on expanding geographical coverage to underrepresented regions like Australia, parts of Africa, and South America to address regional disparities and provide a comprehensive understanding of global pharmaceutical pollution trends. Standardized methodologies for sampling, detection, and analysis should be developed to enhance comparability and reliability. Broader investigations into co-occurring emerging contaminants, such as personal care products and pesticides, are essential to understand combined environmental impacts. Longitudinal studies incorporating historical data are needed to assess trends and persistence over time. Advanced treatment technologies, such as advanced oxidation processes and bioaugmentation, require further evaluation for scalability and cost-effectiveness, especially in low-income regions. Research should also prioritize ecotoxicological impacts on aquatic ecosystems, the synergistic effects of multiple contaminants, and the development of systematic monitoring frameworks. Policy-oriented studies should assess the effectiveness of current regulations and explore "green chemistry" approaches for sustainable pharmaceutical production. Finally, investigating public awareness and behaviours around drug disposal can guide educational campaigns and community-driven solutions for reducing pharmaceutical pollution.

Context-specific research focusing on localized solutions is particularly crucial for effective pharmaceutical pollution management. This includes characterizing regional pharmaceutical usage patterns and conducting targeted screening to identify prevalent compounds in local freshwater systems. Research should explore the optimization of treatment technologies using locally available resources, such as developing biochar from region-specific agricultural wastes (e.g., rice husks in Asia, coconut shells in tropical regions, or corn stover in agricultural areas). Studies should investigate the effectiveness of these locally-produced materials in removing the specific pharmaceutical compounds prevalent in regional water sources. Such localized research approaches would not only improve treatment efficiency but also ensure the sustainability and economic viability of pharmaceutical pollution management strategies in different geographical and socioeconomic contexts.

6. Limitations and strengths of the review

This review has some limitations that readers should consider for a balanced perspective. First, the geographical representation of studies is uneven, with significant underrepresentation from regions such as Australia, parts of Africa, and South America. This disparity reflects the global imbalance in research focus and funding, which limits the ability to generalize findings universally. Additionally, the review focuses on studies published between 2019 and 2024. While this ensures the findings are up-to-date, it excludes earlier foundational research that might provide historical context to pharmaceutical pollution trends.

Another limitation lies in the variability of methodologies used across the studies reviewed. Differences in sampling techniques, detection limits, and analytical approaches pose challenges in comparing results and drawing standardized conclusions about global trends. Furthermore, the review is narrowly focused on pharmaceutical pollutants, excluding other emerging contaminants such as personal care products and industrial chemicals, which often co-occur and could have compounding environmental impacts. Lastly, this review relies on a narrative synthesis rather than a quantitative meta-analysis due to inconsistencies in reported data. While narrative reviews are valuable for summarizing diverse findings, a meta-analysis could have provided more statistically robust insights.

Despite its limitations, this review has several strengths that enhance its value. It provides a comprehensive global perspective by incorporating studies from six continents, shedding light on regional disparities in pharmaceutical pollution and its impact on freshwater systems. Additionally, the review emphasizes emerging wastewater treatment technologies, such as advanced oxidation processes, membrane filtration, and bioaugmentation, offering practical insights for mitigating pharmaceutical contamination. This focus on innovative solutions makes the review relevant for researchers, policymakers, and environmental stakeholders.

The review also highlights critical environmental and public health risks, such as the rise of antibiotic-resistant bacteria and ecological disruptions, with evidence drawn from diverse studies. This approach underscores the importance of addressing pharmaceutical pollutants and adds depth to the discussion. Moreover, the review identifies key knowledge gaps, such as the absence of standardized monitoring frameworks and the need for systematic research on the long-term impacts of pharmaceutical pollutants. By highlighting these gaps, the review not only informs current understanding but also provides a roadmap for future studies and policy development. These strengths position the review as a valuable resource for understanding pharmaceutical pollutants in freshwater systems while acknowledging areas where further research and standardization are needed.

7. Conclusion

This review demonstrates the pervasive presence of pharmaceuticals in ground and surface water sources across six continents, with particularly concerning levels in regions lacking adequate treatment infrastructure. The stark geographical disparities in contamination levels, exemplified by multiple-fold higher concentrations in Africa and Latin America, underscore the urgent need for targeted interventions. With anticipated increases in pharmaceutical consumption globally, this challenge will likely intensify without decisive action.

Several critical strategies emerge from this analysis. First, municipalities must conduct systematic screening to identify locally prevalent pharmaceuticals, as contamination profiles vary significantly with regional healthcare patterns and infrastructure capabilities. Second, while advanced treatment technologies show promise for centralized systems, immediate deployment of point-of-use technologies is crucial for regions lacking adequate infrastructure. The potential of biochar-based systems, particularly when optimized using locally available resources, offers a cost-effective solution for such areas.

Future priorities should include developing standardized monitoring protocols that account for regional variations, improving conventional treatment facilities while implementing advanced technologies where feasible, strengthening pharmaceutical prescription regulations in developing regions and investing in research for more biodegradable pharmaceutical alternatives. Additionally, the integration of both centralized and decentralized treatment approaches, tailored to local conditions and contamination profiles, will be essential for the effective global management of pharmaceutical pollution in freshwater systems.

CRediT authorship contribution statement

Ojima Zechariah Wada: Writing – review & editing, Writing – original draft, Visualization, Resources, Formal analysis, Data curation, Conceptualization, Supervision, Methodology, Investigation.**David Bamidele Olawade:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Conceptualization.

Consent to participate

Not Applicable.

Code availability

Not Applicable.

Ethics approval

Not Applicable.

Consent for publication

Not Applicable.

Funding

No funding.

Declaration of competing interest

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

Data availability

Data will be made available on request.

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