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ASIAN JOURNAL OF SCIENCE AND TECHNOLOGY

ISSN: 0976-3376

Asian Journal of Science and Technology
Vol. 16, Issue, 02, pp. 13449-13457, February, 2025

RESEARCH ARTICLE

PHARMACEUTICALS IN DRINKING WATER: ASSESSING HUMAN EXPOSURE AND ENVIRONMENTAL CONTAMINATION

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ARTICLE INFO

Article History:
Received 06th December, 2024
Received in revised form
13th January, 2025
Accepted 29th January 2025
Published online 22nd February, 2025

Keywords:

Pharmaceutical contamination, water pollution, antimicrobial resistance, sustainable water management.

ABSTRACT

Wetlands pharmaceutical contamination in drinking water has emerged as a critical global challenge, posing significant risks to human health and aquatic ecosystems. Pharmaceuticals enter water sources through household waste, agricultural runoff, and industrial discharges, persisting due to their chemical stability and resistance to conventional treatment methods. The presence of these contaminants contributes to antimicrobial resistance, endocrine disruption, and bioaccumulation, raising concerns about long-term health effects, including reproductive and metabolic disorders. This review comprehensively examines the pathways of pharmaceutical contamination, the associated human health risks, and the environmental consequences. Advanced detection techniques, such as liquid chromatography-mass spectrometry, enable precise monitoring of pharmaceutical residues, while treatment technologies, including advanced oxidation processes, membrane filtration, and activated carbon adsorption, are evaluated for their efficacy in mitigating contamination. The study also highlights critical regulatory gaps, particularly in developing regions, where pharmaceutical pollution levels often exceed global averages. To address these challenges, an integrated approach combining public education, policy reforms, and sustainable pharmaceutical practices is recommended. Strengthening wastewater treatment infrastructure, enforcing stricter regulations, and promoting green chemistry principles in pharmaceutical manufacturing are essential steps toward mitigating contamination at its source. This review provides actionable insights to guide future research, regulatory frameworks, and technological advancements in safeguarding global water resources and public health.

Citation: Nnamso D. Ibuotenang, Peter O. Adigun, Solomon E. Shaibu, Utibe A. Ofon4, Opeyemi K. Fatunla, Oladoja A. Awofisayo 2025. "Pharmaceuticals in Drinking Water: Assessing human exposure and Environmental Contamination", *Asian Journal of Science and Technology*, 16, (02), 13449-13457.

INTRODUCTION

The growing use of pharmaceuticals, a diverse class of emerging contaminants, has raised global environmental concerns in recent years (Pereira *et al*., 2021). Initial detection of pharmaceuticals in the environment dates back to the 1970s, with subsequent studies revealing their widespread presence in aquatic systems (Ogunbanwo *et al*., 2022). While most of these studies have been conducted in Europe and North America, limited research has been performed in Africa, South America, and the Middle East. In the few studies conducted in Africa, high frequencies of pharmaceuticals (60–100%) were detected, often with concentrations exceeding those measured in Western regions (Fekadu, Alemayehu, Dewil, & Bruggen, 2019; S. Shaibu *et al*., 2022). In Kenya, for instance, concentrations as high as 167 µgL−1 were found in sewage effluent and surface waters, while South Africa reported pharmaceuticals' ubiquitous presence in effluent and freshwaters, with concentrations ranging from ng L−1 to µgL−1 (Ogunbanwo *et al*., 2022).

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Several factors may contribute to these high concentrations, including high drug usage with inadequate regulation, the presence of numerous pharmaceutical manufacturing plants, and insufficiently developed sewage treatment facilities (Fekadu, Alemayehu, Dewil, & Bruggen, 2019). In Nigeria, various drug classes, including analgesics, antibiotics, antacids, antihistamines, anticonvulsants, steroids, antimalarials, and antihypertensives, are frequently consumed and often purchased without a prescription. While pharmaceuticals play a crucial role in improving healthcare by preventing or treating human and animal diseases, their presence in drinking water raises environmental concerns (Ebele *et al*., 2020; Gogoi *et al*., 2018). Pharmaceutical residues enter the aquatic environment through various pathways, including improper disposal of unused medications, incomplete drug metabolism, and effluent discharge from wastewater treatment plants Chaturvedi, (Hutchings *et al*., 2019). Pharmaceutical compounds, such as antimicrobial agents, exhibit cytotoxic or cytostatic mechanisms to eliminate microorganisms, allowing the natural immune system to function efficiently (Hutchings *et al*., 2019). The broad effectiveness of these compounds against microbial strains has led to their widespread use worldwide. However, their overuse poses risks to human health and the environment, with the potential emergence of multidrug-resistant

microbes, antibiotic-resistant bacteria (ARB), and antibiotic-resistant genes (ARGs) (Hutchings *et al*., 2019). Small-scale treatment plants and wastewater treatment plants struggle to efficiently remove these pollutants, leading to the spread of antibiotic resistance in aquatic systems (Ogunbanwo *et al*., 2022). The persistence of pharmaceuticals in water bodies and soil causes significant environmental threats. The graphs illustrate a comparative study on pharmaceutical occurrence from 2009 to 2019 and the top 10 countries demonstrating the need for research to raise awareness in highly populated countries, such as India and China. The escalating utilization of pharmaceuticals has raised concerns regarding their potential detrimental effects on human health, aquatic ecosystems, and environmental sustainability. Humans may be exposed to pharmaceutical residues through the consumption of contaminated drinking water, while aquatic organisms are impacted by continuous exposure to low concentrations of these substances.To address these challenges, several treatment methods have been developed to tackle the presence of pharmaceuticals in water sources. These methods encompass advanced oxidation processes (AOPs), membrane filtration, activated carbon adsorption, and biological treatment systems (Chaturvedi *et al*., 2021; Pereira *et al*., 2021). Each of these treatment technologies has advantages and limitations, and the most appropriate method is selected based on factors such as cost-effectiveness, energy requirements, and treatment efficiency.The principal objectives of this review are to provide a comprehensive understanding of the sources and prevalence of pharmaceuticals in drinking water, to summarize current knowledge on human exposure and health effects related to pharmaceuticals in drinking water, and to evaluate the environmental impacts of pharmaceutical contamination in water bodies. Furthermore, the review aims to discuss existing regulations and guidelines for managing pharmaceuticals in drinking water and identify potential strategies for reducing pharmaceutical contamination in drinking water sources and mitigating human exposure.By emphasizing key findings and pinpointing research gaps, this review endeavors to contribute to the existing knowledge base and guide future studies and policy actions related to managing pharmaceuticals in drinking water.

Sources of Pharmaceuticals in Drinking Water

Pharmaceutical Waste from Households: Households are a significant source of pharmaceutical waste, primarily due to the disposal of unused or expired medications. This waste can enter the environment through various pathways, such as flushing down toilets, pouring down sinks, or disposing of medications in trash cans, ultimately leading to water and soil contamination as shown in Figure 1. The presence of pharmaceuticals in the environment can have adverse effects on both aquatic and terrestrial ecosystems, potentially harming wildlife and contributing to the development of antibiotic-resistant bacteria.According to Rogowska, (2022), a study in Sweden revealed that 87% of respondents reported using over-the-counter (OTC) drugs in the previous six months which correspond to the study of Hedenrud, (2019). Similarly, a study by Vatovec *et al*., (2021) conducted among 421 participants in the US found that 85% had purchased OTC drugs within the past 12 months. Another study from 2008–2011 in Germany, involving 7,091 individuals, showed that 40.2% of respondents had used medicines or dietary supplements, such as vitamins or minerals, within the seven days prior to the survey. The global presence of pharmaceuticals in the environment is now well-established. Michael *et al*., (2019) assessed the disposal practices of expired and unused medications among community pharmacies in Anambra State, southeast Nigeria, noting the limited literature on disposal methods used by pharmacists in the country. This study compared local disposal practices with the National Agency for Food and Drug Administration and Control (NAFDAC) guidelines. Improper disposal of expired pharmaceuticals in sewage systems contributes to the rise of antibiotic-resistant microorganisms, potentially leading to dangerous pathogens. Non-biodegradable drugs, such as anti-infectives, cytotoxics, and disinfectants, also harm bacteria essential for sewage treatment. Furthermore, the presence of trace antibiotics in water sources has been linked to increasing antibiotic resistance in humans. Environmental contamination by non-steroidal anti-inflammatory drugs (NSAIDs), like diclofenac, has caused renal failure in vultures after ingesting contaminated carrion, and estrogenic compounds from oral contraceptives, such as 17-α-ethinylestradiol, have been shown to feminize fish, leading to infertility.

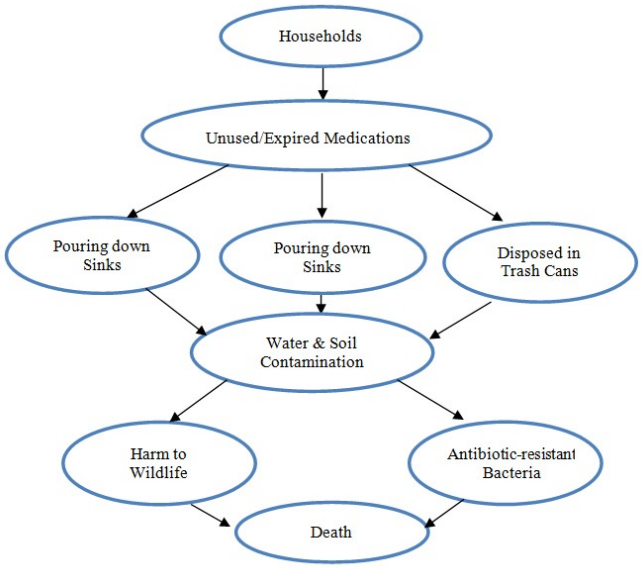

Figure 1. Distribution of household pharmaceutical pathways to water and the environment, highlighting potential adverse effects

In a study of household medicine disposal practices in Maiduguri, northeast Nigeria, Okoro & Peter, (2020) found that 35.0% of participants stored unused or unwanted medicines for future use, while 30.2% gave them to friends or relatives. More than half (59.7%) disposed of expired medicines via household garbage, with a few participants (1.3%) either gifting them or burying them. The study also identified relationships between disposal practices and factors such as gender, age, marital status, and educational level. Most respondents (80.0%) were aware of the harmful effects of improper medicine disposal on public health and the environment. Practices such as flushing medicines down sinks, toilets, or throwing them into rubbish bins contribute significantly to soil and water pollution with active pharmaceutical ingredients, increasing the risk of antibacterial resistance. Additionally, Udobia, (2023) reported that waste management in Uyo, Akwa Ibom State, is unsustainable due to the lack of a structured system for recycling and reusing waste. In Lagos, Akinboro & Onedo, (2022) noted that the average community pharmacy stocks between 2,000 to 5,000 drug items, contributing significantly to pharmaceutical waste. These pharmacies often lack proper disposal systems for expired or unused medications, leading to improper disposal methods such as dumping in general waste bins or sewage systems. This practice exacerbates environmental contamination, as active pharmaceutical ingredients leach into water bodies and soils, posing risks to both human health and ecosystems.

Waste water Treatment Plants and Incomplete Removal: Wastewater treatment plants are essential in managing and treating various types of waste, including pharmaceutical waste (Moslah *et al*., 2018; S. E. Shaibu *et al*., 2024). However, the removal of pharmaceuticals in these plants is often incomplete due to several factors. Inadequate treatment processes, the persistence and resistance of pharmaceutical compounds, limited knowledge of transformation products, and variability in removal efficiency all contribute to the incomplete removal of pharmaceuticals. This incomplete removal leads to the presence of pharmaceutical compounds in surface water, groundwater, and drinking water sources, posing potential risks to human health and the environment. Addressing this issue requires further research into advanced treatment technologies and a better understanding of pharmaceutical compounds' fate during wastewater treatment. Additionally, implementing source control measures can help minimize pharmaceuticals' entry into wastewater treatment

plants (Chaturvedi *et al*., 2021; Gogoi *et al*., 2018; Ofon *et al*., 2022b; Rogowska, 2022). According to Couto *et al*., (2019),a study on the occurrence, fate, and removal of pharmaceutically active compounds in water and wastewater treatment plants revealed that conventional water and wastewater treatment methods are often inadequate for the complete removal of pharmaceuticals. The study assessed 23 drinking water treatment plants and 30 municipal wastewater treatment plants worldwide, focusing on these compounds'risks to human health. The high stability and intrinsic characteristics of pharmaceutical compounds lead to incomplete removal in wastewater treatment plants, with adsorption to sludge and biodegradation being the primary methods of removal. In water treatment plants, processes like chlorination and activated granular carbon application are the most effective removal methods. However, conventional water treatment plants can only reduce, but not eliminate, pharmaceutical compounds (Marais *et al*., 2018; Yu *et al*., 2021). Compounds such as carbamazepine, gemfizobril, and fenofibrate were identified as posing potential health risks, highlighting the need for investments in advanced water and wastewater treatment techniques. Additionally, the study emphasized the necessity for establishing guideline values for drinking water with a broader range of pharmaceutical compounds (Couto *et al*., 2019).

Conventional wastewater treatment techniques often prove inadequate in effectively removing certain pharmaceuticals due to their unique properties, such as hydrophilicity, persistence, and resistance to biological degradation. As a result, these compounds pass through treatment stages and eventually enter natural water bodies (Ofon *et al*., 2022a, 2022b). This issue is particularly evident in the inadequate removal of antibiotics, analgesics, antidepressants, and hormones, which can significantly affect aquatic environments even at low concentrations. Advanced treatment methods, such as ozonation, advanced oxidation processes (AOPs), and activated carbon adsorption, have demonstrated improved removal efficiencies for pharmaceutical contaminants. However, the implementation of these technologies is often limited by higher operational costs and technical challenges (Mansouri *et al*., 2021). The incomplete removal of pharmaceuticals in wastewater treatment plants also highlights the need for stricter regulatory frameworks. Current water quality guidelines often lack specific limits for pharmaceutical residues, leading to limited monitoring and enforcement of these contaminants in water supplies (Ebele *et al*., 2020; Michael *et al*., 2019; Pereira *et al*., 2021).

Agricultural Runoff: Veterinary Pharmaceuticals: Agricultural runoff is a major contributor to water pollution, as it carries veterinary pharmaceuticals into the environment (Fatoki *et al*., 2018). These substances, which include antibiotics, antiparasitics, and growth promoters, are often used in livestock and poultry farming. They can enter the environment through various pathways, such as the application of manure and biosolids as fertilizer on agricultural fields, and runoff from animal feeding operations. When manure containing high concentrations of these pharmaceuticals is applied to farmland, rain, and irrigation can cause the compounds to leach into nearby water bodies.The presence of veterinary pharmaceuticals in agricultural runoff can have detrimental effects on aquatic ecosystems (Barka, 2021). For instance, antibiotics can promote the development of antibiotic-resistant bacteria, posing risks to public health (Liliana Serweci´nska, 2020; Mesa *et al*., 2018). Antiparasitics, like ivermectin, can be toxic to aquatic invertebrates even at low concentrations, disrupting food chains and impacting biodiversity (Mesa *et al*., 2018; Nunes *et al*., 2021). Hormones used in livestock for growth promotion may also disrupt the endocrine systems of wildlife; estrogenic compounds, for example, have been linked to reproductive abnormalities in fish populations (Encarnação *et al*., 2019). Addressing the issue of veterinary pharmaceutical contamination in agricultural runoff requires a multifaceted approach. Improved veterinary drug use practices, better manure management, and the implementation of buffer zones and other best management practices can help reduce runoff from agricultural fields. However, conventional wastewater treatment systems in rural areas are not designed to effectively remove these chemicals (García-Ávila *et al*., 2021; S. E. Shaibu, 2019). Furthermore, the degradation rates of veterinary drugs vary, with some being highly persistent in water. A lack of widespread monitoring and regulation contributes to the problem, as the environmental concentrations of these pharmaceuticals are often poorly understood or underestimated.

Industrial Pharmaceutical Discharges: The substantial contribution of industrial pharmaceutical emissions to water contamination has made pharmaceuticals a serious environmental concern(Caban & Stepnowski, 2021). Wastewater from industrial facilities frequently releases these discharges into water bodies, endangering human health and ecosystems. These discharges might include metabolites, active pharmaceutical ingredients (APIs), and other chemicals utilized during manufacture(Kumar *et al*., 2022).Wastewater treatment plants (WWTPs) often fail to eliminate pharmaceutical residues entirely, according to recent studies as shown in Figure 2 (Khasawneh & Palaniandy, 2021; Tiwari *et al*., 2017).

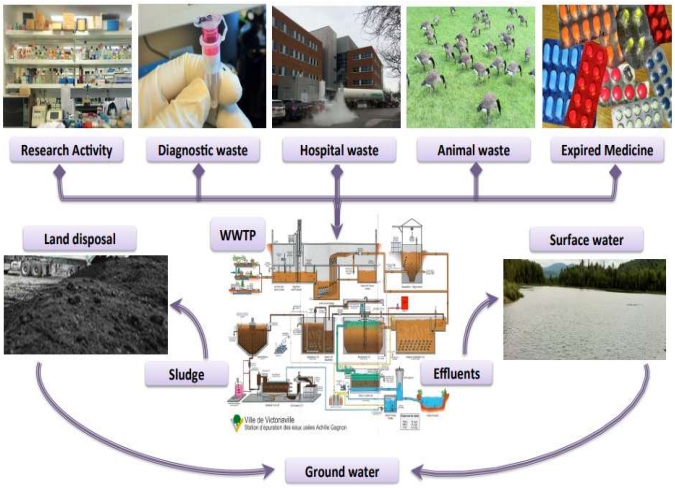

Figure 2. WWTPs Utilize for treatment of Pharmaceutical discharge (Tiwari *et al*., 2017)

The problem is made worse by pharmaceuticals from industrial sources that find their way into lakes, rivers, and even drinking water supplies(Chaturvedi *et al*., 2021; Gogoi *et al*., 2018; Khasawneh & Palaniandy, 2021). For instance, Wilkinson *et al*., (2022)found that pharmaceutical manufacturing sites in countries like China and India, which account for a significant portion of global pharmaceutical production, contribute significantly to the presence of active pharmaceutical ingredients (APIs) in the environment, particularly in nearby water bodies. The most heavily contaminated samples were primarily from African and Asian countries, including Ethiopia, Tunisia, the Democratic Republic of Congo, Kenya, Nigeria, Pakistan, India, Armenia, Palestine, and China. Notably, high levels of pollution were also observed in North American samples from San Jose, Costa Rica, European samples from Madrid, Spain, and Oceania samples from Adelaide, Australia. A significant number of these highly contaminated samples came from low- to middle-income countries with limited or no previous monitoring of APIs in aquatic environments. For example, within the top 10th percentile for cumulative API concentrations across respective catchments, only a handful of publications were available for countries such as Nigeria, Tunisia, Costa Rica, and Palestine, and no prior research existed for Armenia, the Democratic Republic of the Congo, Ethiopia, and Bolivia. In contrast, countries with extensive research on the topic, such as the United States and Germany, had generally lower API concentrations compared to less-studied regions. This suggests that previous research efforts have mainly focused on areas with lower risks to ecosystems and human health. These chemicals' bioaccumulation and persistence in aquatic environments are major problems with industrial pharmaceutical discharges. Microbial communities can be upset by substances like hormones and antibiotics, which can lead to the emergence of antibiotic resistance. Even trace levels of pharmaceutical residues can have a major impact

on aquatic organisms by interfering with their reproductive and hormonal systems, which can lead to a decline in biodiversity, according to Oldenkamp *et al*., (2019).

Furthermore, studies have revealed that industrial pharmaceutical wastes are not just found in underdeveloped nations. Pharmaceutical facilities are another source of API contamination in wealthy nations like the United States and Europe. In contrast to non-industrial sources, pharmaceutical firms were the main cause of the noticeably elevated quantities of opioids and other prescription medicines in wastewater, (Moslah *et al*., 2018; Wilkinson *et al*., 2022). Geological Survey. Recent studies have suggested a number of ways to lessen these effects. Pharmaceutical loads in industrial effluent have been demonstrated to decrease with the use of modern wastewater treatment methods, such as membrane filtration and advanced oxidation processes. Moreover, especially in areas where pharmaceutical businesses are heavily concentrated, regulatory actions are required to improve monitoring of pharmaceutical manufacturing waste. Astudy by Petrie, (2021) found that the environmental impact of pharmaceutical manufacture might be considerably decreased by strengthening monitoring and implementing more stringent discharge limitations. Furthermore, industrial pharmaceutical discharges contribute to the polluting of water bodies with potentially hazardous compounds, making them a major cause of environmental pollution. Stricter laws, improved treatment methods, and international collaboration are all necessary to address this problem and lessen the discharge of pharmaceutical substances into the environment.

Human Exposure to Pharmaceuticals through Drinking Water: Pharmaceutical residues in drinking water pose a growing risk to human health, with multiple pathways leading to exposure as shown Figure 3. The most common route of exposure is ingestion, where pharmaceuticals consumed through contaminated drinking water directly enter the gastrointestinal system. This route accounts for the majority of human exposure, especially for individuals relying on untreated or minimally treated water sources (Praveena *et al*., 2019).

Fig. 3. Human Exposure to Pharmaceuticals (Khasawneh & Palaniandy, 2021)

Skin absorption is another pathway, particularly relevant during activities such as bathing, swimming, or cleaning. Although less significant than ingestion, dermal exposure to certain waterborne pharmaceuticals, such as endocrine disruptors, can still result in bioaccumulation over time (Khan *et al*., 2022; Ohoro *et al*., 2019). The risks associated with chronic low-level exposure to pharmaceuticals are a major concern due to the continuous consumption of contaminated water over time. Pharmaceuticals such as antibiotics, NSAIDs, and hormonal drugs, even in trace amounts, may lead to antimicrobial resistance (AMR), where microorganisms develop resistance to commonly used antibiotics, rendering medical treatments less effective (Mazhandu & Mashifana, 2024; Moslah *et al*., 2018). Furthermore, endocrine disruptors, including synthetic estrogens, interfere with the human endocrine system, potentially causing reproductive and developmental issues, cancers, and metabolic disorders. Chronic exposure to neurotoxic pharmaceuticals, such as psychotropic drugs, can lead to cumulative toxic effects on the nervous system, affecting cognitive and behavioral health (Green *et al*., 2021). Certain populations are more vulnerable to these risks, including pregnant women, whose exposure to pharmaceuticals such as endocrine disruptors can impact fetal development, leading to congenital anomalies. Children are particularly at risk due to their lower body weight and developing systems, making them more susceptible to the effects of pharmaceuticals even at low concentrations. Similarly, immunocompromised individuals face heightened risks from AMR and toxic exposure, which can exacerbate existing health conditions and compromise immune function (Chaturvedi *et al*., 2021; Gogoi *et al*., 2018; Vatovec *et al*., 2021).

Mechanisms of Pharmaceutical Contamination in Water Systems

Fate of Pharmaceuticals in Aquatic Environments: The fate of pharmaceuticals in aquatic environments refers to the processes and transformations that pharmaceutical compounds undergo once they enter bodies of water, such as rivers, lakes, and oceans(Gworek *et al*., 2019).Pharmaceuticals released into the environment may experience various reactions, leading to complete or partial degradation. Degradation involves the gradual breakdown of a compound into simpler molecules through the elimination of individual elements. These processes can occur biotically or abiotically. Based on abiotic mechanisms, pharmaceuticals can be categorized into groups, such as medicines and metabolites that are eliminated through biologically induced mineralization, which relies on bacterial metabolic activity. Other pharmaceuticals may be partially degraded or persistent in the environment(Schwarz *et al*., 2021; Yeshi *et al*., 2022). The amount of pharmaceuticals entering the environment surpasses its capacity for transformation. Different pharmaceutical classes vary in their degree of biological and chemical transformation. The accumulation of pharmaceutical residues in the environment depends primarily on the quantity of pharmaceuticals produced, discharged, and subject to degradation, partial decomposition, and dissolution processes that reduce their concentrations in a specific environmental medium (e.g., water) (Gworek *et al*., 2019). Despite their relatively low persistence, these processes result in increasing levels of pharmaceuticals in the environment. The primary processes reducing pharmaceutical levels include biodegradation, hydrolysis, and direct or indirect photodegradation. For instance, due to their poor hydrolysis capability, pharmaceutical compounds in surface waters undergo abiotic transformation mainly through photolysis, occurring in both natural waters and wastewater. Some pharmaceuticals, like diclofenac and carbamazepine, are resistant to photolysis and persist in the environment (Gworek *et al*., 2019).

Pharmaceutical Classes Found in Drinking Water: The presence of pharmaceuticals in drinking water is an urgent global concern due to their potential health risks and ecological impacts as shown in Table 1. Various classes of pharmaceuticals, including antibiotics, hormonal drugs (endocrine disruptors), nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, psychotropic drugs, and chemotherapeutics, have been detected in water sources worldwide (aus der Beek *et al*., 2016; Fanourakis *et al*., 2020). These compounds enter water systems primarily through wastewater discharge, agricultural runoff, and improper disposal of pharmaceuticals. Among the most concerning classes are antibiotics, which include commonly used compounds such as tetracycline, sulfonamides, and penicillin (Kümmerer, 2009). Antibiotics in drinking water have raised significant concerns about the development of antibiotic resistance, a serious public health issue. Resistance in human pathogens and environmental microorganisms reduces the efficacy of antibiotics in treating diseases, posing challenges for healthcare systems worldwide (Mancuso *et al*., 2021). Moreover, their presence in water systems can disturb microbial communities, affecting biodiversity and critical ecosystem functions (Feng *et al*., 2018). Hormonal drugs, often referred to as endocrine disruptors, are another critical group of contaminants. These compounds, including synthetic estrogens and anti-androgens, can interfere with hormonal systems in both humans

and wildlife. They typically enter drinking water sources via wastewater effluents and agricultural runoff (Chaturvedi *et al*., 2021; Madhav *et al*., 2020). Exposure to endocrine disruptors has been linked to reproductive and developmental issues, including fertility problems, early puberty, and abnormalities in aquatic organisms' sex characteristics (Cargnelutti *et al*., 2021; Green *et al*., 2021). In humans, these compounds have been associated with long-term health risks such as increased incidences of cancers and metabolic disorders. The widespread presence of these compounds underscores the need for effective strategies to prevent their entry into water systems and mitigate their impacts.Nonsteroidal anti-inflammatory drugs (NSAIDs), widely used to manage pain and inflammation, are among the most frequently detected pharmaceutical contaminants in water systems. Common NSAIDs like ibuprofen and naproxen are introduced into water sources through human consumption, wastewater discharge, and agricultural activities (Mlunguza *et al*., 2019). While these drugs play essential roles in healthcare, their ecological impact on aquatic systems is profound. NSAIDs can disrupt the health of fish and invertebrates, leading to behavioral changes, growth retardation, and reproductive issues.

environment. Antidepressants and psychotropic drugs, including fluoxetine (Prozac) and sertraline, are another group of pharmaceutical contaminants that have raised significant concerns. These compounds have been detected in water sources worldwide, raising alarms about their potential impacts on human health and aquatic ecosystems (Batt *et al*., 2006). Antidepressants can influence the behavior and reproduction of aquatic organisms, causing disruptions such as altered fish mating patterns and predation behaviors (Richmond *et al*., 2016). In humans, inadvertent exposure to these drugs through drinking water could lead to nervous system disorders and hormonal imbalances, further emphasizing the need for effective mitigation strategies (Chander *et al*., 2016; Couto *et al*., 2019; Mansouri *et al*., 2021). The persistence of antidepressants in the environment and their widespread use underscores the necessity of advanced removal methods to protect both environmental and public health. Chemotherapeutics and cancer medications, although detected at lower concentrations than other pharmaceutical classes, pose unique challenges due to their high toxicity and persistence in the environment.

Table 1. Classification, Examples, and Properties of Pharmaceutical Drugs (Chander *et al*., 2016)

Pharmaceutical Class	Pharmaceutical Drugs	Nature of Pharmaceutical Drug
Anti-inflammatory	Aspirin, Diclofenac, Ibuprofen	Hydrophilic, Moderate hydrophobic
Lipid regulators	Clofibric acid, Bezafibrate, Fenofibric acid	Hydrophobic
Antiepileptics	Carbamazepine	Moderate hydrophobic
b-blockers	Metoprolol	Hydrophilic
Antibiotics	Ciprofloxacin	Hydrophilic

Table 2. Overview of Analytical Methods for Detecting Pharmaceuticals in Drinking Water

Water Source	Class of Pharmaceuticals	Detected Location	Analytical Procedure	Quantity Detected	Reference
River Water	Antibiotics	Germany	LC-MS/MS	0.1-2.5 µg/L	(Mondragón Velázquez, 2018; Tho Chau Minh Vinh *et al*., 2020)
Wastewater	Analgesics	Spain	GC-MS	0.017 µg/L.	(Caldas *et al*., 2017)
Groundwater	Anti-inflammatory drugs	India	HPLC-UV	0.02–45 ng/L	(Mohiuddin *et al*., 2020)
Surface Water	Antidepressants	United States	LC-MS/MS	245 ng/L	(Lin *et al*., 2018)
Drinking Water	Hormones	China	ELISA	1-100 ng/L	(Zheng *et al*., 2008)
Seawater	Antibiotics	Brazil	LC-MS/MS	(42.3–141.0 ng/L)- (0.001–0.1 ng/L)	(Roveri *et al*., 2021)
Surface Water	Antibiotics, NSAIDs	Nigeria	LC-MS/MS	75 to 129µgL^{-1}	(Roveri *et al*., 2021)
Wastewater Effluent	Antidepressants	USA	HPLC	15–100 ng g^{-1}	(Costa Junior *et al*., 2020)
Medjerda River	organochlorine pesticides	Tunisia	GC-MS	4.41 ng g^{-1} and 29.04 ng g^{-1}	(Necibi & Mzoughi, 2023)
Drinking Water	Endocrine Disruptors	Malaysia	(SPE)-LC-MS/MS)	(<0.470-79.89 ng/L) - (<0.30e7.67 ng/L)	(Ismail *et al*., 2019)
Surface Water	Antibiotics	Kenya	LC-MS/MS	High concentrations	(Fekadu *et al*., 2019)
Industrial Discharges	Active Pharmaceutical Ingredients (APIs)	India	Membrane Filtration	Varied concentrations	(Khasawneh & Palaniandy, 2021)
Surface Water	Antibiotics, Endocrine Disruptors	South Africa	HPLC	High levels	(Fekadu*et al*., 2019
Groundwater	NSAIDs, Antibiotics	India	LC-MS/MS	Low concentrations	(Chaturvedi *et al*., 2021)
Drinking Water	15 NPS, three traditional illicit drugs and two antidepressants.	USA	GC-MS	0.01-1.09 ng/L and0.02-3.64 ng/L	(Peng *et al*., 2019)
Industrial Effluent	Antineoplastics	Germany	Membrane Filtration	High concentrations	(Bukowski *et al*., 2020)
Surface Water	Hormonal Drugs	Malaysia	LC-MS/MS	Trace levels	(Praveena *et al*., 2019)
Surface water	37 pharmaceuticals belonging to 19 therapeutic classes	Nigeria	(HPLC–MS/MS)	ng Lâ''1 range	(Ogunbanwo *et al*., 2022)
Agricultural Runoff	Veterinary Antibiotics	Brazil	GC-MS	Moderate concentrations	(Fatoki *et al*., 2018)
Surface Water	Cytostatic Drugs	Sweden	LC-MS/MS	Trace levels	(Hedenrud, 2019)
Drinking Water	Antibiotics, Endocrine Disruptors	Tunisia	Composite Sampling	Varied concentrations	(Wilkinson *et al*., 2022)
Wastewater Effluent	Lipid Regulators	China	HPLC	Low concentrations	(Cipolatti *et al*., 2021)
Surface Water	NSAIDs	Nigeria	LC-MS/MS	Significant levels	(Schön, 2019) Michael *et al*., 2019
Groundwater	Veterinary Pharmaceuticals	Costa Rica	GC-MS	Trace amounts	(Wilkinson *et al*., 2022)
Agricultural Runoff	Antibiotics	Spain	HPLC	ng Lâ''1 levels	(Khasawneh & Palaniandy, 2021)
Surface Water	Beta-blockers, NSAIDs	Australia	LC-MS/MS	Trace levels	(Mlunguza *et al*., 2019)

Moreover, exposure to these compounds has been shown to alter the feeding behavior and immune responses of aquatic organisms, threatening their survival and disrupting the balance of aquatic ecosystems (Lee *et al*., 2019; Xu *et al*., 2021). These findings highlight the critical need for improved wastewater treatment technologies to minimize the release of NSAIDs into the

Compounds such as cisplatin and methotrexate have been identified in water sources, albeit at trace levels, but their prolonged presence could lead to carcinogenic effects (Bukowski *et al*., 2020). These drugs often enter water systems through hospital wastewater and improper disposal, and their detection highlights gaps in current wastewater treatment processes. Enhancing these processes is

essential to prevent their accumulation in drinking water and to safeguard both human health and aquatic life. The detection of pharmaceuticals in drinking water highlights the complex interplay between human activities, environmental sustainability, and public health. The issue is multifaceted, with concerns ranging from antibiotic resistance and hormonal disruptions to ecological toxicity and chronic health risks. These contaminants have the potential to undermine the effectiveness of medical treatments, alter ecosystems, and pose significant risks to human health, particularly over long-term exposure. Addressing this challenge requires a multi-pronged approach involving ongoing research, enhanced monitoring, and the development of advanced removal strategies. Technologies such as advanced oxidation processes, membrane filtration, and adsorption techniques (e.g., activated carbon and zeolite-based materials) have shown promise in mitigating pharmaceutical contamination (Kumari *et al*., 2024; Mijailovic *et al*., 2022; Oun *et al*., 2018).

Analytical Methods for Detecting Pharmaceuticals in Drinking Water: The detection of pharmaceutical residues in drinking water has become increasingly important due to the potential risks these contaminants pose to human health and environmental sustainability(Gworek *et al*., 2019). Analytical methods for identifying pharmaceuticals in water systems have evolved significantly, focusing on improving sampling techniques, utilizing advanced analytical tools, and enhancing detection limits and accuracy. These advancements are crucial for understanding the extent of contamination and implementing effective mitigation strategies (Richardson & Ternes, 2018). However, sampling is a critical step in detecting pharmaceutical contaminants in drinking water, but it presents several challenges. Proper sampling protocols are essential to ensure representative results and avoid contamination or degradation of the sample during collection, storage, and transport (Magi *et al*., 2018; Richardson & Ternes, 2018). Composite sampling methods, which involve collecting multiple samples over time, are often used to account for temporal variations in contaminant levels. However, these techniques can be time-consuming and require proper preservation to prevent changes in the chemical composition of pharmaceuticals. Factors such as temperature, light, and pH can affect the stability of pharmaceutical residues, necessitating careful sample handling (Lapworth *et al*., 2012). Furthermore, detecting trace concentrations of pharmaceuticals, often in the range of nanograms per liter (ng/L), requires highly sensitive sampling and storage methods to avoid losses during processing (Petrović *et al*., 2020). However, advanced analytical tools have revolutionized the detection and quantification of pharmaceutical residues in water as shown in Table 2. High-performance liquid chromatography (HPLC), liquid chromatography-tandem mass spectrometry (LC-MS/MS), and gas chromatography-mass spectrometry (GC-MS) are among the most widely used methods for identifying pharmaceuticals in water samples. HPLC and LC-MS/MS offer high sensitivity and specificity, making them ideal for detecting a wide range of pharmaceuticals, including antibiotics, NSAIDs, and endocrine disruptors (Hernández *et al*., 2022). These methods are capable of analyzing complex matrices, such as wastewater and surface water, with minimal interference. GC-MS, while also highly effective, is often limited to volatile and thermally stable compounds, requiring additional derivatization steps for non-volatile pharmaceuticals (Fekadu, Alemayehu, Dewil, & Bruggen, 2019). LC-MS/MS, in particular, has emerged as the gold standard for pharmaceutical analysis due to its ability to achieve ultra-low detection limits and high throughput, allowing the simultaneous detection of multiple pharmaceuticals in a single run (Khalikova *et al*., 2024; Tsikas, 2024). Furthermore, the detection limits and accuracy of analytical methods are crucial for assessing pharmaceutical contamination levels in water(Zulkifli*et al*., 2020). Recent advancements in analytical instrumentation have achieved detection limits as low as parts per trillion (ppt), enabling the identification of pharmaceuticals even at trace levels (A. Allwyn Sundarraj, 2024; Progress, 2022). However, achieving such sensitivity requires precise calibration, robust method validation, and the use of high-quality standards. Accuracy is often influenced by matrix effects, which can suppress or enhance signals during analysis, particularly in complex samples like wastewater (Tisler *et al*., 2021). Strategies such as isotope dilution, matrix-matched calibration, and advanced sample preparation techniques, including solid-phase extraction (SPE), have been employed to mitigate these effects and improve analytical accuracy (Cortese *et al*., 2020; Williams *et al*., 2023).

Mitigation Strategies and Policy Recommendations: Mitigating pharmaceutical waste pollution demands a comprehensive approach that integrates source control, public awareness, policy reforms, and sustainable practices (Liu *et al*., 2022). Controlling waste at its origin involves strategies such as reducing unnecessary prescriptions and encouraging rational drug use, as emphasized by (Zulkifli*et al*., 2020). Raising awareness among healthcare providers and patients, alongside facilitating the return of unused medications to authorized facilities, can significantly enhance waste management (Chisholm *et al*., 2021). Public education campaigns also play a pivotal role by informing individuals about the consequences of improper disposal and promoting safe practices, such as mixing unused medications with undesirable substances before disposal, as recommended by the FDA (Freitas & Radis-Baptista, 2021; Lucca *et al*., 2019; Nyaga *et al*., 2020; Yu *et al*., 2021). Changes in consumer behavior regarding medication use and disposal, highlighted by Freitas & Radis-Baptista, (2021), can greatly reduce pollution. On a policy level, enforcing proper waste management regulations and adopting extended producer responsibility (EPR) frameworks can drive pharmaceutical companies to create eco-friendly products and manage post-consumer waste effectively (Faibil *et al*., 2023; Leclerc & Badami, 2020). Additionally, investment in research for biodegradable and non-toxic compounds is essential. Integrating sustainable practices within the pharmaceutical industry is another critical step, involving greener synthesis methods, life cycle assessments (LCA), and eco-friendly packaging (Guiton & Benetto, 2018). By adhering to green chemistry principles, the industry can minimize waste and enhance environmental sustainability. Ultimately, a collaborative effort from all stakeholders, including the public, policymakers, and the pharmaceutical industry, is vital to mitigate the environmental impacts of pharmaceutical pollution effectively (Isoni *et al*., 2022; Miettinen & Khan, 2022).

CONCLUSION

Pharmaceutical contamination in drinking water remains a significant global challenge with profound implications for environmental sustainability and public health. Pharmaceuticals enter water systems through various pathways, including household waste, agricultural runoff, and industrial discharges, and persist due to their chemical stability and resistance to conventional treatment methods. These contaminants pose risks such as antimicrobial resistance, endocrine disruption, and ecological harm, affecting both human and aquatic life.Despite advancements in detection and treatment technologies, such as advanced oxidation processes, membrane filtration, and activated carbon adsorption, the removal of pharmaceutical residues remains incomplete. The limitations of these methods, coupled with the lack of widespread monitoring and regulation, exacerbate the issue. Regions with limited resources, particularly in developing countries, face the highest risks due to inadequate wastewater management systems and limited public awareness of proper disposal practices.Mitigating the impact of pharmaceutical pollution requires a multifaceted approach. Public education campaigns are essential to raise awareness about the consequences of improper disposal and promote safe practices. Stricter regulatory frameworks and extended producer responsibility (EPR) policies can drive the pharmaceutical industry toward the development of environmentally friendly products and better waste management practices. Additionally, integrating green chemistry principles, such as greener synthesis methods and eco-friendly packaging, can significantly reduce pharmaceutical waste at its source. Collaboration among stakeholders, including policymakers, industries, healthcare providers, and the public, is critical to addressing this issue effectively. Investments in research and development, particularly for sustainable pharmaceutical practices and advanced treatment technologies, are necessary to minimize environmental and health risks. By adopting an integrated

approach that combines prevention, treatment, and education, society can work toward safeguarding water resources and ensuring a sustainable future for generations to come. Continued global efforts are imperative to tackle this growing environmental challenge comprehensively.

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