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Review Research paper

Pharmaceutical Wastes as Emerging Groundwater Contaminants: A Review of Their Sources, Fate, Health Impacts, and Techniques for Analytical Detection and Treatment

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ABSTRACT

Pharmaceutical wastes are emerging as significant groundwater contaminants, raising concerns over their long-term impacts on public health and ecosystems. This review examines the major sources of contamination—such as wastewater treatment plants (WWTPs), septic systems, industrial discharges, and agricultural runoff—and explores how physicochemical properties and subsurface interactions influence their environmental fate. Although advanced analytical tools like liquid chromatography–tandem mass spectrometry (LC-MS/MS) have improved detection at trace levels, challenges in effective removal persist. Frequently detected contaminants include non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, antidepressants, and hormone-disrupting compounds, often present in concentrations ranging from nanograms to micrograms per liter. Promising treatment technologies, including advanced oxidation processes and activated carbon adsorption, are discussed alongside their limitations. This review highlights the urgent need for comprehensive monitoring programs, cost-effective remediation methods, and further investigation into the chronic effects of low-dose pharmaceutical exposure.

INTRODUCTION

Pharmaceuticals are essential to modern medicine and are widely used in both human and veterinary healthcare for treating infections, alleviating pain, regulating hormones, and managing psychological conditions. Major classes include antibiotics, anti-inflammatories, hormones, β-blockers, and lipid regulators (Xiang et al., 2021; Boxall et al., 2012). However, the widespread use of these compounds, coupled with their partial metabolism and poor removal in conventional treatment systems, has resulted in their persistent accumulation in the environment—particularly in groundwater (Ortúzar et al., 2022).

Pharmaceutical residues reach groundwater through various pathways, including effluent discharge from wastewater treatment plants (WWTPs), leaking sewer systems, agricultural runoff, industrial effluents, landfill leachates, and improper drug disposal (Shaheen et al., 2022). Consequently, groundwater—an essential source of drinking water—is increasingly contaminated with a diverse array of pharmaceutical compounds, such as antibiotics, antidepressants, hormones, and anti-inflammatory agents (Morin-Crini et al., 2022; Nag et al., 2023).

Despite significant advancements in analytical detection—particularly through techniques like liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS)—the effective removal of pharmaceuticals remains a challenge. Most existing treatment systems are not designed to target such compounds, and their chronic, low-level presence poses potential long-term risks to ecosystems and human health. Furthermore, transformation products generated during degradation processes may be equally or more toxic and persistent than the parent compounds.

Although awareness of pharmaceutical contamination is increasing, comprehensive reviews specifically focused on their occurrence and behavior in groundwater systems remain limited. This review addresses that gap by synthesizing current knowledge on the sources, environmental fate, health risks, detection methods, and treatment technologies related to pharmaceutical contaminants in groundwater. The review also highlights emerging research challenges and emphasizes the need for improved regulatory and remediation frameworks.

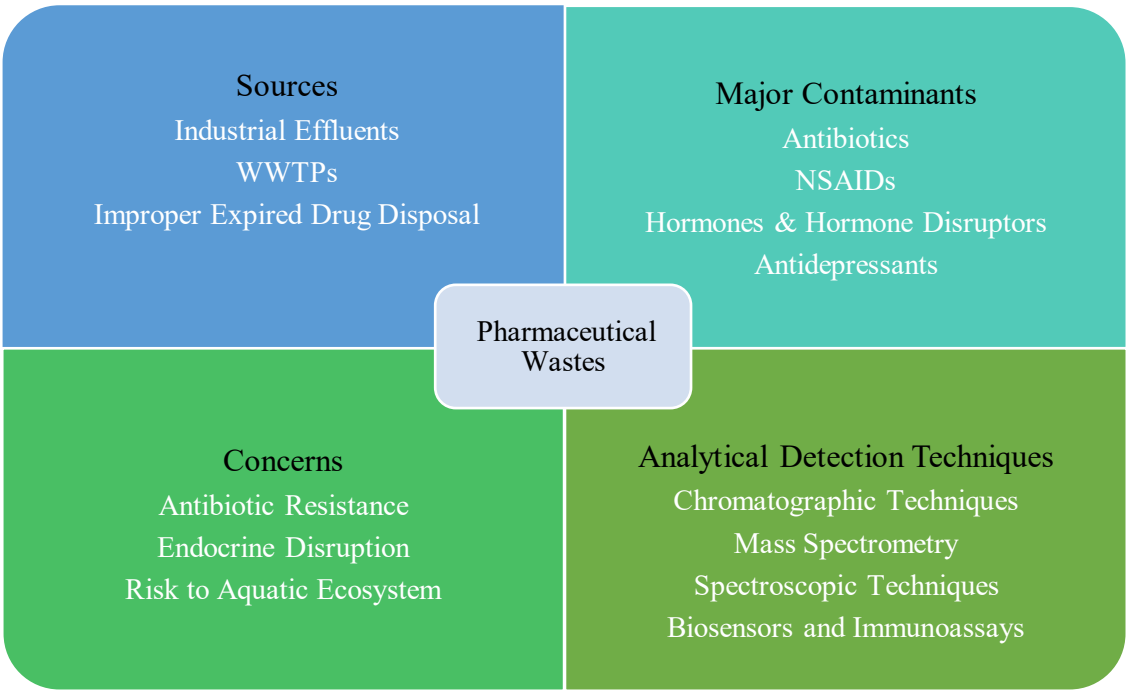

Fig.1. Conceptual Overview of Pharmaceutical Wastes in the Environment

2. MATERIALS AND METHODS

This review was conducted following PRISMA guidelines. Peer-reviewed studies published between 2005 and 2024 were retrieved from databases including Scopus, Web of Science, PubMed, MEDLINE, AGRIS, UGC CARE, and Reaxys.

2.1 Search Strategy

Search terms included combinations of "pharmaceutical contaminants," "groundwater pollution," "NSAIDs fate," "LC-MS/MS detection," and "treatment technologies," using Boolean operators.

2.2 Selection Criteria

Included studies focused on pharmaceutical contamination in groundwater, covering sources, fate, detection, health risks, and treatment. Excluded were non-peer-reviewed articles, surface water-only studies, or those lacking methodological rigor.

2.3 Screening and Data Extraction

Out of 450 initial articles, 400 remained after duplicates were removed. After abstract screening and full-text review, 92 studies were selected. Extracted data included compound types, concentrations, analytical methods, and treatment outcomes. Results were synthesized thematically and presented in tables where applicable.

3. OCCURRENCES & SOURCES OF PHARMACEUTICAL CONTAMINANTS

Pharmaceutical residues are increasingly detected in groundwater globally, typically at concentrations ranging from nanograms to micrograms per liter. Their presence is primarily attributed to anthropogenic sources and the limited removal efficiency of wastewater treatment systems. Key contributors include municipal WWTPs, leaky sewer lines, industrial effluents, agricultural runoff, and improper drug disposal (Lapworth et al., 2012; Luo et al., 2014).

A nationwide study conducted in China investigated 35 pharmaceutical compounds in influent and effluent samples from 12 WWTPs across different cities. The results revealed significant regional variation, with WWTPs in northern cities exhibiting higher influent concentrations than those in the south. Caffeine was reported at the highest influent concentration, reaching up to 1775.98 ng/L. Despite advanced infrastructure in some facilities, the overall removal efficiency was low: only 14.3% of pharmaceuticals achieved a mean removal efficiency greater than 70%, while 51.4% were removed at rates below 30% (Liu et al., 2017). These findings highlight not only the prevalence of pharmaceutical pollutants in urban wastewater systems but also the inefficiency of existing treatment frameworks, especially in rapidly urbanizing regions.

In contrast, many European countries have adopted tertiary treatment technologies—such as ozonation, activated carbon adsorption, and membrane filtration—resulting in higher removal efficiencies (up to 80–95% for selected compounds). However, even these advanced systems are often ineffective at fully removing persistent pharmaceuticals such as carbamazepine and diclofenac (Zhang et al., 2008; Luo et al., 2014).

Pharmaceuticals also enter groundwater through leaky sewer systems, surface runoff, improper disposal, and agricultural practices. In urban areas, aging infrastructure allows compounds like estrogens and NSAIDs to migrate into shallow aquifers, as documented in Kraków, Poland (Rusiniak et al., 2021). In rural areas, veterinary pharmaceuticals from manure, biosolids, and reclaimed water used in irrigation contribute to diffuse contamination (Kümmerer, 2009). Industrial effluents represent another major source, particularly in regions with inadequate environmental regulation. For instance, elevated levels of ibuprofen and naproxen were detected in soil and groundwater near pharmaceutical manufacturing facilities in Pakistan (Ashfaq et al., 2017), while hospital-associated WWTPs in South Africa were found to discharge multiple pharmaceuticals including antibiotics, β-blockers, and antihistamines (Kanama et al., 2018).

These examples illustrate that pharmaceutical contamination in groundwater is both widespread and multifactorial. Urban areas tend to be affected by centralized WWTP inefficiencies and infrastructure leaks, while rural and peri-urban zones are impacted more by agricultural runoff and decentralized disposal practices. Regional differences in regulation, treatment technology, and pharmaceutical consumption patterns further influence contaminant profiles.

Table 1: Prevalence and levels of frequently identified pharmaceutical pollutants across various matrices in multiple countries. Abdulmalik M. Alqarni 2024.

Pharmaceutical Contaminants	Classification	Occurrence	Concentration	Country	References
Ofloxacin and ciprofloxacin	Antibiotics	WWTP influent	1000–2200 ng/L	Italy	Verlicchi et al. 2012.
Tramadol,ofloxacin, gemfibrozil, atenolol, caffeine, and cetirizine	Analgesic, antibiotics, lipid regulator, β-blocker,stimulant and antihistamine	Irrigation water	1100–4400 ng/L	Spain	García-Valverde et al. 2023.
Estrone, 17b-estradiol, estriol, 2-hydroxyestrone, 16α-hydroxyestrone, 4-hydroxyestrone, 2-hydroxyestradiol, 4- hydroxyestradiol, 17-epiestriol, 16 keto-estradiol, and 16-epiestriol	Steroidal hormones	WWTP (effluent & influent)	n.d.–62.9 ng/L	China	Tang et al. 2020
		River water	n.d.–51.7 ng/L		
Ketoprofen, diclofenac, and indomethacin	Analgesic/NSAIDs	Sludge	4.4–77 ng/g	Japan	Matsuo et al. 2011.
Amoxicillin	Antibiotics	STP	172 ng/L	India	Mutiyar & Mittal et al. 2013.
Atenolol, ciprofloxacin, sulfamethoxazole, ranitidine	β-blocker, Antibiotics and antihistamine	WWTP (effluent and influent)	34–3585 ng/L	Saudi Arabia	Mostafa et al. 2023.

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STP sewage treatment plant; n.d.: Not detected

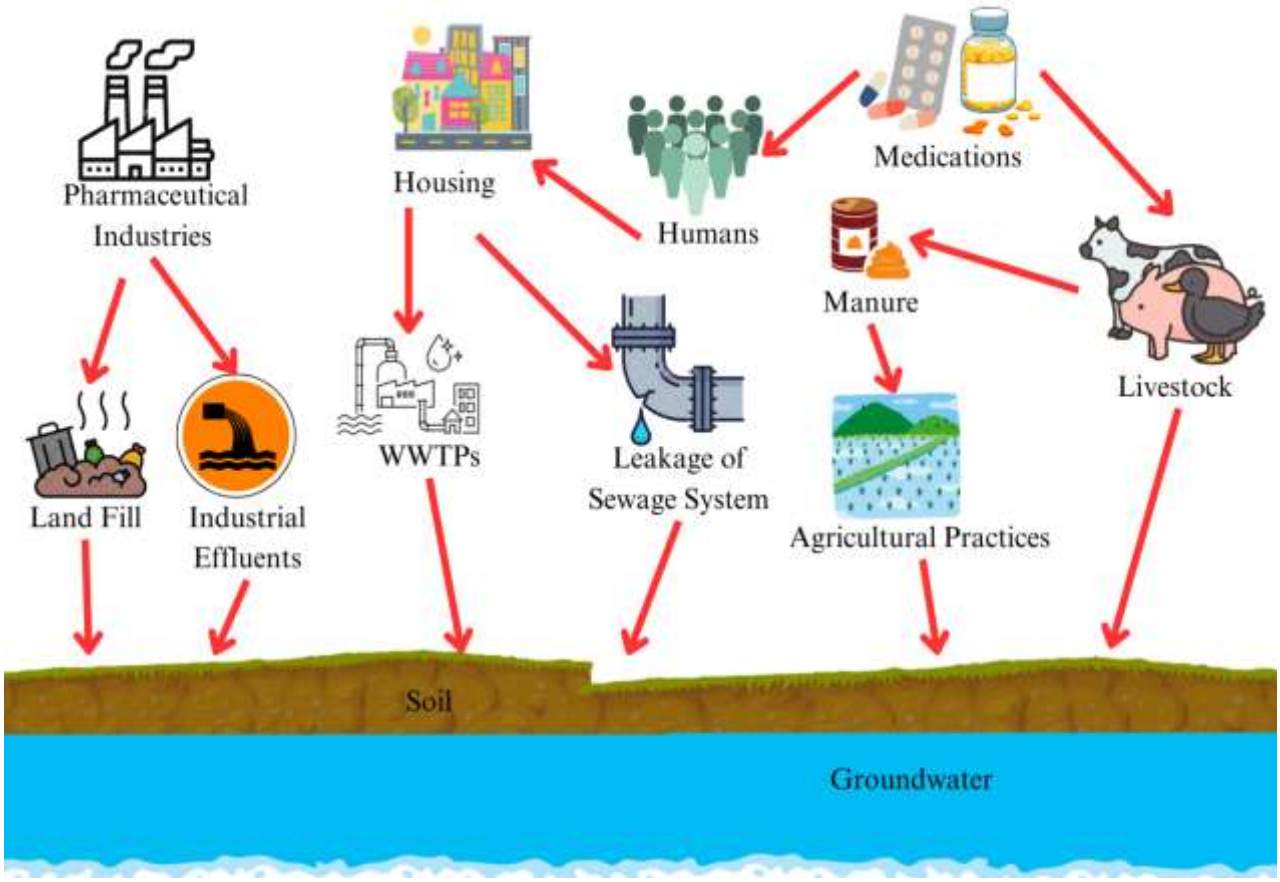

Fig.2. Overview Schematic Representations of Various Sources of Pharmaceutical Contaminants in Groundwater

4. FATE AND TRANSPORT IN GROUNDWATER

The behavior of pharmaceuticals in groundwater is governed by their physicochemical properties—such as solubility, polarity, molecular weight, and ionization potential—as well as site-specific environmental conditions. Hydrophilic compounds like acetaminophen and caffeine migrate more readily through aquifers, whereas hydrophobic or ionizable compounds, such as carbamazepine and diclofenac, tend to adsorb to organic matter, limiting their mobility but enhancing persistence (Lv et al., 2019; Clara et al., 2004).

Environmental factors including redox conditions, pH, temperature, and microbial activity influence degradation rates and transport dynamics (Jelic et al., 2011). Some pharmaceuticals persist in aquifers for extended periods, long after their initial release, reflecting their environmental stability (Lapworth et al., 2012).

Wastewater treatment efficiency also affects pharmaceutical transport. Advanced technologies like membrane bioreactors and sequencing batch reactors provide improved removal but still leave detectable residues of compounds such as ofloxacin and clarithromycin (Liu et al., 2017; Zhang et al., 2008).

These findings highlight the complexity of pharmaceutical behavior in subsurface environments and the need for refined models to assess long-term contaminant mobility and exposure risk (Ruhoy & Daughton, 2008; Petrie et al., 2015).

Table 2: Different classes and nature of pharmaceutical drug. Vikas Chander, Bhavtosh Sharma et al. 2016.

Pharmaceutical classes	Pharmaceutical drugs	Nature of Pharmaceutical drug
Anti-inflammatory	Aspirin Diclofenac Ibuprofen	Hydrophilic Varies Moderate hydrophobic
Antidepressants	Clofibric acid Bezafibrate Fenofibric acid	Moderate hydrophobic Hydrophobic Hydrophobic
Antiepileptics	Carbamazepine	Moderate hydrophobic
Antibiotics	Ciprofloxacin	Hydrophilic

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4.1 Transformation Products and Metabolites

The degradation of pharmaceutical compounds in the environment often leads to the formation of transformation products (TPs), which may be more persistent, mobile, or toxic than their parent molecules (Kümmerer, 2009; aus der Beek et al., 2016). For instance, carbamazepine commonly transforms into carbamazepine-10,11-epoxide, a compound known for its environmental stability and comparable toxicity (Miao et al., 2005).

Transformation processes—such as microbial metabolism, hydrolysis, photolysis, and partial oxidation—produce by-products with altered physicochemical properties, often resulting in increased water solubility and reduced sorption to soils. These characteristics enhance their transport through aquifers, contributing to their widespread detection in groundwater (Patel et al., 2019).

Because treated wastewater and landfill leachates often contain both parent compounds and TPs, the continuous release of these mixtures results in pseudo-persistent environmental exposure. Even as individual compounds degrade, their sustained input maintains relatively stable concentrations in groundwater.

Despite their significance, TPs are frequently overlooked in environmental monitoring and regulation. This omission hampers risk assessments, as TPs can differ substantially in toxicity and behavior from their

precursors. There is a critical need to expand monitoring frameworks and analytical protocols to specifically target TPs and develop tailored remediation strategies (Petrie et al., 2015).

5. PHARMACEUTICAL CONTAMINANTS (PCS)

Pharmaceuticals are categorized based on their mechanisms of action, chemical structure, interaction with biological systems, and therapeutic use. The primary classes of pharmaceutical contaminants in the environment include antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), hormonal agents (including endocrine disruptors), and antidepressants.

5.1 Antibiotics

Antibiotics are widely used in both human and veterinary medicine to prevent and treat bacterial infections. While these compounds have greatly advanced medical outcomes, their extensive and often indiscriminate use has led to their pervasive presence in aquatic environments, where they now represent a major class of environmental contaminants (Bilal et al., 2019; Gillings, 2014). The most commonly detected antibiotic pollutants include fluoroquinolones, macrolides, tetracyclines, and sulphonamides (Sonkar et al., 2024).

These compounds enter the environment through multiple pathways, including domestic wastewater discharge, agricultural runoff, hospital effluents, and pharmaceutical manufacturing waste. Consequently, antibiotics have been detected at varying concentrations in seawater, surface water, groundwater, and even treated drinking water supplies (Bilal et al., 2019).

Their environmental presence poses significant risks to both aquatic and terrestrial ecosystems. In aquatic systems, antibiotics can adversely affect planktonic organisms, which occupy the foundational level of the food web. Exposure has been shown to disrupt their physiological, morphological, and behavioral functions, leading to shifts in interspecies dynamics and ecosystem structure (Gunathilaka et al., 2023). Similarly, in terrestrial environments, antibiotic residues in soil can alter microbial community composition, thereby disturbing nutrient cycling and ecosystem balance (Brooks et al., 2008).

One of the most pressing concerns associated with environmental antibiotic contamination is the proliferation of antibiotic-resistant bacteria, which poses a critical threat to both public and animal health (Gangar and Patra, 2023; Gillings, 2014). Resistant microorganisms have been detected in wild-caught marine and terrestrial species, including those intended for human consumption (Gillings, 2014). In addition to fostering resistance, antibiotics can also be toxic to non-target species, further compromising ecosystem stability (Gangar and Patra, 2023).

An emerging concern is the development of the so-called "plastisphere"—microbial communities that colonize plastic debris in aquatic environments. These surfaces have been identified as vectors for antibiotic-resistant bacteria and resistance genes, thereby facilitating the spread of resistance across marine ecosystems (Andryukov et al., 2022).

5.2 Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

NSAIDs are among the most widely prescribed medications for pain, inflammation, and fever. Common examples include paracetamol, diclofenac, and ibuprofen, all of which have been frequently detected in aquatic environments (Parolini, 2020). These compounds primarily enter water systems as excreted metabolites.

NSAIDs are known to bioaccumulate in aquatic organisms such as *Mytilus galloprovincialis*, leading to toxic effects such as oxidative stress, hepatotoxicity, immunosuppression, and developmental abnormalities (Elizalde-Velázquez & Gómez-Oliván, 2020). Sublethal effects can occur even at environmentally relevant concentrations. For example, NSAID exposure has been linked to male-biased sex ratios and altered gene expression in zebrafish (Bereketoglu et al., 2020).

5.3 Hormones & Hormone Disruptors

Hormonal pharmaceuticals and endocrine-disrupting chemicals (EDCs) are exogenous compounds that mimic, block, or otherwise interfere with endogenous hormonal signaling pathways. These substances have been increasingly associated with adverse physiological and developmental effects in both aquatic organisms and humans (Falco and Laforgia, 2021; Streifer and Gore, 2021).

In aquatic environments, EDCs have been shown to impair reproductive and behavioral functions in fish, potentially leading to long-term disruptions in population dynamics (Hotchkiss et al., 2008). Notably, several EDCs are capable of inducing epigenetic modifications, which may be heritable across generations, thereby compounding their ecological and health risks (Fudvoye et al., 2014). In humans, exposure to EDCs has been implicated in a range of health conditions, including infertility, thyroid disorders, precocious puberty, metabolic dysfunctions such as obesity and diabetes, and skeletal abnormalities (Pironti et al., 2021; Turan, 2021). Moreover, these compounds may interfere with neurodevelopment, contributing to elevated risks of neurological and cognitive disorders (Streifer and Gore, 2021).

5.4 Antidepressants

Antidepressants are pharmaceutical agents prescribed for the management of depression and other related psychiatric disorders. They are typically categorized into four main classes: tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) (Carreno and Frazer, 2022). In recent years, the widespread detection of these compounds—particularly SSRIs—in aquatic environments has emerged as a significant ecological concern.

Experimental studies utilizing artificial stream mesocosms have demonstrated that environmentally relevant concentrations of fluoxetine and citalopram (20 μg/L) can lead to measurable ecological disturbances. These include a reduction in gross primary productivity by up to 29% and a decline in biofilm community respiration by at least 43%. Additionally, treated streams exhibited earlier emergence of dipteran midges compared to control conditions (Richmond et al., 2016). These results suggest that even low-level

concentrations of SSRIs can substantially alter aquatic ecosystem function, potentially disrupting trophic interactions and the life cycles of aquatic organisms.

6. IMPACTS OF PHARMACEUTICALS ON HUMAN HEALTH

Pharmaceutical contaminants in groundwater raise growing concerns for public health, particularly through **chronic low-dose exposure** via **drinking water**, **food crops**, and **recreational use of groundwater-fed systems**. While concentrations are generally in the **ng/L to low µg/L range**, certain compounds have been detected at levels exceeding risk thresholds in various studies (aus der Beek et al., 2016; Lapworth et al., 2012).

Risk assessment frameworks commonly use the **Hazard Quotient (HQ)**, **Risk Quotient (RQ)**, and **Excess Cancer Risk (ECR)** to evaluate human exposure:

- **HQ** is the ratio of exposure concentration to a reference dose (RfD).
- **RQ** compares environmental concentrations to predicted no-effect concentrations (PNECs).
- **ECR** estimates lifetime cancer risk from chronic exposure to carcinogenic substances.

For instance, **carbamazepine**, frequently detected in groundwater across Europe and Asia, has been reported with **HQ values approaching or exceeding 1**, indicating potential chronic health risks (Mompelat et al., 2009). Similarly, **diclofenac** and **sulfamethoxazole** often present **RQ values >1** in both WWTP effluents and adjacent aquifers, especially near urban or industrial hotspots (Petrovic et al., 2003; Rizzo et al., 2019).

Recent studies have shown that **infants and immunocompromised individuals** are particularly vulnerable to compounds with **endocrine-disrupting potential**, such as **estrone** and **17β-estradiol**, found in some drinking water wells at levels exceeding **10 ng/L** (Kleywegt et al., 2008). These concentrations, although low, are within ranges known to **disrupt hormonal regulation** during developmental windows of exposure (Sumpter and Johnson, 2005).

In a meta-analysis of global occurrence and risk studies, (Patel et al., 2019) highlighted that at least **18 commonly detected pharmaceuticals** in environmental waters exceed their Predicted No-Effect Concentration (PNEC) or acceptable daily intake (ADI) thresholds in localized scenarios. Among them, **ofloxacin**, **clarithromycin**, and **erythromycin-H_2O** were frequently identified as high-risk, particularly in areas with high WWTP effluent discharge and limited water reuse treatment infrastructure.

Moreover, many existing risk assessments **fail to account for cumulative exposure**, **synergistic effects**, or **transformation products**, which may enhance or compound toxicological effects. The limited scope of monitoring efforts—often focused solely on parent compounds—underestimates potential human health risks (Petrie et al., 2015).

Therefore, future assessments should incorporate **multi-compound exposure models**, **population-specific vulnerability assessments**, and expanded **monitoring frameworks** that include both parent pharmaceuticals and transformation products. This is especially critical in regions dependent on groundwater for potable use and lacking advanced treatment technologies.

7. ANALYTICAL TECHNIQUES FOR DETECTION OF PHARMACEUTICALS

The analysis of pharmaceutical residues in environmental matrices demands high sensitivity and specificity due to the low concentrations at which these compounds typically occur. Chromatographic methods, particularly when coupled with mass spectrometric detection, are extensively utilized for their ability to separate, detect, and quantify diverse pharmaceutical compounds across complex matrices.

7.1 Chromatographic Techniques

7.1.1 High-Performance Liquid Chromatography (HPLC)

High-Performance Liquid Chromatography (HPLC) High-Performance Liquid Chromatography (HPLC) is a widely used technique in the analysis of pharmaceutical residues due to its high resolution, precision, and reproducibility. It separates analytes based on their polarity and interactions with stationary and mobile phases. HPLC, when coupled with Ultraviolet Detector (UV), Diode Array Detector (DAD), or MS detectors, offers robust sensitivity and quantification. For instance, Petrović et al. (2013) identified 81 pharmaceuticals in Serbian surface waters using Ultra Performance Liquid Chromatography with Mass Spectrometry (UPLC-MS), with ibuprofen concentrations up to 20.1 μg/L. Similarly, Cai et al. (2014) reported carbamazepine at 38.24 ng/L in Beijing tap water using HPLC-MS/MS. However, matrix effects such as ion suppression may reduce accuracy, which can be mitigated through solid-phase microextraction (SPME) and micellar desorption (MD) (Padrón et al., 2009; Cahill et al., 2004).

7.1.2 Gas Chromatography (GC)

Gas Chromatography (GC) is especially suitable for volatile and thermally stable pharmaceutical compounds. GC coupled with mass spectrometry (GC-MS) is commonly used for identifying analgesics, NSAIDs, and antibiotics. Farré et al. (2001) and Sadkowska et al. (2017) detected ibuprofen and diclofenac in river and wastewater samples using GC-MS techniques. Derivatization is often necessary for polar compounds, increasing sample preparation time and potential for analyte loss (Quintana et al., 2007).

7.2 Mass Spectrometry -Based Hyphenated Techniques

7.2.1 Liquid Chromatography-Mass Spectrometry (LC-MS)

Liquid Chromatography–Mass Spectrometry (LC-MS) combines chromatographic separation with molecular detection, offering high sensitivity for a wide range of pharmaceutical compounds, both polar and non-polar. Detection limits typically range from 1 to 1000 ng/L depending on the sample matrix and instrument configuration (Ferrer & Thurman, 2012). Nonetheless, matrix-induced ion suppression may impact quantitative accuracy, which necessitates the use of internal standards and thorough calibration procedures (Rodrigues et al., 2024).

7.2.2 Gas Chromatography-Mass Spectrometry (GC-MS)

GC-MS is employed for thermally stable pharmaceuticals and is ideal for analyzing volatile residues. Reddersen and Heberer (2003) reported detection of 19 pharmaceutical compounds with GC-MS using selective ion monitoring (SIM), achieving Limits of detection (LODs) in the range of 1–10 ng/L. While highly selective, GC-MS is limited by its requirement for analyte volatility or chemical derivatization.

7.2.3 Tandem Mass Spectrometry coupled with Liquid Chromatography (LC-MS/MS)

LC-MS/MS utilizes multiple reaction monitoring (MRM) to improve specificity and reduce background noise in complex matrices. Boix et al. (2014) and Gracia-Lor et al. (2009) successfully quantified a wide range of pharmaceuticals including sulfamethoxazole and ketoprofen in environmental waters at sub-ng/L levels. Sample preparation typically includes solid-phase extraction (SPE), and method validation often requires the use of isotope-labeled internal standards.

Table 3: Analytical approaches for detecting pharmaceutical compounds of different classes in various locations

Class of Pharmaceutical	Pharmaceutical Compound	Concentration	Analytical Technique	Location	References
Antibiotic, Fluoroquinolone	Ciprofloxacin Enrofloxacin ofloxacin	1400 µg/L 210 µg/L 55 µg/L			
Antihistamine	Cetirizine	2100 µg/L	LC-MS	Hyderabad, India	Fick et al. 2009
Beta -adrenoreceptor antagonist	Metoprolol	4 µg/L			
Anti-Epilepsy	Carbamazepine	26,329.6 ng/L	UPLC - ESI-MS/MS	Eastern Cape Province, South Africa	Vumazonke et al. 2020
Antibiotic	Sulfamethoxazole	6968 ng/L			
Anti-inflammatories	Naproxen Ibuprofen	0.16 µg/L 0.17 µg/L	HPLC - PDA	Kwazulu-Natal Province, South Africa	Ngubane et al. 2019

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LC-MS, Liquid Chromatography –Mass Spectrometry

UPLC- ESI-MS/MS, Ultra- Performance Liquid Chromatography Electrospray Ionization Tandem mass Spectrometry

HPLC – PDA, High-Performance Liquid Chromatography with a Photodiode Array Detector

7.3 Spectroscopic Techniques

7.3.1 UV-Visible Spectroscopy

UV-Vis spectroscopy is a cost-effective screening method based on the Beer–Lambert principle of light absorption. While useful for high-concentration assessments in relatively clean matrices, its applicability in complex environmental samples is restricted due to low specificity and interference from natural organic matter (Singh et al., 2021; Hussain et al., 2020).

7.3.2 Fluorescence Spectroscopy and Infrared (IR) Spectroscopy

Fluorescence spectroscopy, especially using excitation-emission matrix (EEM) analysis, offers high sensitivity for naturally fluorescent pharmaceuticals, although background signal interference may compromise accuracy (Jing et al., 2022). Infrared spectroscopy, particularly Fourier-transform IR (FTIR) and attenuated total reflectance (ATR) modes, is employed for functional group identification. However, spectral distortions due to water absorption present analytical challenges (Hahn et al., 2010; Goldberg and Chaffotte, 2005).

7.4 Advanced and Emerging Techniques

7.4.1 Biosensors and Immunoassays

Biosensors and immunoassays represent innovative, high-throughput platforms for the rapid detection of pharmaceuticals in aquatic systems. Electrochemical and optical biosensors offer real-time monitoring with high specificity, while immunoassays provide robust sensitivity via antigen–antibody interactions (Sanvicens et al., 2011; Cháfer-Pericás et al., 2010). However, issues such as cross-reactivity, matrix effects, and limited standardization constrain their widespread implementation (Adrián et al., 2009; Petz, 2009).

Table 4. Comparative evaluation of analytical techniques for pharmaceutical contaminant detection in environmental matrices.

Technique	LOD (ng/L)	Sensitivity	Selectivity	Application	References
HPLC	50–100	Moderate	Moderate–High	Quantification of target drugs	Ahmed, 2024; Cai et al., 2014

GC-MS	1–50	High	High	Volatile pharmaceuticals	Farré et al., 2001; Sadkowska et al., 2017
LC-MS/MS	<1–10	Very High	Very High	Multi-residue trace analysis	Boix et al., 2014; Gracia-Lor et al., 2009
UV-Vis	1000–5000	Low	Low	Screening of APIs	Singh et al., 2021
Fluorescence	<100	High	Moderate–High	Naturally fluorescent drugs	Jing et al., 2022
IR (FTIR, ATR)	500–2000	Moderate	Low–Moderate	Functional group ID	Hahn et al., 2010
Biosensors	<50	High	High	On-site screening	Sanvicens et al., 2011
Immunoassays	<10	High	High	Hormonal drugs, antibiotics	Cháfer-Pericás et al., 2010

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8 Treatment Technologies

8.1 Advanced Oxidation Processes

Advanced Oxidation Processes (AOPs) are highly effective technologies for degrading pharmaceutical contaminants in water. They function by generating hydroxyl radicals (•OH), which are extremely reactive species capable of breaking down complex organic pollutants into carbon dioxide and water (Stefan, 2017; Wang & Xu, 2012). These radicals are produced through mechanisms such as ultraviolet (UV) radiation, photocatalysis, ozonation, Fenton reactions, and electrochemical oxidation (Khader et al., 2024). AOPs are particularly effective in treating recalcitrant compounds like antibiotics and NSAIDs, which are often resistant to conventional biological processes (Michael et al., 2013; Zawadzki, 2022). However, AOPs require significant energy input and chemical reagents, leading to high operational costs. Their efficiency can also be affected by pH, background matrix composition, and the presence of halide ions. In some cases, partial oxidation may result in the formation of toxic by-products, necessitating careful optimization and monitoring (Taoufik et al., 2021; Stefan, 2017).

8.2. Membrane Filtration

Membrane filtration is a pressure-driven separation technique that employs semi-permeable membranes to remove pharmaceuticals based on size exclusion and charge interactions. Four main types exist: microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO), with NF and RO being most effective for pharmaceutical removal due to their finer pore sizes (Scott, 1995; Cevallos-Mendoza et al., 2022). Removal efficiencies for many pharmaceuticals often exceed 90%, with reports of up to 99% for certain

compounds (Iqbal et al., 2023). Despite high effectiveness, membrane fouling remains a significant limitation, reducing efficiency and increasing energy consumption. Additionally, not all pharmaceuticals are retained, and small polar compounds may pass through certain membranes (Rosman et al., 2018). Hybrid systems such as membrane bioreactors (MBRs), which combine biological degradation and physical filtration, are being explored to enhance treatment performance and operational efficiency (Hernando et al., 2007).

8.3. Activated Carbon Adsorption

Activated carbon adsorption is a well-established and effective method for removing pharmaceutical residues from aqueous media. The technique relies on physical and chemical interactions such as pore filling, hydrogen bonding, and electrostatic forces between pharmaceutical molecules and the high-surface-area carbon material (Wang et al., 2021). Adsorption capacity depends on pore structure, surface area, and the physicochemical properties of both the pharmaceutical and the carbon surface. Studies have shown that microporous carbons derived from sources like pinecones and Butia capitata endocarp effectively adsorb ketoprofen, paracetamol, and other drugs (Kerkhoff et al., 2021; Yu et al., 2023). Isotherm models such as Langmuir, Freundlich, and Redlich–Peterson are used to describe adsorption behavior (Delgado et al., 2019). Challenges include competitive adsorption from co-existing organics, expensive regeneration, and decreased performance over time due to fouling and pore blockage (Zieliński et al., 2022; Heusser et al., 2023)

Table 5. Comparative summary of pharmaceutical treatment technologies

Technology	Removal Efficiency	Advantages	Limitations	Scalability	References
Advanced Oxidation Processes (AOPs)	70–100%	Effective for recalcitrant compounds, broad spectrum	High cost, toxic by-products, energy intensive	Medium to High	Stefan, 2017; Michael et al., 2013
Membrane Filtration (NF/RO)	90–99%	High selectivity, physical barrier	Membrane fouling, high energy demand	High	Scott, 1995; Iqbal et al., 2023
Activated Carbon Adsorption	50–95%	Cost-effective, high adsorption capacity	Competitive adsorption, regeneration costs	High	Wang et al., 2021; Zieliński et al., 2022

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9. CONCLUSIONS

Pharmaceuticals and their transformation products (TPs) persist in groundwater due to incomplete removal by conventional treatment technologies, particularly under real-world environmental conditions. Current research often overlooks key factors such as mixture toxicity, chronic low-dose exposure, and site-specific hydrogeological variability—limiting the effectiveness of risk assessments and management strategies. While

analytical techniques have advanced, treatment technologies and regulatory frameworks remain fragmented and inadequate.

Key Recommendations

1. Establishing unified regulatory standards for pharmaceuticals and TPs in groundwater;
2. Integrating **multi-barrier treatment solutions**—such as membrane processes integrated with advanced oxidation processes (AOPs)—that are both scalable and adaptable to real-world conditions;
3. Developing affordable, real-time monitoring tools and decentralized filtration systems;
4. Expanding environmental surveillance frameworks to include TPs; and
5. Incentivizing green drug design and responsible disposal through take-back programs.

A coordinated, cross-disciplinary approach is essential to advance regulatory policies, technological innovation, and research efforts for safeguarding groundwater quality.

Author Contributions: Bendalam Moulika (Author 1) was responsible for collecting relevant research articles and review papers on pharmaceutical contamination, with a specific focus on groundwater, from authentic databases such as Scopus, Web of Science, PubMed, MEDLINE, AGRIS, UGC CARE, and Reaxys-indexed journals. She also prepared the original draft of the manuscript. Edupuganti Naga Dhanamjaya Rao (Author 2) and Ayyagari Venkata Surya Satya Anand (Author 3) contributed by reviewing and supervising the work.

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REFERENCES

1. Adrián, J., Obregon, R., Ramón-Azcon, J., Fernández, F., Tort, N., Muriano, A., Marco, M.-P., 2009. Biosensors for Pharmaceuticals and Emerging Contaminants Based on Novel Micro and Nanotechnology Approaches. springer berlin heidelberg, pp. 47–68.
2. Ahmad, M., Jamal, A., Tang, X.-W., Al-Sughaiyer, M.A., Al-Ahmadi, H.M., Ahmad, F., 2020. Assessing Potable Water Quality and Identifying Areas of Waterborne Diarrheal and Fluorosis Health Risks Using Spatial Interpolation in Peshawar, Pakistan. Water 12, 2163. https://doi.org/10.3390/w12082163
3. Alqarni, A.M., 2024. Analytical Methods for the Determination of Pharmaceuticals and Personal Care Products in Solid and Liquid Environmental Matrices: A Review. Molecules 29, 3900. https://doi.org/10.3390/molecules29163900
4. Andryukov, B., Besednova, N., Zaporozhets, T.A., 2022. Microplastics and Their Role in the Maintenance and Spread of Antibiotic Resistance Genes in Marine Ecosystems. Antibiotics and Chemotherapy 67, 61–70. https://doi.org/10.37489/0235-2990-2022-67-7-8-61-70
5. Ashfaq, M., Khan, K.N., Rehman, M.S.U., Mustafa, G., Nazar, M.F., Sun, Q., Iqbal, J., Mulla, S.I., Yu, C.-P., 2017. Ecological risk assessment of pharmaceuticals in the receiving environment of pharmaceutical wastewater in Pakistan. Ecotoxicology and Environmental Safety 136, 31–39. https://doi.org/10.1016/j.ecoenv.2016.10.029
6. Bereketoglu, C., Pradhan, A., Olsson, P.-E., 2020. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Cause Male-Biased Sex Differentiation in Zebrafish. Aquatic Toxicology 223, 105476. https://doi.org/10.1016/j.aquatox.2020.105476

7. Bilal, M., Mahmood, S., Rasheed, T., Iqbal, H., 2019. Antibiotics traces in the aquatic environment: Persistence and adverse environmental impact. Current Opinion in Environmental Science & Health 13. https://doi.org/10.1016/j.coesh.2019.11.005
8. Boix, C., Ibáñez, M., Sancho, J.V., Rambla, J., Aranda, J.L., Ballester, S., Hernández, F., 2014. Fast determination of 40 drugs in water using large volume direct injection liquid chromatography–tandem mass spectrometry. Talanta 131, 719–727. https://doi.org/10.1016/j.talanta.2014.08.005
9. Boxall, A.B.A., Rudd, M.A., Brooks, B.W., Caldwell, D.J., Choi, K., Hickmann, S., Innes, E., Ostapyk, K., Staveley, J.P., Verslycke, T., Ankley, G.T., Beazley, K.F., Belanger, S.E., Berninger, J.P., Carriquiriborde, P., Coors, A., DeLeo, P.C., Dyer, S.D., Ericson, J.F., Gagné, F., Giesy, J.P., Gouin, T., Hallstrom, L., Karlsson, M.V., Larsson, D.G.J., Lazorchak, J.M., Mastrocco, F., McLaughlin, A., McMaster, M.E., Meyerhoff, R.D., Moore, R., Parrott, J.L., Snape, J.R., Murray-Smith, R., Servos, M.R., Sibley, P.K., Straub, J.O., Szabo, N.D., Topp, E., Tetreault, G.R., Trudeau, V.L., Van Der Kraak, G., 2012. Pharmaceuticals and Personal Care Products in the Environment: What Are the Big Questions? Environ Health Perspect 120, 1221–1229. https://doi.org/10.1289/ehp.1104477
10. Brooks, B., Maul, J., Belden, J., 2008. Antibiotics in Aquatic and Terrestrial Ecosystems, in: Encyclopedia of Ecology. pp. 210–217. https://doi.org/10.1016/B978-008045405-4.00370-0
11. Cai, M.-Q., Wang, R., Zhang, L.-Q., Feng, L., 2014. Determination of selected pharmaceuticals in tap water and drinking water treatment plant by high-performance liquid chromatography-triple quadrupole mass spectrometer in Beijing, China. Environmental Science and Pollution Research 22, 1854–1867. https://doi.org/10.1007/s11356-014-3473-8
12. Carreno, F.R., Frazer, A., 2022. Antidepressant Drugs, in: Comprehensive Pharmacology. Elsevier, pp. 308–324. https://doi.org/10.1016/B978-0-12-820472-6.00044-X
13. Cevallos-Mendoza, J., Amorim, C., Rodríguez-Díaz, J., Montenegro, M., 2022. Removal of Contaminants from Water by Membrane Filtration: A Review. Membranes 12, 570. https://doi.org/10.3390/membranes12060570
14. Cháfer-Pericás, C., Maquieira, Á., Puchades, R., 2010. Fast screening methods to detect antibiotic residues in food samples. TrAC Trends in Analytical Chemistry 29, 1038–1049. https://doi.org/10.1016/j.trac.2010.06.004
15. Chander, V., Sharma, B., Negi, V., Aswal, R.S., Singh, P., Singh, R., Dobhal, R., 2016. Pharmaceutical Compounds in Drinking Water. Journal of Xenobiotics 6. https://doi.org/10.4081/xeno.2016.5774
16. Clara, M., Strenn, B., Gans, O., Martinez, E., Kreuzinger, N., Kroiss, H., 2005. Removal of selected pharmaceuticals, fragrances and endocrine disrupting compounds in a membrane bioreactor and conventional wastewater treatment plants. Water Research 39, 4797–4807. https://doi.org/10.1016/j.watres.2005.09.015
17. De Falco, M., Laforgia, V., 2021. Combined Effects of Different Endocrine-Disrupting Chemicals (EDCs) on Prostate Gland. International journal of environmental research and public health 18, 9772. https://doi.org/10.3390/ijerph18189772
18. Delgado, N., Capparelli, A., Navarro, A., Marino, D., 2019. Pharmaceutical emerging pollutants removal from water using powdered activated carbon: Study of kinetics and adsorption equilibrium. Journal of Environmental Management 236, 301–308. https://doi.org/10.1016/j.jenvman.2019.01.116
19. Elizalde-Velázquez, G.A., Gómez-Oliván, L.M., 2020. Introduction and Historical Findings That Focused Nonsteroidal Anti-Inflammatory Drugs as Emerging Pollutant, in: Gómez-Oliván, L.M. (Ed.), Non-Steroidal Anti-Inflammatory Drugs in Water, The Handbook of Environmental Chemistry. Springer International Publishing, Cham, pp. 1–40. https://doi.org/10.1007/698_2020_540
20. Farré, M., Ferrer, I., Ginebreda, A., Figueras, M., Olivella, L., Tirapu, L., Vilanova, M., Barceló, D., 2001. Determination of drugs in surface water and wastewater samples by liquid chromatography–mass spectrometry: methods and preliminary results including toxicity studies with Vibrio fischeri. Journal of Chromatography A 938, 187–197. https://doi.org/10.1016/s0021-9673(01)01154-2
21. Ferrer, I., Thurman, E.M., 2012. Analysis of 100 pharmaceuticals and their degradates in water samples by liquid chromatography/quadrupole time-of-flight mass spectrometry. Journal of Chromatography A 1259, 148–157. https://doi.org/10.1016/j.chroma.2012.03.059
22. Fick, J., Söderström, H., Lindberg, R.H., Phan, C., Tysklind, M., Larsson, D.G.J., 2009. Contamination of surface, ground, and drinking water from pharmaceutical production. Environmental Toxicology and Chemistry 28, 2522–2527. https://doi.org/10.1897/09-073.1
23. Fudvoye, J., Parent, A.-S., Bourguignon, J.-P., 2014. Chapter One - Endocrine-Disrupting Chemicals and Human Growth and Maturation: A Focus on Early Critical Windows of Exposure, in: Vitamins and Hormones. elsevier, pp. 1–25.
24. Gangar, T., Patra, S., 2023. Antibiotic persistence and its impact on the environment. 3 Biotech 13. https://doi.org/10.1007/s13205-023-03806-6
25. García-Valverde, M., Aragonés, A.M., Andújar, J.A.S., García, M.D.G., Martínez-Bueno, M.J., Fernández-Alba, A.R., 2023. Long-term effects on the agroecosystem of using reclaimed water on commercial crops. Science of The Total Environment 859, 160462. https://doi.org/10.1016/j.scitotenv.2022.160462
26. Gillings, M., 2014. Pollution by antibiotics and resistance genes: dissemination into Australian wildlife, in: Stow, A., Maclean, N., Holwell, G.I. (Eds.), Austral Ark. Cambridge University Press, pp. 186–196. https://doi.org/10.1017/CBO9781139519960.011
27. Goldberg, M.E., Chaffotte, A.F., 2005. Undistorted structural analysis of soluble proteins by attenuated total reflectance infrared spectroscopy. Protein Science 14, 2781–2792. https://doi.org/10.1110/ps.051678205
28. Gracia-Lor, E., Sancho, J.V., Hernández, F., 2009. Simultaneous determination of acidic, neutral and basic pharmaceuticals in urban wastewater by ultra high-pressure liquid chromatography-tandem mass spectrometry. Journal of Chromatography A 1217, 622–632. https://doi.org/10.1016/j.chroma.2009.11.090

29. Gunathilaka, M.D.K., Bao, S., Xuan, L., Li, Y., Pan, Y., 2023. Antibiotic Pollution of Planktonic Ecosystems: A Review Focused on Community Analysis and the Causal Chain Linking Individual- and Community-Level Responses. Environmental science & technology 57. https://doi.org/10.1021/acs.est.2c06787
30. Hahn, H., Huck, C.W., Pezzei, C., Pallua, J.D., Bonn, G.K., Huck-Pezzei, V., 2010. Infrared-Spectroscopy: A Non-Invasive Tool for Medical Diagnostics and Drug Analysis. Current Medicinal Chemistry 17, 2956–2966. https://doi.org/10.2174/092986710792065063
31. Hernando, M.D., Fernández-Alba, A.R., Radjenovic, J., Petrovic, M., Barceló, D., 2007. Chapter 4.2 Removal of pharmaceuticals by advanced treatment technologies, in: Comprehensive Analytical Chemistry. elsevier, pp. 451–474.
32. Heusser, A., Dax, A., Mcardell, C.S., Udert, K.M., 2023. High content of low molecular weight organics does not always affect pharmaceutical adsorption on activated carbon: The case of acetate, propionate and ethanol in source-separated urine. Water Research X 21, 100199. https://doi.org/10.1016/j.wroa.2023.100199
33. Hotchkiss, A.K., Ankley, G.T., Foster, P.M., Hartig, P.C., Wilson, V.S., Rider, C.V., Gray, C.L., Gray, L.E., Blystone, C.R., 2008. Fifteen Years after "Wingspread"—Environmental Endocrine Disrupters and Human and Wildlife Health: Where We are Today and Where We Need to Go. Toxicological Sciences 105, 235–259. https://doi.org/10.1093/toxsci/kfn030
34. Hussain, C.M., Rawtani, D., Pandey, G., Tharmavaram, M., 2020. Chapter 3 - UV-visible and fluorescence spectroscopy for forensic samples, in: Handbook of Analytical Techniques for Forensic Samples. elsevier, pp. 37–54.
35. Iqbal, A., Cevik, E., Bozkurt, A., Mustafa, A., Asiri, S., Alagha, O., Qahtan, T.F., 2023. Tailored multifunctional molybdenum-iron nanosheets for enhanced membrane filtration and excellent electrocatalytic performance for hydrogen evolution reaction. Journal of Cleaner Production 421, 138486. https://doi.org/10.1016/j.jclepro.2023.138486
36. Jelic, A., Gros, M., Ginebreda, A., Cespedes-Sánchez, R., Ventura, F., Petrovic, M., Barcelo, D., 2011. Occurrence, partition and removal of pharmaceuticals in sewage water and sludge during wastewater treatment. Water Research 45, 1165–1176. https://doi.org/10.1016/j.watres.2010.11.010
37. Jing, Z.-B., Wu, Q.-Y., Wang, W.-L., Zhu, P., Lu, Y., Nong, Y.-J., 2022. Fluorescence analysis for water characterization: measurement processes, influencing factors, and data analysis. Journal of Water Reuse and Desalination. https://doi.org/10.2166/wrd.2022.065
38. Kanama, K.M., Daso, A.P., Mpenyana-Monyatsi, L., Coetzee, M.A.A., 2018. Assessment of Pharmaceuticals, Personal Care Products, and Hormones in Wastewater Treatment Plants Receiving Inflows from Health Facilities in North West Province, South Africa. Journal of Toxicology 2018, 3751930. https://doi.org/10.1155/2018/3751930
39. Kerkhoff, C.M., Boit Martinello, K.D., Franco, D.S.P., Netto, M.S., Georgin, J., Foletto, E.L., Piccilli, D.G.A., Silva, L.F.O., Dotto, G.L., 2021. Adsorption of ketoprofen and paracetamol and treatment of a synthetic mixture by novel porous carbon derived from Butia capitata endocarp. Journal of Molecular Liquids 339, 117184. https://doi.org/10.1016/j.molliq.2021.117184
40. Khader, E.H., Muslim, S.A., Saady, N.M.C., Ali, N.S., Salih, I.K., Mohammed, T.J., Albayati, T.M., Zendehboudi, S., 2024. Recent advances in photocatalytic advanced oxidation processes for organic compound degradation: A review. Desalination and Water Treatment 318, 100384. https://doi.org/10.1016/j.dwt.2024.100384
41. Kleywegt, S., Pileggi, V., Yang, P., Hao, C., Zhao, X., Rocks, C., Thach, S., Cheung, P., Whitehead, B., 2011. Pharmaceuticals, hormones and bisphenol A in untreated source and finished drinking water in Ontario, Canada — Occurrence and treatment efficiency. Science of The Total Environment 409, 1481–1488. https://doi.org/10.1016/j.scitotenv.2011.01.010
42. Kümmerer, K., 2009. The presence of pharmaceuticals in the environment due to human use – present knowledge and future challenges. Journal of Environmental Management 90, 2354–2366. https://doi.org/10.1016/j.jenvman.2009.01.023
43. Lapworth, D.J., Baran, N., Stuart, M.E., Ward, R.S., 2012. Emerging organic contaminants in groundwater: A review of sources, fate and occurrence. Environmental Pollution 163, 287–303. https://doi.org/10.1016/j.envpol.2011.12.034
44. Liu, H.-Q., Lam, J.C.W., Li, W.-W., Yu, H.-Q., Lam, P.K.S., 2017. Spatial distribution and removal performance of pharmaceuticals in municipal wastewater treatment plants in China. Science of The Total Environment 586, 1162–1169. https://doi.org/10.1016/j.scitotenv.2017.02.107
45. Luo, Y., Guo, W., Ngo, H.H., Nghiem, L.D., Hai, F.I., Zhang, J., Liang, S., Wang, X.C., 2014. A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. Science of The Total Environment 473–474, 619–641. https://doi.org/10.1016/j.scitotenv.2013.12.065
46. Lv, J., Zhang, L., Chen, Y., Ye, B., Han, J., Jin, N., 2019. Occurrence and distribution of pharmaceuticals in raw, finished, and drinking water from seven large river basins in China. Journal of Water and Health 17, 477–489. https://doi.org/10.2166/wh.2019.250
47. Matsuo, H., Sakamoto, H., Arizono, K., Shinohara, R., 2011. Behavior of Pharmaceuticals in Waste Water Treatment Plant in Japan. Bull Environ Contam Toxicol 87, 31–35. https://doi.org/10.1007/s00128-011-0299-7
48. Michael, I., Frontistis, Z., Fatta-Kassinos, D., 2013. Chapter 11 - Removal of Pharmaceuticals from Environmentally Relevant Matrices by Advanced Oxidation Processes (AOPs), in: Comprehensive Analytical Chemistry. elsevier, pp. 345–407.
49. Mompelat, S., Le Bot, B., Thomas, O., 2009. Occurrence and fate of pharmaceutical products and by-products, from resource to drinking water. Environment International 35, 803–814. https://doi.org/10.1016/j.envint.2008.10.008

50. Morin-Crini, N., Torri, G., Lu, Z., Pandey, A., Li, C., Ribeiro, A.R.L., Liu, G., Lichtfouse, E., Hocquet, D., Stock, F., Balaram, V., Crini, G., Carmona, E., Giraldo, L., Teixeira, M.R., Picos-Corrales, L.A., Moreno-Piraján, J.C., 2022. Worldwide cases of water pollution by emerging contaminants: a review. Environmental Chemistry Letters 20, 2311–2338. https://doi.org/10.1007/s10311-022-01447-4
51. Mostafa, A., Shaaban, H., Alqarni, A., Al-Ansari, R., Alrashidi, A., Al-Sultan, F., Alsulaiman, M., Alsaif, F., Aga, O., 2023. Multi-class determination of pharmaceuticals as emerging contaminants in wastewater from Eastern Province, Saudi Arabia using eco-friendly SPE-UHPLC-MS/MS: Occurrence, removal and environmental risk assessment. Microchemical Journal 187, 108453. https://doi.org/10.1016/j.microc.2023.108453
52. Nag, S., Das, J., Roy, S., Saha, K., Sarkar, S., 2023. Emerging Environmental Contaminants: Sources, Consequences, and Future Challenges. de gruyter, pp. 223–234.
53. Ngubane, N.P., Naicker, D., Ncube, S., Chimuka, L., Madikizela, L.M., 2019. Determination of naproxen, diclofenac and ibuprofen in Umgeni estuary and seawater: A case of northern Durban in KwaZulu–Natal Province of South Africa. Regional Studies in Marine Science 29, 100675. https://doi.org/10.1016/j.rsma.2019.100675
54. Ortúzar, M., González-López, J., Olicón-Hernández, D.R., Esterhuizen, M., Aranda, E., 2022. Pharmaceutical Pollution in Aquatic Environments: A Concise Review of Environmental Impacts and Bioremediation Systems. Frontiers in Microbiology 13. https://doi.org/10.3389/fmicb.2022.869332
55. Padrón, M.E.T., Ferrera, Z.S., Rodríguez, J.J.S., 2009. Coupling of solid-phase microextraction with micellar desorption and high performance liquid chromatography for the determination of pharmaceutical residues in environmental liquid samples. Biomedical Chromatography 23, 1175–1185. https://doi.org/10.1002/bmc.1240
56. Parolini, M., 2020. Adverse Effects Induced by Nonsteroidal Anti-inflammatory Drugs on Freshwater Invertebrates. https://doi.org/10.1007/698_2020_547
57. Patel, M., Kumar, R., Kishor, K., Mlsna, T., Pittman, C.U., Mohan, D., 2019. Pharmaceuticals of Emerging Concern in Aquatic Systems: Chemistry, Occurrence, Effects, and Removal Methods. Chem. Rev. 119, 3510–3673. https://doi.org/10.1021/acs.chemrev.8b00299
58. Petrie, B., Barden, R., Kasprzyk-Hordern, B., 2015. A review on emerging contaminants in wastewaters and the environment: Current knowledge, understudied areas and recommendations for future monitoring. Water Research 72, 3–27. https://doi.org/10.1016/j.watres.2014.08.053
59. Petrović, M., Škrbić, B., Živančev, J., Ferrando-Climent, L., Barcelo, D., 2013. Determination of 81 pharmaceutical drugs by high performance liquid chromatography coupled to mass spectrometry with hybrid triple quadrupole–linear ion trap in different types of water in Serbia. Science of The Total Environment 468–469, 415–428. https://doi.org/10.1016/j.scitotenv.2013.08.079
60. Petz, M., 2009. Recent applications of surface plasmon resonance biosensors for analyzing residues and contaminants in food. Monatshefte für Chemie - Chemical Monthly 140, 953–964. https://doi.org/10.1007/s00706-009-0142-6
61. Pironti, C., Proto, A., Bianco, P.M., Motta, O., Ricciardi, M., Montano, L., 2021. Endocrine-Disrupting Compounds: An Overview on Their Occurrence in the Aquatic Environment and Human Exposure. Water 13, 1347. https://doi.org/10.3390/w13101347
62. Quintana, J., Carpinteiro, J., RodríGuez, I., 2007. Chapter 2.5 Analysis of acidic drugs by gas chromatography, in: Comprehensive Analytical Chemistry. elsevier science technology, pp. 185–218.
63. Reddersen, K., Heberer, T., 2003. Multi-compound methods for the detection of pharmaceutical residues in various waters applying solid phase extraction (SPE) and gas chromatography with mass spectrometric (GC-MS) detection. Journal of Separation Science 26, 1443–1450. https://doi.org/10.1002/jssc.200301533
64. Richmond, E., Rosi, E., Lee, S., Thompson, R., Grace, M., 2016. Antidepressants in stream ecosystems: Influence of selective serotonin reuptake inhibitors (SSRIs) on algal production and insect emergence. Freshwater Science 35, 000–000. https://doi.org/10.1086/687841
65. Rizzo, L., Manaia, C., Merlin, C., Schwartz, T., Dagot, C., Ploy, M.C., Michael, I., Fatta-Kassinos, D., 2013. Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: A review. Science of The Total Environment 447, 345–360. https://doi.org/10.1016/j.scitotenv.2013.01.032
66. Rodrigues, T.B., Cunha, R.L., Barci, P.E.P., Santos-Neto, Á.J., Lanças, F.M., 2024. Analysis of human biological samples using porous graphitic carbon columns and liquid chromatography-mass spectrometry: a review. Analytical and bioanalytical chemistry. https://doi.org/10.1007/s00216-024-05458-8
67. Rosman, N., Salleh, W.N.W., Mohamed, M.A., Jaafar, J., Ismail, A.F., Harun, Z., 2018. Hybrid membrane filtration-advanced oxidation processes for removal of pharmaceutical residue. Journal of Colloid and Interface Science 532, 236–260. https://doi.org/10.1016/j.jcis.2018.07.118
68. Ruhoy, I.S., Daughton, C.G., 2008. Beyond the medicine cabinet: An analysis of where and why medications accumulate. Environment International 34, 1157–1169. https://doi.org/10.1016/j.envint.2008.05.002
69. Rusiniak, P., Kmiecik, E., Wątor, K., Duda, R., Bugno, R., 2021. Pharmaceuticals and personal care products in the urban groundwater – preliminary monitoring (case study: Kraków, Southern Poland). Urban Water Journal 18, 364–374. https://doi.org/10.1080/1573062X.2021.1893354
70. Sadkowska, J., Kumirska, J., Stepnowski, P., Caban, M., Chmielewski, M., 2017. Environmental aspects of using gas chromatography for determination of pharmaceutical residues in samples characterized by different composition of the matrix. Archives of Environmental Protection 43, 3–9. https://doi.org/10.1515/aep-2017-0028

71. Sanvicens, N., Mannelli, I., Salvador, J.-P., Valera, E., Marco, M.-P., 2011. Biosensors for pharmaceuticals based on novel technology. TrAC Trends in Analytical Chemistry 30, 541–553. https://doi.org/10.1016/j.trac.2011.01.006
72. Scott, K., 1995. Section 10 - Water purification, in: Handbook of Industrial Membranes. elsevier, pp. 521–572.
73. Shaheen, J.F., Sizirici, B., Yildiz, I., 2022. Fate, transport, and risk assessment of widely prescribed pharmaceuticals in terrestrial and aquatic systems: A review. Emerging Contaminants 8, 216–228. https://doi.org/10.1016/j.emcon.2022.04.001
74. Singh, D., Kaushik, A., Chauhan, V., Chaudhar, S., 2021. A REVIEW ON INSTRUMENTATION AND VALIDATION METHOD OF UV-VISIBLE SPECTROSCOPY AND HPLC FOR THE ANALYSIS OF DRUGS. International Research Journal of Pharmacy 12, 14–21. https://doi.org/10.7897/2230-8407.1203126
75. Sonkar, V., v, V., Nishil, B., Shashidhar, T., 2024. Review on antibiotic pollution dynamics: insights to occurrence, environmental behaviour, ecotoxicity, and management strategies. Environmental Science and Pollution Research 31. https://doi.org/10.1007/s11356-024-34567-1
76. Stefan, M.I., 2017. Advanced Oxidation Processes for Water Treatment - *Fundamentals* and Applications. Water Intelligence Online 16, 9781780407197. https://doi.org/10.2166/9781780407197
77. Stefan, M.I., 2017. Advanced Oxidation Processes for Water Treatment - *Fundamentals* and Applications. Water Intelligence Online 16, 9781780407197. https://doi.org/10.2166/9781780407197
78. Streifer, M., Gore, A.C., 2021. Epigenetics, estrogenic endocrine-disrupting chemicals (EDCs), and the brain. Advances in pharmacology (San Diego, Calif.) 92, 73–99. https://doi.org/10.1016/bs.apha.2021.03.006
79. Sumpter, J.P., Johnson, A.C., 2005. Lessons from Endocrine Disruption and Their Application to Other Issues Concerning Trace Organics in the Aquatic Environment. Environ. Sci. Technol. 39, 4321–4332. https://doi.org/10.1021/es048504a
80. Tang, Z., Liu, Z., Wang, H., Dang, Z., Yin, H., Zhou, Y., Liu, Y., 2020. Trace determination of eleven natural estrogens and insights from their occurrence in a municipal wastewater treatment plant and river water. Water Research 182, 115976. https://doi.org/10.1016/j.watres.2020.115976
81. Taoufik, N., Boumya, W., Achak, M., Sillanpää, M., Barka, N., 2021. Comparative overview of advanced oxidation processes and biological approaches for the removal pharmaceuticals. Journal of Environmental Management 288, 112404. https://doi.org/10.1016/j.jenvman.2021.112404
82. Ternes, T.A., Joss, A., Siegrist, H., 2004. Peer Reviewed: Scrutinizing Pharmaceuticals and Personal Care Products in Wastewater Treatment. Environ. Sci. Technol. 38, 392A-399A. https://doi.org/10.1021/es040639t
83. Turan, S., 2021. Endocrine disrupting chemicals and bone. Best Practice & Research Clinical Endocrinology & Metabolism 35, 101495. https://doi.org/10.1016/j.beem.2021.101495
84. Verlicchi, P., Al Aukidy, M., Galletti, A., Petrovic, M., Barceló, D., 2012. Hospital effluent: Investigation of the concentrations and distribution of pharmaceuticals and environmental risk assessment. Science of The Total Environment 430, 109–118. https://doi.org/10.1016/j.scitotenv.2012.04.055
85. Vumazonke, S., Khamanga, S.M., Ngqwala, N.P., 2020. Detection of Pharmaceutical Residues in Surface Waters of the Eastern Cape Province. IJERPH 17, 4067. https://doi.org/10.3390/ijerph17114067
86. Wang, J.L., Xu, L.J., 2012. Advanced Oxidation Processes for Wastewater Treatment: Formation of Hydroxyl Radical and Application. Critical Reviews in Environmental Science and Technology 42, 251–325. https://doi.org/10.1080/10643389.2010.507698
87. Wang, T., He, J., Lu, J., Zhou, Yi, Wang, Z., Zhou, Yanbo, 2021. Adsorptive removal of PPCPs from aqueous solution using carbon-based composites: A review. Chinese Chemical Letters 33, 3585–3593. https://doi.org/10.1016/j.cclet.2021.09.029
88. Xiang, Y., Wu, H., Li, L., Ren, M., Qie, H., Lin, A., 2021. A review of distribution and risk of pharmaceuticals and personal care products in the aquatic environment in China. Ecotoxicology and Environmental Safety 213, 112044. https://doi.org/10.1016/j.ecoenv.2021.112044
89. Yu, H., Mikšík, F., Thu, K., Miyazaki, T., 2023. Characterization and optimization of pore structure and water adsorption capacity in pinecone-derived activated carbon by steam activation. Powder Technology 431, 119084. https://doi.org/10.1016/j.powtec.2023.119084
90. Zawadzki, P., 2022. Visible Light–Driven Advanced Oxidation Processes to Remove Emerging Contaminants from Water and Wastewater: a Review. Water, Air, & Soil Pollution 233. https://doi.org/10.1007/s11270-022-05831-2
91. Zhang, Y., Geißen, S.-U., Gal, C., 2008. Carbamazepine and diclofenac: Removal in wastewater treatment plants and occurrence in water bodies. Chemosphere 73, 1151–1161. https://doi.org/10.1016/j.chemosphere.2008.07.086
92. Zieliński, B., Miądlicki, P., Przepiórski, J., 2022. Development of activated carbon for removal of pesticides from water: case study. Scientific Reports 12. https://doi.org/10.1038/s41598-022-25247-6