J MEDICINE 2026; 27: 114-127

Review Article

Pharmaceutical Remnants and Residues in Water and Its Impact on Human Health and Aquatic Life

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Abstract

Background and aims: *Drugs that have expired, unused, spilled, recalled, damaged, contaminated, or removed from circulation for other reasons are referred to as pharmaceutical waste. Pharmaceuticals and their waste pose a threat to human health and contribute significantly to environmental deterioration. Using a variety of sophisticated experimental approaches, numerous pharmaceutical compounds have been found in considerable amounts in groundwater, surface water, subsurface water, household waste water, municipal waste water, and industrial effluents. The current review focuses on pharmaceutical wastes' effects on water quality, including their prevalence, characteristics, and environmental fate that endangers human health.*

Methods: *Keywords including pharmaceutical wastes, pharmacological action of drug residue, drug waste in water, drug residue in environment, antibiotics in water, illicit drug substances, pharmaceutical waste disposal, wastewater treatment, and human health were used to search research databases including Google Scholar, EBSCO, PubMed, Springer, Science Direct, and NIH. The data was collected from the books, literatures and websites were then analyzed, discussed and properly summarized.*

Results: *Pharmaceuticals, nanomaterials and cosmeceuticals are the products and their metabolite substances that are present in surface water, drinking water and wastewater are not well known in many cases. Even at low concentrations, many active pharmaceutical ingredients (APIs) maintain their biological activity, which might affect aquatic environments and have an impact on human health. So, public health is seriously at danger due to their unknown toxicity, teratogenicity, and carcinogenicity profile as well as a lack of monitoring and control mechanisms.*

Conclusion: *To reduce environmental and human health risk, effective waste management, government policy, organization policy and public awareness are crucial to ensure that discarded pharmaceuticals wouldn't contribute to exacerbate ecological problems and human health.*

Keywords: *Pharmaceutical waste, Drug residue, Toxicity, Human health, Aquatic life*

DOI: *https://doi.org/10.3329/jom.v27i2.92246*

Received: *03-02-2026* ***Accepted:*** *25-04-2026*

Introduction:

Pharmaceutical residues in water bodies, including hormones, lipid regulators, antibiotics, NSAIDs, anti-retroviral medications, and β-blockers, have drawn a lot of attention, because of their detrimental impact on aquatic ecosystems and human health.[1] Concerns including drug-resistant populations, infertility, cancer, endocrine disruption, and reduced plant and animal development might result from these persistent chemicals' harmful effects, even at trace quantities (ng/L).[2,3] Pharmaceutical pollutants are often found in surface water, reclaimed wastewater. Different drugs including vancomycin, ampicillin, penicillin, amoxicillin, diclofenac, paracetamol, carbamazepine, efavirenz, aspirin, paracetamol, and ibuprofen are also found in aquatic sources and soil.[4] Pharmaceutical compounds typically enter aquatic ecosystems through stormwater runoff, leaching from landfills, indiscriminate disposal of hospital and household waste, and discharges from pharmaceutical industrial and domestic sewage.[5] Various drugs concentration found in ground, surface and drinking water is shown in (**Table 1**).

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Table 1. Pharmaceuticals approximate concentration ranges in water environment reports

Pharmaceutical group	Example	Surface Water (ng/L)	Groundwater (ng/L)	Drinking Water (ng/L)	Detection Method
Antibiotics	Sulfamethoxazole, Ciprofloxacin, Erythromycin, Amoxicillin	15-2500	10-400	2-90	Solid-Phase Extraction (SPE) followed by Liquid Chromatography–Tandem Mass Spectrometry (LC-MS/MS)
Antidepressant	Carbamazepine, Fluoxetine, Sertraline	10-850	5-100	1-35	SPE + LC-MS/MS
Analgesics and Anti-inflammatories	Ibuprofen, Diclofenac, Naproxen, Ketoprofen, Aspirin	20-3000	5-270	2-40	SPE + LC-MS/MS
Cardiovascular Drugs	Atenolol, Metoprolol, Propranolol, Atorvastatin	25-1000	10-150	3-20	SPE + LC-MS/MS
Hormones and Endocrine Disruptors	Estradiol, Ethinylestradiol, Androgens, Bisphenol A	0.5-75	<5-15	<1-6	**SPE + LC-MS/MS**; GC-MS/MS
Lipid Regulators	Clofibric acid, Gemfibrozil	30-800	2-75	2-10	SPE + LC-MS/MS
Anticancer Drugs	Cyclophosphamide, Ifosfamide, Tamoxifen, Methotrexate, Cyclophosphamide, Capecitabine	5-35	<10	<1-4	SPE + LC-MS/MS (High-sensitivity Triple Quadrupole LC-MS/MS)
Antiepileptics	Carbamazepine, Phenytoin	70-4600	20-300	1-50	**SPE + LC-MS/MS;** HPLC-UV for routine analysis

(Note: Values are consolidated and analyzed from European, Asian, and North American monitoring studies and from different websites)

Methods

Research databases including Google Scholar, PubMed, EBSCO, Springer, Science Direct, and NIH database were searched using following keywords including '*pharmaceutical wastes, pharmacological action of drug residue, drug waste in water, drug residue in environment, antibiotics in water, illicit drug substances, pharmaceutical waste disposal, wastewater treatment, and human health'*. All relevant searches were done using books and scientific literature from the databases. The gathered information was examined, discussed over, and summarized. For this narrative review, literature only written in the English language were chosen and included in the analysis. Preprint and conference papers were excluded from review analysis. No formal bias assessment tool was applied to this narrative literature review.

Results and discussion

Sources and types of waste from pharmaceuticals: Through production procedures, ingestion, and inappropriate disposal, pharmaceuticals and their byproducts usually enter the environment.[18] Although there is a lack of quantitative data about the precise percentage that various sources contribute to total pharmaceutical pollution due to regional and pharmaceutical compound variations, moreover, important sources include the following:

Pharmaceutical: Industrial chemical residues used to make medicines and active pharmaceutical ingredients (APIs) can pollute the water cycle through indirect discharges like leaks and direct discharges like industrial effluent. While isolated hotspots may still develop, this source is usually thought to be minor worldwide in comparison to the quantities expelled by patients.[19] The first research revealing extremely high pharmaceutical emissions from Indian medicine manufacturing facilities were released in 2007. With an estimated total daily emission of 44 kg, ciprofloxacin is the most involved antibiotic. This amount is sufficient to treat nearly 44,000 people of Sweden over the course of five days. High levels of APIs linked to factory discharges were documented by similar studies conducted in the USA, Europe, and other Asian countries, such as China, Korea, Taiwan, and Pakistan. Despite these studies, there is still a great deal of incoherence in the data about pharmaceutical industrial pollution.[20]

Veterinary: Environmental pollution is largely caused by pharmaceuticals used in agriculture, aquaculture, and veterinary care. Like humans, between 30% and 90% of the medications that animals ingest are eliminated in their feces either unaltered or as metabolites. Veterinary drugs are discharged straight into water bodies in aquaculture. These compounds are also capable of entering the soil, surface water, and groundwater due to the common practice of recycling animal manure.[19] To produce precise quantitative statistics on the contribution of veterinary medications to total environmental pollution, extensive study is necessary.

Hospital: Long-term care homes, hospitals, and other healthcare facilities are major contributors to pharmaceutical materials getting into sewage systems. Their total contribution to pharmaceutical pollution in wastewater varies according on the type of medicine, despite the fact that the pharmaceutical load in wastewater is huge. According to a research by the European Union (EU), 20% of pharmaceutical residues in wastewater come from hospitals in Europe.[21] According to studies done in Sweden and Norway, the majority of medications contribute between 1% and 3%. This is mostly due to the fact that increasingly complicated care is being given in private homes and that a substantial portion of hospital prescription drugs are used at home.[22] Hospitals in the Copenhagen area of Denmark are responsible for around 24% of the total antibiotic burden. Even more important may be the role of several hospital-specific drugs, such as contrast agents, cytostatics, and endocrine therapies.[23]

Household: Pharmaceuticals are a major source of domestic environmental pollution since between 30 and 90 percent of pharmaceuticals taken orally are eliminated by people and end up in aquatic systems, sometimes being fully removed by without treatment procedures. Furthermore, medications included in creams and ointments may be washed off the skin, which increases the likelihood that they may be found in wastewater.[23,24] For instance, it is estimated that residential wastewater in Europe accounts for almost 80% of pharmaceutical residue in the environment, mostly from human urine and the disposal of unused medications.[21]

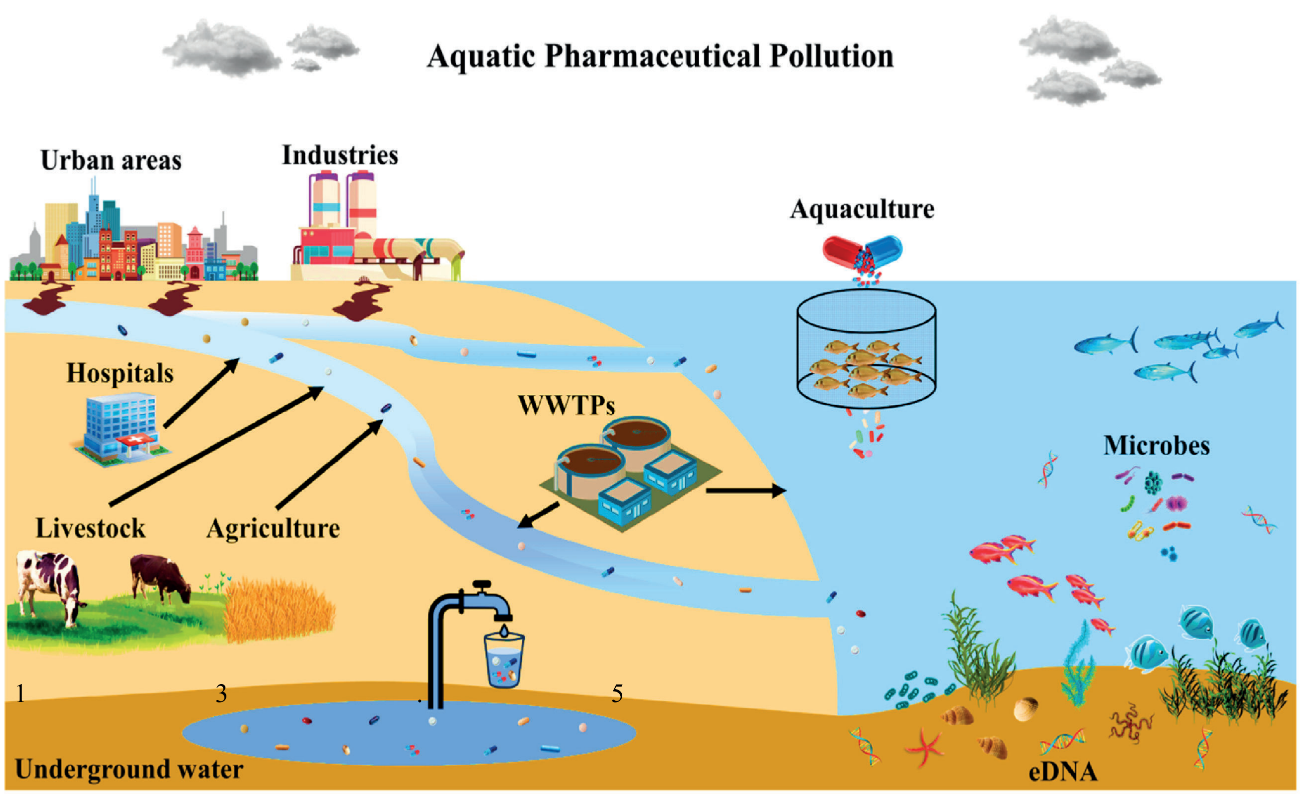

Figure 1. Pharmaceuticals' sources in the aquatic environment, adapted from [32] under CC BY license

Table 2. Common pharmaceutical drugs and residues found in environment

Drug Class	Drug	Toxicity	Reference
Antibiotic	Amoxicillin (AMX)	Promotes antibiotic-resistant bacteria; toxic to aquatic microorganisms at high concentrations	[33]
	Ciprofloxacin (CPF)	Highly toxic to algae and bacteria; promotes antimicrobial resistance	[34]
	Tetracycline (TTC)	Inhibits algal growth; affects microbial communities	[34]
	Erythromycin (EMC)	Very toxic to cyanobacteria and algae; disrupts aquatic microbial ecosystems	[34]
	Chloramphenicol(CMC)	Toxic to aquatic bacteria and fish embryos; may affect hematopoietic systems	[35]
	Sulfamethoxazole(SFM)	Antibiotic resistance development	[36]
Beta blocker	Propranolol (PRO)	Affects physiology of fish, reproduction, and behavior	[37]
	Atenolol (ATE)	Chronic cardiovascular effects in fish and aquatic invertebrates	[35]
	Metoprolol (MET)	×	[35]
NSAIDs	Diclofenac (DIC)	Highly toxic to aquatic animals	[36]
	Mefenamic acid (MA)	-	[34]
	Acetaminophen (ACE)	Low acute toxicity but chronic exposure may damage fish liver and kidneys	[33]
Anti-hypertensive	Amlodipine (AML)	Developmental negative effects on aquatic organisms	[35]
	Chlorothiazide (CTZ)	Chronic growth inhibition of aquatic invertibrates	[38]
	Nifedipine (NIF)	Phototoxicity; affects fish embryos and aquatic invertebrates	[39]
	Perindopril (PER)	-	[39]
Hormones	Norethindrone (NOE)	Affects fish reproduction	[40]
	Cyproterone (CYP)	Affects fish endocrine system	[24]
	Norgestrol (NOG)	Highly bioaccumulative; endocrine disruption at very low concentrations	[41]
	Progesterone (PG)	Alters reproduction and endocrine function in aquatic organisms	[41]
Anti-hyperglycemic	Metformin (MET)	Low bioaccumulation	[35]
	Glibenclamide (GLB)	Metabolic toxicity in fish	[42]
		-	[42]
Anti-inflammatory	Dexamethasone (DEX)	Immunosuppression and endocrine disruption in aquatic organisms	[40]
	Ibuprofen	Causes oxidative stress, reproductive toxicity, and developmental effects in fish and invertebrates	-

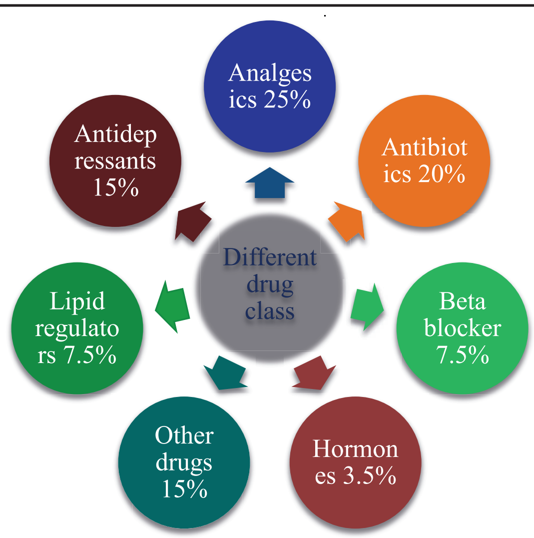

Figure 2. Apaproximate percentage of pharmaceutical load in water body

Impact of pharmaceuticals on microorganism: Numerous sources, such as untreated water used for cleaning, irrigation, and domestic tasks, allows pharmaceutical pollutants to reach aquatic systems. As a result, germs that are resistant to antibiotics grow fast. Although pharmaceuticals are mostly made to cure people and animals, they can also have the same pharmaco-dynamic effects on species with comparable biological traits when they enter an aquatic environment.[43] Important activities in aquatic environments, such as organic breakdown, nitrogen fixation, and denitrification, are usually controlled by certain bacterial species. Antibiotics have the ability to interfere with each of these processes. These bacterial groups may be inhibited or have their activity changed by antibiotics, which might disrupt organic matter breakdown, nitrogen cycle, and other vital ecological processes. Water quality, nutrient dynamics, and the wellbeing of aquatic creatures may all be impacted (Figure

3), as well as the general stability and functionality of the aquatic environment.[44,45] The cycling of nutrients and other essential functions that sustain aquatic food webs depend heavily on microbes. Whole ecosystems may be affected in a cascade of ways if these communities are damaged (Table 3). Sub-therapeutic and chronic drug concentrations can both function as environmental stresses that hinder ability of bacteria to survive and perform metabolic processes.[44,46]

Table 3. Impact of pharmaceutical substances in water on microorganisms

Pharmaceutical substance	Microorganism impact	Mechanism of action
Antibiotics (e.g., tetracycline, ciprofloxacin, amoxicillin)	Development of antibiotic resistance in bacteria	Selective pressure favors resistant strains; horizontal gene transfer
Chemotherapy drugs (e.g., cyclophosphamide, methotrexate)	Cytotoxic effect on bacteria and fungi	DNA damage and inhibition of cell division
Antidepressants (e.g., fluoxetine, sertraline)	Alters microbial diversity and biofilm formation	Interferes with serotonin pathways that impact quorum sensing in microorganisms
Antifungals (e.g., fluconazole, ketoconazole)	Inhibits aquatic fungal communities	Disruption of ergosterol synthesis in fungal membranes
Antivirals (e.g., acyclovir, oseltamivir)	Changes the harmony of the viral community in water	Inhibition of viral DNA/RNA replication enzymes

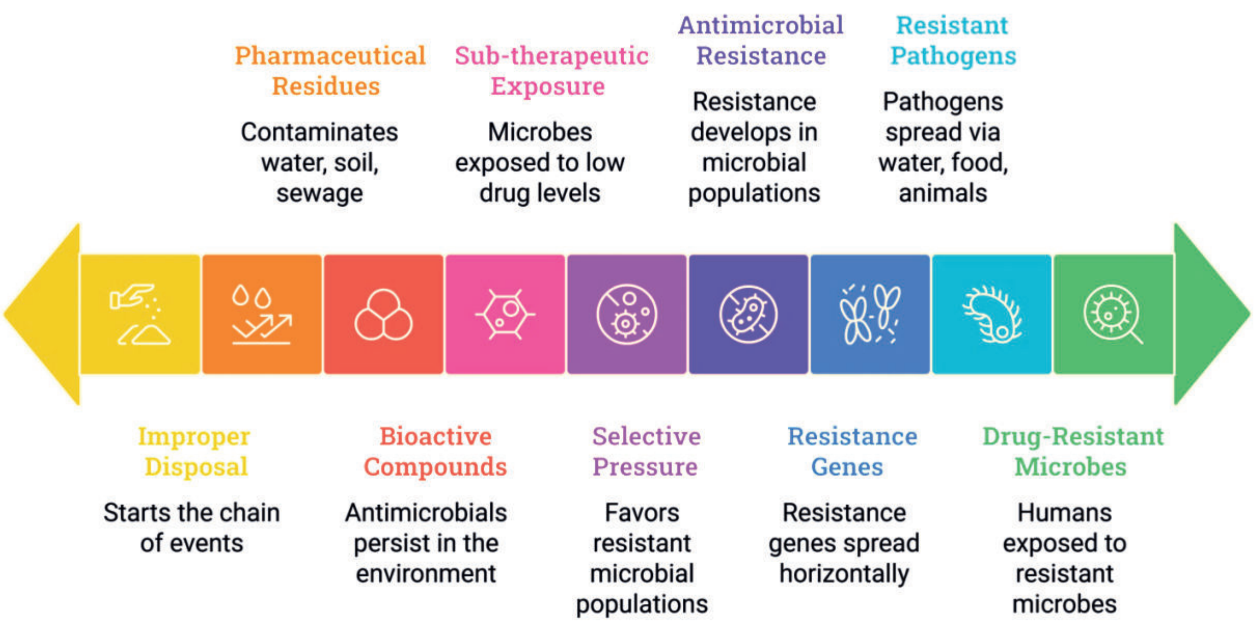

Figure 3. Impact of wasted drugs on microbes and ultimate health consequences

A few broad examples include Naproxen produces chronic toxicity to phytoplankton and 690 mg/dm^3 of acute toxicity to Oncorhynchus mykiss species and 12.3 mg/dm^3 to cyanobacteria, depending on the nature of organism. Since diclofenac exhibits acute toxicity among non-steroidal anti-inflammatory medicines (NSAIDs), it puts a lot of strain on aquatic animals, including fish. For fish, diclofenac's "median effective concentration" is 14.5 mg/dm^3, but for phytoplankton, it is 22.43 mg/dm^3. Diclofenac has long-term toxicity to phytoplankton. Chronic diclofenac exposure to Oncorhynchus mykiss affects kidneys and gills. Carbamazepine and diclofenac may be harmful to aquatic microorganisms.[47-49]

The ecological harm that illicit drug substances do to water systems: As illegal narcotics are produced and used in large quantities, they are continuously released into the water system.[50] Examining the prevalence of "illegal drugs and their metabolites" from an eco-toxicological perspective is necessary since research has shown that they may have detrimental effects on the aquatic system.[51] There are few and unmethodical investigations on the ecological harm of illicit narcotics in "scientific journalism." Information about the ecotoxicity of cocaine, morphine, and amphetamine to marine life is limited. Amphetamine sulfate's toxicity to recently isolated Daphnia and *Oncorhynchus mykiss* was investigated. The results of the Multicenter Evaluation of in-vitro cytotoxicity revealed that the 50 compounds employed were relatively more hazardous.[52] A problem resulting from a mutation in many genes that affect dopaminergic transmission in the brain and retina was discovered during the behavioral screening of cocaine sensitivity in Danio Renio.[53] According to a study on the cyto-genotoxic effects of cocaine on *Dreissena polymorpha*, there was a significant increase in micronucleated cells, apoptosis, and primary DNA damage.[54] By monitoring the change in plasma morphine content over a 100-hour period, the pharmacokinetics of morphine entering seawater-acclimated *Oncorhynchus mykiss* and pseudopleuronectes americanus were described.[55] Therefore, based on the knowledge currently available, it is reasonable to assume that the stimulatory or inhibitory effects of illicit substances vary depending on the molecule and the organism being tested.

Nanomaterials in aquatic system: In various industries, nanomaterials are becoming an increasingly significant portion of global material flows that significantly impact human life and well-being.[56] The pharmaceutical and medical industries, which include nanopharmaceuticals, nanobiomaterials, and nanootheranostics, among others, are the area where nanomaterials are used. Given how widely and extensively these materials are utilized, it is imperative to consider what will happen to the increasing quantity of used nanoparticles found in the environment.[57] The most prevalent nanomaterials in the worldwide market in terms of mass flow were silica, titania, alumina, and iron and zinc oxides. These materials were mostly used in paint, optoelectronics, cosmeceuticals, energy, catalysts, and environmental applications. According to estimates, between 63 and 91 percent of the world's output of nanoparticles, which totaled weighted between 260,000 and 309,000 metric tons, was released into the environment in 2010 and may have found its way into freshwater and wastewater sources.[58,59]

Table 4. Nanopharmaceuticals in aquatic systems with their potential effects

Type of nano-pharmaceuticals	Source	Entry into aquatic system	Environmental fate	Key concerns
Silver nanoparticles (AgNPs)	Antimicrobial agents, wound dressings, coatings	Wastewater discharge, hospital effluents	Can aggregate, dissolve into Ag^z ions	Bioaccumulation and microorganism toxicity
Lipid-based nanocarriers (liposomes, solid lipid nanoparticles)	Drug delivery for cancer, infections	Excretion from patients, medical waste into sewage	Biodegradable, but can interact with organic matter	May affect nutrient cycle in water
Polymeric nanoparticles (PLGA, PEGylated NPs)	From controlled drug delivery release	Medical waste into water	Degradable into lactic/glycolic acid	Not clearly known but may have long term effect on aquatic system
Carbon nanotubes (CNTs)	Drug delivery, biosensors	Industrial and research waste	Persistent, hydrophobic, adsorb pollutants	High amount of persistence, bioaccumulation
Iron oxide nanoparticles	MRI contrast agents, drug delivery	Medical wastewater	Settle in sediments, can dissolve to Fe ions	Sediment accumulation, iron overload risk
Dendrimers	Drug delivery	Hospital effluents	Cationic charge interacts with membranes	High reactivity, cytotoxicity risk

As a result, the environmental presence of nanoparticles and their possible effects on living things and human health are prevalent (Table 4). These nanoparticles have been shown to have ecotoxicological effects on microorganisms, plants, invertebrates, and fish. They can also partially aggregate, form transient complexes with solid particles in suspensions, precipitate as sediments, accumulate in organisms, and enter fresh water resources before entering food materials. The physicochemical properties of nanoparticles and the features of the surrounding environment have a significant impact on their destiny.[60,61] Our understanding about the possible health impacts of nanoparticles in water resources is poor, despite the fact that existing toxicity data indicates a minimal environmental risk of nanoparticles to both human health and the environment.[62] This issue necessitates ongoing study to further our knowledge in a variety of domains, such as ecotoxicology, nanotoxicology, environmental fate and transport mechanisms, analytical measurement, and physicochemical characterization.[63-64]

Pharmaceutical waste entering into water and food cycle: Wastewater may include numerous pathogenic bacteria, chemical and pharmaceutical residues, and other hazardous chemical. Salts, metals, metalloids, leftover medications, organic chemicals, endocrine disrupting substances, and active residues of personal care items are a few examples of the chemical pollutants.[65] The amount of wastewater treatment, pollutant characteristics, human exposure, and local risk factors are some of the elements that affect the nature and seriousness of health concerns. While chemical and pharmaceutical contamination is the greatest health issue in high-income and developing nations, infectious outbreaks continue to be the biggest worry in low-income nations.[66] For this, several developing countries deal with both kinds of health issues. The majority of pharmaceutical manufacturing facilities and academic research institutions are situated within the city, where they focus on the synthesis of novel chemicals, medicines, and nanomaterials. However, untreated or partially treated effluent that contains various chemicals and heavy metals could end up in certain nearby drinking water wells. The problem becomes more pressing when we know that the majority of cities lack a thorough wastewater treatment plan and that untreated wastewater may be utilized to irrigate and cultivate crops for direct human consumption.[67,68] A glimpse about pharmaceutical waste in water, and its health impact on both human and aquatic life depicted in (Table 5); (Figure 4).

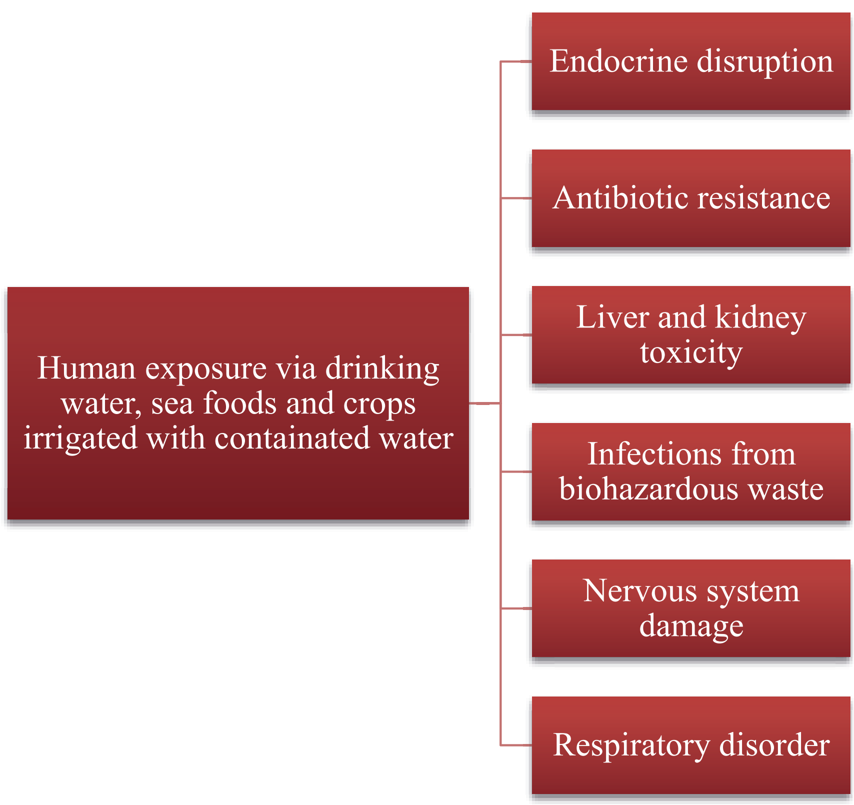

Figure 4. *Pharmaceutical waste residue causes different harmful health impact*

Table 5. Pharmaceutical waste in water and its health impact

Source of Pharmaceutical Waste	Examples of Contaminants	Pathway into Aquatic System	Impact on Aquatic Life	Impact on Human Health
Hospital and clinical waste	Analgesics, cytotoxic medications, and antibiotics	Improper disposal, untreated hospital effluents	Antibiotic resistance in microbes, toxic effects on fish	Risk of mutagenic, carcinogenic, or antibiotic resistance
Household disposal (flushing, trash)	Painkillers, antidepressants, contraceptives	Domestic wastewater, landfill leachate	Fish hormone disruption (feminization, decreased fertility)	Hormonal imbalance, reproductive issues
Pharmaceutical manufacturing units	Bulk drugs, solvents, APIs (active pharmaceutical ingredients)	Industrial discharge into rivers and lakes	Reduced biodiversity and bioaccumulation in aquatic species	Chronic toxicity, organ damage upon long-term exposure
Agricultural use (veterinary drugs, aquaculture)	Antibiotics, antiparasitics, growth promoters	Runoff from farms and aquaculture ponds	Alters microbial ecology, toxic to aquatic invertebrates	Indirect exposure via food chain, antibiotic resistance
Ineffective treatment of waste water	Mixture of various drugs (NSAIDs, beta-blockers, hormones)	Incomplete removal during sewage treatment	Accumulation in sediments, affects fish behavior and physiology	Low-dose chronic exposure, possible neurological and endocrine effects

In Poland, high antibiotic use not only exacerbates environmental issues but also poses serious health dangers to the general population. The difficulties wastewater treatment plants face and the ensuing soil pollution emphasize how urgently comprehensive steps are needed to address antibiotic-related problems and guarantee the preservation of the environment and public health.[69] There are risks to the environment and human health when farm animals and fish are given subtherapeutic dosages of antibiotics to speed up their growth. Through a variety of routes, including the application of manure to land and airborne dispersion, this practice releases antibiotics that are difficult to break down into the environment. Animal waste adds to the environmental concentration of active antibiotic metabolites, raising worries about food antibiotic residues, antibiotic-resistant bacterial growth, and aquatic ecosystem damage. Responsible antibiotic management in agriculture is necessary to address these issues and reduce negative impacts on the environment and public health.[70] The levels of several antibiotics, including ciprofloxacin, norfloxacin, ofloxacin, erythromycin, and trimethoprim/sulfamethoxazole, range from nanograms per liter (ng/L) to (ig/L) in hospital wastewater from major cities in China, Malaysia, Vietnam, and other regions. These concentrations are largely comparable to those found in India and some European countries, though some extreme values have been reported in pharmaceutical effluents in Vietnam. The high rates of manufacture and environmental persistence of these medications are the reasons for their prevalence. Because of the proliferation of antibiotic residues and the emergence of antibiotic resistance, such pervasive pollution raises questions regarding the possible effects on the environment and human health.[71]

Human health implications: One of the most significant health concerns is the development of antimicrobial resistance (AMR) in human. Antibiotics such as amoxicillin, ciprofloxacin, tetracycline, erythromycin, chloramphenicol, and sulfamethoxazole persist in aquatic environments and exert selective pressure on environmental microorganisms. This promotes the emergence and spread of antibiotic-resistant bacteria and resistance genes, making bacterial infections increasingly difficult to treat and reducing the effectiveness of life-saving antimicrobial therapies. Non-steroidal anti-inflammatory drugs (NSAIDs), including diclofenac, ibuprofen, mefenamic acid, and acetaminophen, are among the most frequently detected pharmaceutical contaminants worldwide. Excessive exposure to these compounds is associated with gastrointestinal ulceration, renal impairment, hepatotoxicity, and an increased risk of cardiovascular disease.

Antidepressant medications, including citalopram, fluoxetine, paroxetine, sertraline, venlafaxine, and duloxetine, contain psychoactive ingredients that are used to treat mental illness, eating disorders, obsessive-compulsive disorder, panic disorder, and attention-deficit disorder. Modifying the amounts of neurotransmitters in the brain, especially serotonin, dopamine, and norepinephrine, is how these antidepressants work.[72] Cyclophosphamide, an antineoplastic medication, inhibits human granulosa cells' ability to secrete progesterone. Pharmaceuticals in the drinking water system pose a serious risk to the elderly, infants, those with liver or renal disease, and even newborns. As fluorouracil can cross the blood-placenta barrier and have an embryotoxic and teratogenic impact, the presence of anticancer medications in drinking water poses a risk to expectant mothers.[73]

The World Health Organization has identified antibiotic-resistant bacteria as one of the biggest hazards to world health, and antibiotic residues in the environment might encourage the growth of these bacteria. Common illnesses may become incurable due to the spread of antibiotic-resistant strains, which would raise rates of morbidity and death. In addition to increasing healthcare expenses, this issue puts a burden on healthcare systems since doctors are forced to use more costly and less effective treatment choices.[74,75] It is also yet unclear how exposure to drugs affects the body and mind, especially during critical times like pregnancy or early childhood development. There is growing evidence that some drugs might cause behavioral problems, developmental difficulties, and other health problems in children if they are exposed to these medications during pregnancy. Knowing how pharmaceutical waste affects public health over the long run is essential because of the changes in the healthcare system.[76]

Chronic exposure to the adverse effects of pharmaceuticals in drinking water can have significant effects on human health. If a person consumes around two liters of water each day and the concentration of a "pharmaceutical compound in drinking water is 5 ng/dm^3," then the individual consumes reaches nearly 10 ng of this medication every day. This little dosage amounts to 3650 ng annually. This rate would be 255,500 ng if it were multiplied by the average human life expectancy of 70 years. Human health may suffer as a result of this unintentional consumption.[77,78]

Responsibilities of pharmaceutical company to reduce drug waste and public policy: Prescriptions should be optimal, reasonable, and effective in order to lessen the impact of medications on the environment. Otherwise, they will result in a rise in usage and the accumulation of unnecessary drugs.[79] The above-mentioned use and accumulation of medications and other pharmaceutical items may be influenced by several variables. Irrational antibiotic use has the potential to significantly increase the amount of pharmaceutical-induced environmental pollution. Collecting leftover or expired medications from patients is one strategy a pharmacy may take to reduce the environmental effect of pharmaceutical and medical items. Pharmacies are able to get accredited for their waste management operations. Standard operating procedures for gathering patients' unused and expired medications and getting rid of pharmaceutical waste should be their focus.[80,81]

The usage of antibiotics, improper waste disposal, and environmental contamination are all significantly influenced by the knowledge gap among people, particularly in poor nations. Antibiotic abuse has been identified as one of the main causes of antimicrobial resistance. A research was conducted in Lebanon, where 30% of the population uses antibiotics and 50% of the population engages in self-medication. It was discovered that the degree of knowledge, attitudes, and misconceptions around antibiotics contributed to this abuse.[82] Appropriate steps should be taken (**Table 6**) and campaigns should be organized to inform and raise patient knowledge of the appropriate disposal of unwanted or out-of-date medications as well as the proper and responsible use of drugs.

Hospital management: Hospital pharmaceutical management is the organized process of ensuring that patients receive safe, effective, and high-quality medicines when they need them. It covers every stage of the medication-use process, including medicine selection, procurement, storage, distribution, dispensing, administration, and monitoring. Effective hospital pharmaceutical management plays a vital role in reducing the release of pharmaceutical residues into water bodies. By ensuring the rational use of medicines, hospitals minimize unnecessary prescribing, dispensing, and drug wastage, thereby reducing the amount of unused pharmaceuticals that may enter wastewater systems.[83]

Proper inventory management is essential to maintain medicine quality and prevent shortages or expiration. Hospital pharmacists also contribute by promoting antimicrobial stewardship and rational prescribing practices, which can reduce excessive consumption of antibiotics and lower the release of active pharmaceutical ingredients into wastewater. Clinical pharmacists also monitor treatment outcomes, identify and report adverse drug reactions (ADRs), counsel patients on the proper use of medicines, and promote evidence-based, rational prescribing.[84-86]. Hospitals can further reduce pharmaceutical pollution by segregating pharmaceutical waste from general waste, implementing wastewater pretreatment systems, and adopting advanced treatment technologies such as activated carbon adsorption, ozonation, membrane filtration, and advanced oxidation processes to remove pharmaceutical residues before wastewater is discharged into the environment.

Proper procurement and inventory management help to prevent overstocking and medicine expiration. Safe collection and disposal of expired, unused, and contaminated medicines through approved pharmaceutical waste management systems prevent their direct discharge into sinks, toilets, or municipal waste streams.

Table 6. Steps needed to reduce pharmaceutical waste in water sources

Serial no.	Steps	Focus Area	Description	Practice Field
1	Proper disposal programs	Public awareness and infrastructure	Encourage safe disposal instead of flushing or open dumping	Medicine take-back programs, pharmacy drop-off bins, hospital collection points
2	Green Pharmacy	Drug design properly	Make less harmful or biodegradable medications	Designing medicine formulations that are environmentally friendly and break down more quickly
3	Hospital and Industry Waste Management	Source control	Prevent pharmaceutical factories and healthcare facilities from directly releasing their trash	On-site pre-treatment, segregation of chemical/biological waste
4	Regulation and Policy Enforcement	Governance and monitoring	Establish stricter guidelines for the disposal of pharmaceutical waste and environmental monitoring	National pharmaceutical disposal guidelines, environmental quality standards
5	Recycling and Recovery	Resource management	Recovery of useful chemicals or energy from pharmaceutical waste	Technologies for recycling pharmaceuticals and energy recovery from combustion
6	Public Awareness	Community engagement	Educate individuals on safe practices and the dangers of pharmaceutical pollution	Campaigns in schools, media awareness programs, community workshops
7	Wastewater Treatment Upgrades	Technological implementation	Improve treatment plants to remove pharmaceutical residues	Advanced oxidation, membrane filtration, activated carbon adsorption
8	Rational Use of Drug	Prescription	Reduce medication abuse and unnecessary over-prescriptions to prevent the buildup of unused drugs	Appropriate clinical guidelines, electronic prescription monitoring, patient education

Conclusion:

The problem of pharmaceutical waste in water is complicated and has significant effects on the environment and human health. There is a long-term concern since current wastewater treatment technology cannot completely remove pharmaceutical residues. Reducing pharmaceutical contamination in aquatic systems requires a multifaceted strategy that includes increased regulation, technical advancement, and public involvement. A collaborative action plan by government agencies, academic institutions, and the pharmaceutical sector and a systematic approach are necessary for effective health risk management.

Conflicts of interest: The author declares that there is no conflict of interest.

Acknowledgement: None.

Financial disclosure: This study did not receive any targeted funding from any public, private, or non-profit organizations.

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