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A Review of Pharmaceuticals in Aquatic Environments Risk Assessment and Ecological Impacts

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Abstract

Pharmaceuticals are enduring, active compounds that, when released into the natural surroundings, impact the equilibrium of ecosystems. The rising prevalence of drugs and their transformation byproducts in the surroundings has garnered increased attention. Numerous commonly prescribed medications, particularly analgesics and antimicrobial agents, are employed in quantities comparable to agricultural pesticides yet are not subjected to equivalent environmental risk assessments. The environmental destiny and actions of pharmaceuticals necessitate more investigation. People and veterinary medications and their substances are disseminated in the environment through many pathways. Drugs and their metabolites have been documented in underground and groundwater, potable water, particles, soil, wastewater, drainage waste, and animal tissues. The paper addresses concerns regarding the disposition and effects of medicines in the surroundings and in handling sewage, ecological toxicology, and risk assessment procedures.

Keywords:

Pharmaceuticals, aquatic environments, risk assessment, marine.

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Introduction

The contamination of aquatic ecosystems has emerged as a global issue, garnering public concern and compelling researchers and authorities to intensify their endeavors to avert further environmental deterioration (Bashir et al., 2020). A range of contaminants, including herbicides, heavy metallic ones, polycyclic fragrant hydrocarbons, and, more lately, microplastic fragments and pharmaceuticals, infiltrate aquatic ecosystems through human actions, jeopardizing the well-being of flora, fauna, and people due to their immediate danger and the possibility of chronic buildup. Physical, psychological, and biological cleanup techniques are advancing to address this issue. Phytoremediation, which utilizes macro - and micro-algae for rehabilitation, appears viable because of its cost-effectiveness, environmental sustainability, and eco-friendliness (Kafle et al., 2022). Phytoremediation is effective for extracting heavy metals from sewage, and current research is extensively exploring the capacity of algae to eliminate additional anthropogenic pollutants, including pharmaceuticals (Singh & Gurudiwan, 2024).

Pharmaceuticals are formulated to exhibit a particular advantageous mechanism of action in either people or animals and encompass any substance containing a naturally occurring compound utilized for (i) the assessment, therapy, or avoidance of illnesses or health conditions in human healthcare; (ii) the improvement of skin health in the personal care sector; or (iii) the management of intestinal illnesses to improve livestock productivity during growth and ensure long-term viability in the agricultural industry (Khan et al., 2024). Over 3k medications have been authorized in the European Union only. Some different kinds of pharmaceuticals, such as antibiotics, lipid metabolic regulators, hormonal representatives, anti-epileptic substances, and β-blockers, Non-Steroidal Anti-Inflammatory Substances (NSAIDs) (Bindu et al., 2020), are the power source of the most frequently used medications employed to mitigate inflammation and alleviate pain due to their anti-inflammatory, analgesics and antibiotics characteristics. Substantial quantities of these chemicals are ingested daily owing to their extensive accessibility in several over-the-counter medicinal formulations. The pharmaceutical business is a crucial and consistently expanding sector globally, with rising revenues over the past decade (Milanesi et al., 2020). The escalating environmental pollution by medicines is attributable to heightened use and the inadequacies of standard wastewater procedures, which do not effectively eliminate several pharmaceutical chemicals (Đurić & Djuric, 2024).

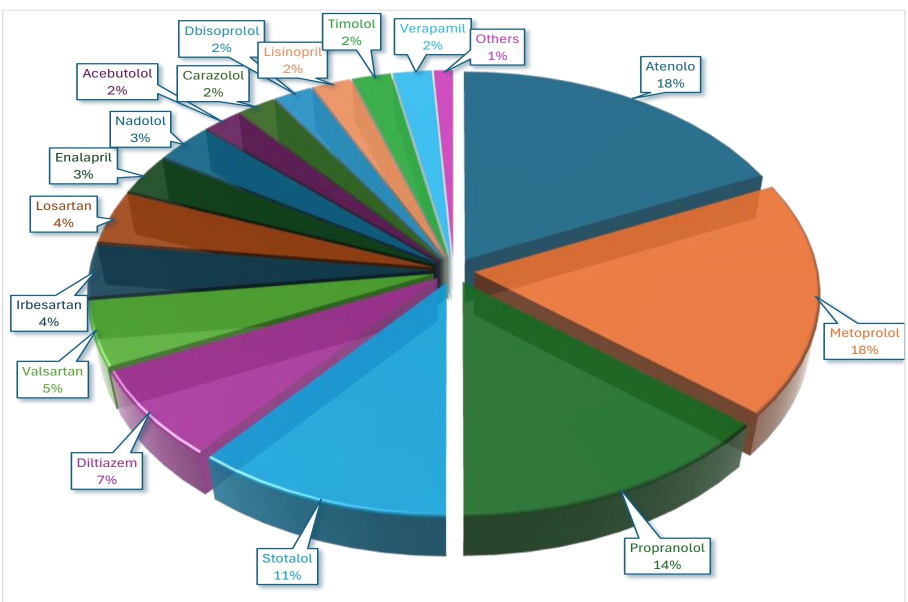

Figure 1. Scientific circle analysis of chemicals

Figure 1 indicates that scientific circles have predominantly focused on beta-blockers, including atenolol, metoprolol, propranolol, and sotalol. Studies identify the fast expansion of the pharmaceutical sector, advancements in agriculture, and inadequate removal of beta-blockers from sewage as contributing causes to the occurrence of these chemicals in aquatic environments (Samal et al., 2022). The medications within this therapeutic category are among the most extensively utilized drugs globally (Balagopal, 2019).

Therefore, a study that offers a survey of sources, a synopsis, and a critical assessment of the existing information regarding pharmaceuticals in the surroundings, together with potential restoration strategies, is necessary. The objectives of this overview are: (i) to investigate the prevalence of pharmaceuticals as pollutants of recent interest in wastewater, groundwater, and beverages, along with their toxicology to non-target beings worldwide, and to outline standard wastewater treatments that are largely ineffective against pharmaceutical pollutants; (ii) to introduce various algal-based methods for eliminating contaminants as cost-effective alternatives to traditional wastewater therapies; (iii) to delineate various kinds of algae farms and the variables that significantly affect contaminant removal effectiveness; and (iv) to discuss the issues and benefits of phytoremediation.

Background

The extensive utilization of medications results in their ongoing release into the surroundings. The principal sources of pharmaceutical pollution in wastewater worldwide are (i) urban home effluents, (ii) medical pollutants, (iii) animal agriculture, including the excretion of medicines and their byproducts, and (iv) pharmaceutical manufacturing (Ramesh et al., 2023). Universities and healthcare facilities significantly contribute medicines to water waste through patient medication excretion and laboratories, diagnosis, and research operations. The overall concentration of medicines in urban wastewater is influenced by several factors, including the administered dosage, the proportion excreted, and the chemical makeup of the individual component. The primary pathways for pharmaceuticals to enter terrestrial agricultural land include veterinary medication usage in livestock, improper disposal of old medications, and feed components containing various pharmaceuticals (Krzemiński et al., 2020). The use of antibiotics in agriculture is constrained and governed in several nations. Antibiotics can still be utilized to address animal diseases via veterinarian prescriptions. Pharmaceutical production facilities are particularly concerning because of significantly elevated efflux levels and point source pollution, particularly in underdeveloped nations where adequate wastewater management is deficient.

After medicines enter wastewater from the above sources, they migrate into aquatic environments such as surface water (lakes, rivers, and oceans), groundwater, debris, soil, and water for drinking. The presence of medicines in aquatic environments differs by region and is influenced by patterns of drug intake. The utilization of medications is contingent upon seasonal illness surges. Antibiotic usage stemming from diseases leads to heightened discharges into sewage and waterways throughout the fall and winter (Chinemerem Nwobodo et al., 2022). Likewise, the intake of antihistamines rises periodically in response to pollen production and ensuing allergy management. The current epidemic has led to heightened pharmaceutical consumption, causing a significant rise in drug concentrations in aquatic environments. Due to the pandemic's volatility and unforeseen mutations, more data is needed about this matter (Alamer & Shadadi, 2023; Farajizadeh & Bakhsh, 2015).

Pharmaceuticals pose an environmental hazard because they substantially impact several non-target aquatic creatures with analogous biological tasks and sensors (Świacka et al., 2021). The danger posed by these chemicals in water correlates directly with their unaltered state; their parent molecules undergo further transformation through both abiotic and biotic mechanisms (microbiological alteration, hydrolysis, or photosynthesis) in natural water bodies or during wastewater treatments (Talebi Fard & Leung, 2011).

Studies indicate that medications demonstrate both short-term (acute) toxicity and necessitate consideration of long-term (chronic) consumption (Denny, 2024). Acute toxicology refers to the effects caused by a single exposure or repeated exposures within a brief timeframe, typically manifesting as a deadly outcome (mortality or immobility). Chronic toxicology refers to the emergence of detrimental consequences due to extended and recurrent exposure to obstacles, typically manifesting as sub-lethal outcomes like growth suppression, structural or biochemical modifications, or behavioral disturbances.

New pollutants encompass several categories of molecules, including medicines, personal care items, gasoline ingredients, hormone disruptors, and illegal narcotics (Sudarsan et al., 2024). Pharmaceuticals are possibly hazardous compounds lacking regulation criteria identified in surroundings and natural waterways for a brief duration. They must be observed due to their perhaps harmful effects on non-target species. Tracking medicines is intricate due to their diverse, active chemical compositions, their varied effects on living creatures, and the absence of terrestrial toxicity information.

Ecological Impacts

In aquatic environments (freshwater and ocean), many processes govern the accumulation of active chemicals. Among the most fundamental techniques, abiotic transformation techniques include ultraviolet (UV) light deterioration, sorption, hydrolysis, sedimentation solubility, and anaerobic and anaerobic decomposition. The effectiveness of the methods is determined based on the properties and makeup of the substance utilized in the medicine and the environmental conditions (Ahmed et al., 2022). Aerobic and adiabatic biodegradation effectively removes medication from contaminated water sources. Further studies have revealed that diclofenac biodegrades within 10 days after being absorbed into muck. Sedimentation, breakdown, and photosynthesis facilitate drug changes in wastewater or water filtration facilities and, occasionally, in surface water.

Direct and indirect photosynthesis is a principal method for transforming pharmacological microcontaminants in water bodies. Principal photolysis occurs due to direct exposure to sunlight, whereas natural photosensitive compounds are essential for secondary photolysis.

Three primary possible outcomes categorize pharmaceuticals:

- As demonstrated with aspirin, the compound is formed from minerals in water and carbon-carbon monoxide.
- The chemicals undergo metabolism but remain in water-soluble kinds of the parent material, allowing them to traverse wastewater therapy facilities and ultimately enter receiving water organizations, potentially affecting aquatic living things if the compounds exhibit biological activity.
- The polymers are lipid-soluble and exhibit slow degradation, resulting in a portion retained in the sewage.

If the sludge is applied to agricultural areas, the substances inside it will influence the development of several microorganisms. The substances utilized in the manufacture of medicinal medications and growth stimulants in the farming of animals are likely to be collected and incorporated into the waste of animals, eventually ending up in dung.

Over the decades, aquatic life has been associated with over 300 distinct pharmaceuticals at quantities varying from trace to considerable levels. As medications are perpetually discharged into the atmosphere, several chemicals and their byproducts will likely remain available to animals and people throughout their lifespan. In terrestrial and aquatic ecosystems, it is plausible that medications will impact non-target creatures.

Certain medications have been linked to detrimental impacts on aquatic environments and have demonstrated distinct negative impacts on human well-being (Narwal et al., 2023). Despite their detection at very minor amounts with little toxic effects, it has been proven that several drugs, including both synthetic and endogenous hormone goods, pose considerable risks to the aquatic ecosystem. Moreover, pharmaceutical chemicals present in both ground and surface water have been identified and detected as a result of the direct or indirect impact of sewage. These pollutants have been documented in fish and algae in varied quantities globally.

Significant apprehension surrounds the potential accessibility, bioaccumulation, and durability of released medications. Moreover, the release of drugs together raises major worries as the aggregate health and ecological impacts of these substances have long been uncertain. Besides the possible environmental hazards, the prolonged ingestion of waters with trace levels of medicines impacts the wellness of humans. The concentrations of chemical substances in potable water are far lower than those utilized in therapeutic applications; hence, the toxicity limits for most pharmaceutical leftovers remain undefined.

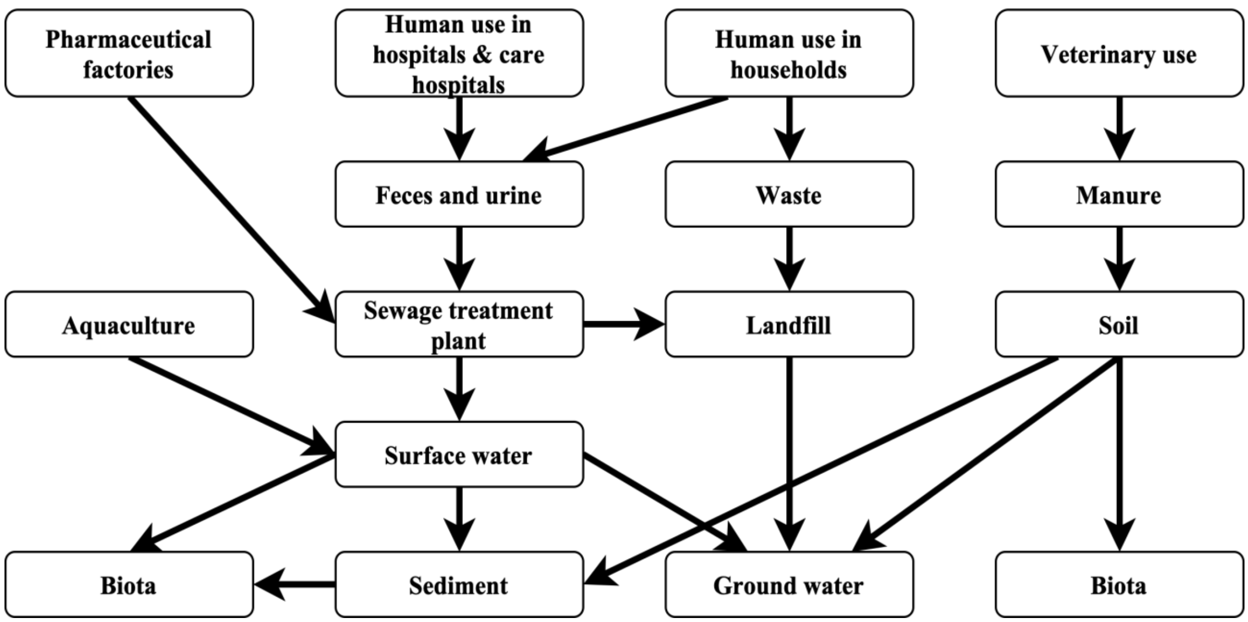

Figure 2. Pharmaceutical processing

About 180 pharmaceuticals have been documented from wastewater processing facilities, sludges, subsurface, and freshwater globally Figure 2. Pharmacological chemicals have been identified and measured in distant Arctic regions (Staszak et al., 2022). The information gathered on the mean levels of medication across various ecological sections and nations indicate that psychoactive and controlled substances, including tramadol, hydrocodone or amphetamine, heroin (benzoylecgonine), opiates, and methadone, have only recently been detected in exterior and wastewater. Periodic and seasonal changes were assessed, revealing swings in paraxanthine, cocaine, amphetamines, and nicotine levels, with ingestion estimations derived from the total quantities identified in wastewater.

Risk Assessment

Sweden has been identified as one of the foremost nations with significant concentrations of drug residues in its water resources, attributed in part to the presence of several pharmaceutical institutes. Sweden, home to premier healthcare institutions, has faced significant concerns regarding the harmful effects of pharmaceuticals on aquatic systems and human health for a long time. Most pharmaceuticals for animals detected in surface and groundwater were documented in Sweden from 1987 to 1995.

The total consumption of medicines in Sweden remained around 42 tons of active material annually. In 1986, the administration of antibiotics for growth promotion was prohibited, and its application was restricted solely to veterinarian reasons. In 1998, the expected yearly quantity of antiparasitic medicines was roughly 16 tons. Before excretion via urine, medicinal substances are converted into phase I or II intermediates and interact with the surroundings. Phase I processes predominantly encompass oxidation and hydrolysis; in some instances, the byproducts are more toxic and harmful than the original chemical. Phase II events include combination, typically resulting in the deactivation of molecules.

Effects on Aquatic Ecosystems

The effects of medicinal products on aquatic environments are categorized into two types. According to the nature of the pharmaceutical wastewater derived from the harmful impacts on marine wildlife and According to the breakdown of the pharmaceutical drainage

These encompass the following:

1. Elevated levels of organic substances (alcohols, methanol)
2. Inhibitory and toxic agents (antibiotics)
3. Gradually disintegrating organic chemicals and resistant macromolecules (aromatic substances, chlorine solvents)
4. Soaps and detergents containing surfactants.

Elevated Levels of Organic Materials

- ***Depletion of Oxygen***

Flats are more susceptible to pollution than rivers since rivers possess self-purification processes. In minimal amounts, these wastewater discharges have negligible consequences and are beneficial sources of organic contaminants that contribute nutrients to stream aquatic life. Whenever these pollutants accumulate in substantial quantities, they can cause extensive harm to the environment by diminishing the oxygen levels in water and reducing the light needed for reproduction.

- ***Eutrophication (Algal Proliferation)***

Eutrophication transpires when a water body is too loaded with ammonium and nitrogen components, resulting in increased proliferation of plants and microalgae. Pharmaceutical waste waters comprise organic molecules such as acetone and alcoholic beverages, utilized as solvents and denaturants in denatured alcohol.

- ***Inhibitory and Harmful Substances (Antibiotics)***
    - ***Antimicrobial Resistance***

The release of waste from pharmaceuticals enhances immunity to antibiotics. Pharmaceutical contaminants lead to the rise of resistant microbes. In contrast, the escalating administration and adoption of antimicrobial treatments have led to a surge in pharmaceuticals in clean water, adversely affecting human well-being.

The dumping of active pharmaceutical components into rivers adversely affects bacterial populations and has resulted in medication resistance. Treatment of medications arises via the emergence of resistant bacteria in wastewater, together with potential gene transfers resulting from continuous contact with antimicrobial agents.

- ***Hematological and Endocrine Dysregulations in Fish***

Steroidal drugs, including hormones, glucocorticoids, and testosterone, have been detected in low amounts in aquatic environments. Continuous exposure to artificial estrogen has caused endocrine and metabolic disturbance in fish. This has led to gender equality for male fish subjected to this wastewater. This scenario involves the male fish displaying intersex characteristics and compromised reproductive capabilities. Researchers have clarified that exposure to steroidal estrogen has compromised reproduction in adolescent and male zebrafish. Other instances include feminizing male fish given estrogen, which can substantially affect fish populations.

Oxazepam, a pharmacological agent for anxiety, can affect fish habits in aquatic habitats and markedly disrupt their actions and food intake rates, even at low doses. In addition to the hormonal and hematopoietic impacts on fish in pharmaceutical-contaminated waterways, decreased oxygen levels in these aquatic environments due to pharmaceutical by-products have been identified. The existence of resistant molecules leads to oxygen reduction in an aqueous biocoenosis. The particles of suspended matter impede light from reaching algal and cyanobacteria, which are essential for ecological agriculture. This impacts the wellness of the ecosystem's indigenous plants and wildlife.

Gradually Biodegradable Organic Acids and their Resistant Components

- ***Impairment of Immunological Reactions in Aquatic Wildlife***

These categories of contaminants are designated as immunotoxic or cancerous. They are accountable for the impacts on the immune systems of fish. Extended exposure has been shown to influence fish’s macrophage activity and lymphocyte growth. Immunotoxicological evaluation studies indicate that xenobiotic-induced reduction of natural reactions significantly impacts resistance to pathogens more than the inhibition caused by acquired immune system reactions.

- ***Surfactant-Containing Detergents and Shampoos***

Surfactants are amphiphilic monomers composed of hydrophobic caps and hydrophilic ends. Residual detergents enter wastewater either because they are untreated or neglected due to the limitations of a single treatment method. This means they are dispersed over numerous environments, including water and soil. Surfactants, owing to their distinctive functional characteristics, are widely utilized in the healthcare sector for diverse applications, including the decontamination of equipment post-drug production, enhancement of drug solubility and strength, stabilization of semisolid preparation textures, facilitation of interpreting, and improvement of chemical as well as physical formulations for medicines.

Current Studies and Remedies

Current methodologies for sewage treatment utilize bioremediation methods to effectively address non-degradable chemicals found in sewage, ranging from trace levels to substantial concentrations. One such strategy is using algae biomass for trash breakdown and reuse of water. Microalgae has progressively been seen as an alternative to traditional wastewater treatment methods. This is primarily due to microalgae's capacity to recover fertilizers while reducing costs and lowering the release of greenhouse gases. The efficacy of phytoremediation is contingent upon several conditions, including the kind of algae employed, the properties of the toxicant targeted, pH, temperatures, accessibility to light, oxygen levels, fertilizer supply, moisture, the environment, and salt.

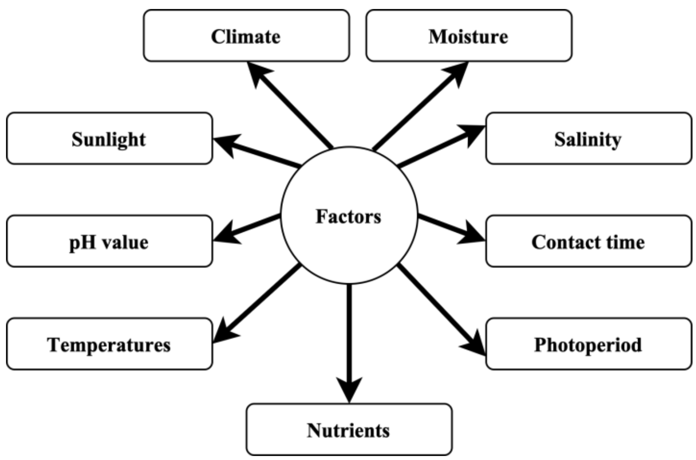

Figure 2. Factors impacting the efficiency

In comparison, microalgae-based systems utilize marginally less power (0.3 kWh/m3), conserving almost half of the power now employed in traditional water treatment by reducing energy expenditure. The capacity of microalgae to produce and develop substantial biomass for integration into sewage treatment plants is contingent upon its photosynthesis effectiveness and the availability of sunlight. Even some obstacles to using this method for water-land reclamation, particularly in Africa, arise because only a few firms have effectively employed this technology globally. This is attributed to the need for more complete knowledge of how the procedure is repeated on a large scale. Despite its various benefits, the method has yet to achieve widespread application. Another problem is that microalgae cultivation requires extended hydrodynamic retention times of 8-11 days. The pursuit of pollutant removal within shorter time frames needs more study.

Environmental Risk Assessments

Medicines in aquatic ecosystems have emerged as a significant environmental issue. Owing to their intricate chemical composition, these substances are not eliminated during wastewater processing, and their unaltered versions or secondary metabolites influence the pollution of ground and surface water. The existence of medicines in the surroundings, even at minimal amounts, presents a possible risk to living creatures and necessitates new regulations concerning their detection, proof of identity, and clearance from aquatic ecosystems. Monitoring is necessary to assess the prevalence of medicines in the surroundings, along with their movement and effects on living creatures. The issue of drug contamination in the surrounding area is complex. It necessitates the collaborative efforts of different research fields, while the pollution of ecological systems by pharmaceuticals compels the development and implementation of successful removal techniques during wastewater treatment.

The presence of some non-steroidal anti-inflammatory medicines in aquatic environments, due to their widespread accessibility, and practical strategies for eliminating them during wastewater processing processes have been previously documented. Ineffective water filtering and urban sewage treatment jeopardize both drinking water consumers and microorganisms inhabiting the consumers of cleansed wastewater. In the long run, inadequate sanitation leads to heightened organism sensitivity to specific drugs, necessitating greater dosages to attain the intended effect. The study provided literature evaluations about the findings of investigations on the precise levels of NSAIDs in wastewater processed and released into the atmosphere.

A collaborative team of scientists from the US and China investigated gemfibrozil's prevalence, behavior, and longevity (a hypolipemic agent) in soil and water environments. Specimens of processed and unprocessed wastewater from drainage treatment facilities and freshwater specimens from regions watered with processed sewage were analyzed. The study indicated that gemfibrozil levels in unprocessed and chemically processed wastewaters ranged from 3.51 to 65.2 µg/L and from 0.07 to 20.5 µg/L. The values in groundwater varied from undetectable levels to 7.12 µg/L. The findings indicated that gemfibrozil in sewage utilized for irrigating agricultural areas can infiltrate aquifers.

The potential risk posed by drugs left in the natural environment has gained significance in policies related to environmental preservation and industries. Identifying drugs in environmental evaluations raised awareness of this issue, particularly within science. The probability of a substance inducing adverse ecological impacts is evaluated throughout the risk assessment procedure.

The existence of pharmaceutical component combinations in the environment necessitates the execution of environmental risk evaluations for these chemicals. Ecological danger evaluations focus on specific medicinal compounds. These substances do not exist in isolation within the surroundings; instead, they are a combination of diverse, active chemicals, their byproducts, and conversion byproducts. Combinations of these chemicals have distinct toxicological consequences relative to individual compounds; nonetheless, understanding this phenomenon still needs to be improved. The issue with tracking pharmaceuticals lies in selecting suitable analytical techniques for specific ecological evaluations. Pharmaceuticals in aquatic environments do not provide acute toxicity risks to living creatures.

The persistent exposure to medications results in toxic consequences, necessitating a deeper evaluation of the dangers and risks of their environmental introduction; the potential impacts on aquatic creatures remain primarily unknown. The application of Quantification Structure-Activity Relationship (QSAR) modeling to forecast the toxicity of pharmacological compounds utilized in healthcare is controversial.

Conclusion

Pharmaceuticals released into the surroundings undergo numerous reactions, resulting in their entire or partial degradation. The methods for reducing pharmaceutical concentrations in the surroundings primarily include biological degradation, breakdown, and photodegradation (either direct or indirect).

The danger of harmful emissions by pharmaceuticals increasingly affects drinking water reports, with recorded quantities ranging from ng/L to µg/L; yet, complete information remains insufficient. Ozonation, improved oxidation techniques, chemical separation techniques, absorption of carbon dioxide, and membrane-based procedures are efficiently employed in the water treatment of pharmaceutical wastes.

Due to their intricate chemical composition, pharmaceuticals are not eliminated during the processing of wastewater, resulting in the presence of their unaltered forms or compounds in both ground and surface water, posing a threat to ecosystems. The existence of drugs in surroundings, even at minimal amounts, poses a possible risk to living species and necessitates additional legislation. Moreover, the surveillance of pharmaceuticals is essential to assess their prevalence and dispersion in surroundings, along with their effects on living creatures.

Author Contributions

All Authors contributed equally.

Conflict of Interest

The authors declared that no conflict of interest.

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