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ECOTOXICOLOGICAL ASSESSMENT OF PHARMACEUTICAL RESIDUES IN AQUATIC AND TERRESTRIAL ECOSYSTEMS

Regeena

Rajputana College of Pharmacy, Bangalore, Karnataka, India

Corresponding Author
Regeena

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ABSTRACT

Pharmaceutical residues have emerged as significant environmental contaminants due to their continuous introduction into aquatic and terrestrial ecosystems through human and veterinary usage, industrial discharge, and improper disposal practices. These biologically active compounds, including antibiotics, analgesics, hormones, and antineoplastic agents, are frequently detected in surface water, groundwater, soil, and sediments at trace concentrations. Despite their low levels, their persistence, bioaccumulation potential, and capacity to induce biological effects raise serious ecotoxicological concerns. In aquatic ecosystems, pharmaceutical residues can affect fish, algae, plankton, and invertebrates, leading to physiological alterations, reproductive dysfunction, and behavioral changes. In terrestrial systems, these contaminants influence soil microbial communities, plant growth, and soil fauna, potentially disrupting ecosystem processes such as nutrient cycling. The development of antimicrobial resistance due to environmental exposure to antibiotics further exacerbates public health risks. Ecotoxicological assessment involves evaluating the toxicity, exposure pathways, and environmental fate of these compounds using laboratory and field-based studies, biomarkers, and predictive modeling approaches. However, challenges remain in assessing the combined effects of complex mixtures and transformation products. This review provides a comprehensive overview of the occurrence, fate, and ecotoxicological effects of pharmaceutical residues in diverse ecosystems, highlighting current assessment methodologies, regulatory frameworks, and mitigation strategies. Understanding these impacts is essential for developing effective environmental management practices and safeguarding ecosystem and human health.

Keywords: Ecotoxicology; Terrestrial ecosystems; Environmental risk assessment; Ecological impact.

INTRODUCTION

The widespread use of pharmaceuticals in human and veterinary medicine has led to the continuous release of drug residues into the environment, making them a class of emerging contaminants of global concern. These residues, including antibiotics, nonsteroidal anti-inflammatory drugs, hormones, antidepressants, and anticancer agents, are introduced into aquatic and terrestrial ecosystems through various pathways such as wastewater discharge, agricultural runoff, and improper disposal. Unlike conventional pollutants, pharmaceutical compounds are designed to exert biological activity at low concentrations, which raises concerns about their potential impact on non-target organisms even at trace levels. In aquatic environments, pharmaceutical residues have been detected in rivers, lakes, and groundwater, where they can affect a wide range of organisms, including fish, algae, and invertebrates[1]. These effects may include endocrine disruption, altered growth and reproduction, and behavioral changes. In terrestrial ecosystems, pharmaceuticals can accumulate in soil through the application of bio solids and manure, influencing soil microbial communities, plant health, and

soil fauna. The persistence and transformation of these compounds in the environment are influenced by factors such as chemical structure, environmental conditions, and microbial activity. Partial degradation can result in the formation of metabolites that may retain or enhance biological activity, complicating toxicity assessments. Bioaccumulation and bio magnification processes can further amplify the ecological impact of these contaminants. Eco toxicological assessment plays a crucial role in understanding the potential risks associated with pharmaceutical residues by evaluating their toxicity, exposure pathways, and environmental fate. This involves the use of laboratory toxicity tests, field studies, biomarkers, and predictive models to assess the effects on various organisms and ecosystems[2]. However, challenges such as the presence of complex mixtures, limited data on chronic exposure, and variability in environmental conditions make risk assessment difficult. Regulatory frameworks for pharmaceutical contaminants are still evolving, and there is a need for standardized methodologies and comprehensive monitoring systems. As pharmaceutical consumption continues to rise globally, there is an urgent need to develop sustainable strategies for managing these contaminants. This review aims to provide a detailed understanding of the Eco toxicological assessment of pharmaceutical residues in aquatic and terrestrial ecosystems, highlighting key challenges and future directions.

Overview of Pharmaceutical Residues in the Environment

Pharmaceutical residues are increasingly recognized as emerging environmental contaminants due to their continuous release and persistence in various ecosystems. These residues include a broad spectrum of compounds such as antibiotics, analgesics, anti-inflammatory drugs, hormones, antiepileptic's, and anticancer agents, which are extensively used in human and veterinary medicine. Unlike traditional pollutants, pharmaceutical compounds are biologically active and specifically designed to interact with molecular targets at low concentrations, making their presence in the environment particularly concerning. They are frequently detected in surface water, groundwater, soil, sediments, and even drinking water, often at trace levels ranging from nomograms to micrograms per liter. The pseudo-persistent nature of these compounds results from their continuous input into the environment, even if they are partially degradable. Environmental conditions such as pH, temperature, sunlight, and microbial activity influence their stability and transformation[3]. The presence of pharmaceutical residues poses risks to non-target organisms, including aquatic life, soil microorganisms, and plants, potentially affecting physiological functions and ecological balance. In addition, the combined effects of multiple pharmaceuticals present as mixtures can lead to synergistic or antagonistic interactions, complicating toxicity assessment. The widespread detection of these compounds has raised concerns about their long-term ecological and human health impacts, particularly in regions with inadequate wastewater treatment infrastructure. Advances in analytical technologies have improved detection capabilities, yet challenges remain in monitoring and assessing their environmental distribution. Addressing pharmaceutical contamination requires a comprehensive understanding of their sources, fate, and ecological effects, along with the implementation of effective regulatory frameworks and sustainable management strategies[4].

Sources and Occurrence of Pharmaceutical Residues

Pharmaceutical residues originate from multiple sources and are widely distributed across environmental compartments, reflecting the extensive use of drugs in modern society. One of the primary sources is the excretion of metabolized drugs and their metabolites from humans and animals, which enter municipal wastewater systems and subsequently reach natural water bodies. Hospitals and healthcare facilities contribute significantly to pharmaceutical contamination through effluents containing high concentrations of various drugs, particularly antibiotics and anticancer agents. Pharmaceutical manufacturing industries also release active pharmaceutical ingredients and intermediates into the environment through industrial discharge, often at higher concentrations than those found in domestic wastewater. In agricultural settings, veterinary drugs used in livestock and poultry farming are introduced into the environment through manure application, which can contaminate soil and water systems[5]. Aquaculture practices further contribute to the direct release of pharmaceuticals into aquatic environments. Improper disposal of unused or expired medications, such as flushing them down toilets or discarding them in landfills, exacerbates environmental contamination. Wastewater treatment plants are not specifically designed to remove pharmaceutical compounds, resulting in their partial elimination and continuous discharge into surface waters. Sludge generated during treatment processes may contain accumulated drug residues, which can be transferred to agricultural land when used as fertilizer. Monitoring studies have reported the presence of pharmaceuticals in rivers, lakes, groundwater, and even drinking water supplies worldwide. Seasonal variations, population density, and healthcare practices influence the occurrence and concentration of these contaminants. Understanding the sources and occurrence of pharmaceutical residues is essential for developing targeted strategies to reduce environmental contamination and mitigate associated risks.[6]

Table 1: Sources and Pathways of Pharmaceutical Residues in the Environment

Source of Contamination	Pathway Description	Potential Environmental Impact
Excretion from Humans and Animals	Drugs and metabolites entering municipal wastewater systems	Contamination of rivers, lakes, and groundwater
Pharmaceutical Manufacturing Effluents	Industrial discharge containing active pharmaceutical ingredients	High concentrations of biologics in surface waters
Agricultural Runoff	Veterinary drugs from livestock and poultry farming	Soil and water contamination, affecting ecosystems

Environmental Distribution and Exposure Pathways

The environmental distribution of pharmaceutical residues is governed by complex processes involving transport, transformation, and interactions with environmental components, leading to widespread contamination across aquatic and terrestrial ecosystems. Once released, pharmaceuticals can be transported through surface water systems, infiltrate into groundwater, or accumulate in soil and sediments. In aquatic environments, these compounds are dispersed through rivers, lakes, and oceans, where they may remain dissolved or adsorb onto suspended particles. Soil acts as both a sink and a source of pharmaceutical residues, particularly when contaminated sludge or manure is applied as fertilizer. Leaching processes can facilitate the movement of these compounds from soil into groundwater, posing risks to drinking water sources. Exposure pathways for organisms include direct uptake from contaminated water, ingestion of contaminated food or sediment, and dermal absorption[6]. Aquatic organisms such as fish and invertebrates are particularly vulnerable due to continuous exposure, while terrestrial organisms may be exposed through soil and plant uptake. Bioavailability of pharmaceuticals is influenced by their physicochemical properties, environmental conditions, and interactions with organic matter. Additionally, atmospheric pathways, although less studied, may contribute to the distribution of certain volatile compounds. Human exposure can occur through the consumption of contaminated water and food, highlighting the potential public health implications. The presence of multiple pharmaceuticals in the environment can lead to combined exposure scenarios, increasing the complexity of risk assessment. Understanding environmental distribution and exposure pathways is critical for assessing ecological risks and developing effective mitigation strategies.[7]

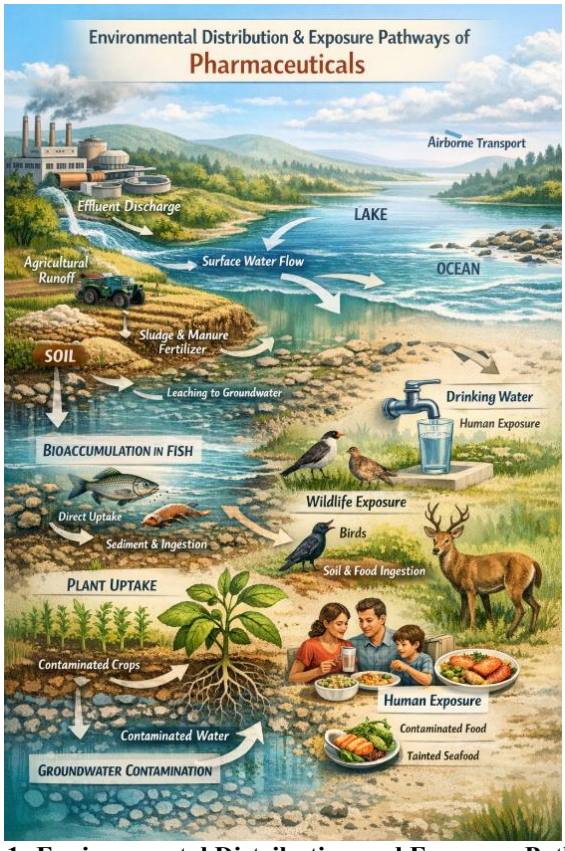

Figure 1: Environmental Distribution and Exposure Pathways.

Soil Contamination and Leaching into Groundwater

Soil contamination by pharmaceutical residues is a significant environmental concern, particularly in agricultural regions where biosolids and manure are commonly applied as fertilizers. These materials often contain residual pharmaceuticals from human and veterinary sources, which can accumulate in soil over time. The interaction of pharmaceutical compounds with soil components, such as organic matter and minerals, influences their retention, mobility, and degradation. While some compounds may bind strongly to soil particles, reducing their mobility, others remain more soluble and can be transported through the soil profile. Leaching is a critical process that facilitates the movement of these soluble compounds into groundwater systems, which serve as major sources of drinking water. Factors such as soil composition, pH, rainfall, irrigation practices, and the physicochemical properties of the pharmaceuticals play a key role in determining leaching potential [8]. Persistent compounds are particularly concerning, as they can remain in soil for extended periods and gradually migrate into groundwater. The presence of pharmaceuticals in groundwater has been reported in various regions, raising concerns about long-term exposure and potential health risks. Soil microorganisms may contribute to the degradation of these compounds, but their efficiency varies depending on environmental conditions and compound structure. Additionally, the accumulation of pharmaceuticals in soil can affect microbial diversity and activity, potentially disrupting nutrient cycling and soil fertility. Monitoring and managing soil contamination is essential to prevent groundwater pollution and protect ecosystem health. Implementing sustainable agricultural practices and improving waste management strategies can help reduce the environmental burden of pharmaceutical residues [9].

Fate and Transformation of Pharmaceutical Residues

The environmental fate and transformation of pharmaceutical residues are influenced by a combination of physical, chemical, and biological processes that determine their persistence, mobility, and ecological impact. Once released into the environment, pharmaceuticals may undergo various transformation processes, including biodegradation, photo degradation, hydrolysis, and oxidation. These processes can lead to the formation of transformation products or metabolites, which may differ in toxicity and persistence compared to the parent compounds. Environmental factors such as temperature, pH, sunlight exposure, and microbial activity play a crucial role in determining the rate and extent of these transformations. Hydrophobic compounds tend to adsorb onto soil and sediment particles, while hydrophilic compounds remain dissolved in water, facilitating their transport[2]. In aquatic environments, photo degradation induced by sunlight can significantly reduce the concentration of certain pharmaceuticals, whereas in soil systems, microbial activity is a driver of degradation. However, incomplete degradation can result in the accumulation of intermediate products, some of which may retain biological activity. The continuous input of pharmaceuticals into the environment contributes to their pseudo-persistence, even if they are partially degradable. Understanding the fate and transformation of pharmaceutical residues is essential for assessing their environmental impact and developing effective remediation strategies. Advanced analytical techniques and modeling approaches are increasingly used to study these processes and predict the behavior of pharmaceuticals in different environmental compartments [10].

Biodegradation and Microbial Transformation

Biodegradation and microbial transformation are key processes in the natural attenuation of pharmaceutical residues in the environment, involving the breakdown of complex compounds into simpler, less harmful substances by microorganisms. Bacteria, fungi, and algae possess diverse enzymatic systems capable of degrading a wide range of pharmaceuticals, including antibiotics, hormones, and analgesics. These processes are primarily mediated by enzymes such as oxidases, reductases, hydrolases, and lyases, which facilitate the transformation of pharmaceutical molecules through various biochemical pathways. The efficiency of biodegradation depends on factors such as the chemical structure of the compound, environmental conditions, and the composition of microbial communities [11]. Easily biodegradable compounds are rapidly metabolized, whereas structurally complex or highly stable pharmaceuticals may resist degradation. Microbial transformation can result in complete mineralization or partial degradation, leading to the formation of intermediate metabolites that may retain biological activity. In wastewater treatment systems, microbial processes play a significant role in reducing pharmaceutical concentrations, although complete removal is not always achieved. Advances in biotechnology, including the use of engineered microorganisms and microbial consortia, have enhanced the potential for targeted biodegradation of persistent compounds. However, environmental variability and competition with native microorganisms can affect the performance of these systems. Understanding microbial transformation mechanisms is essential for optimizing bioremediation strategies and improving environmental management practices [12].

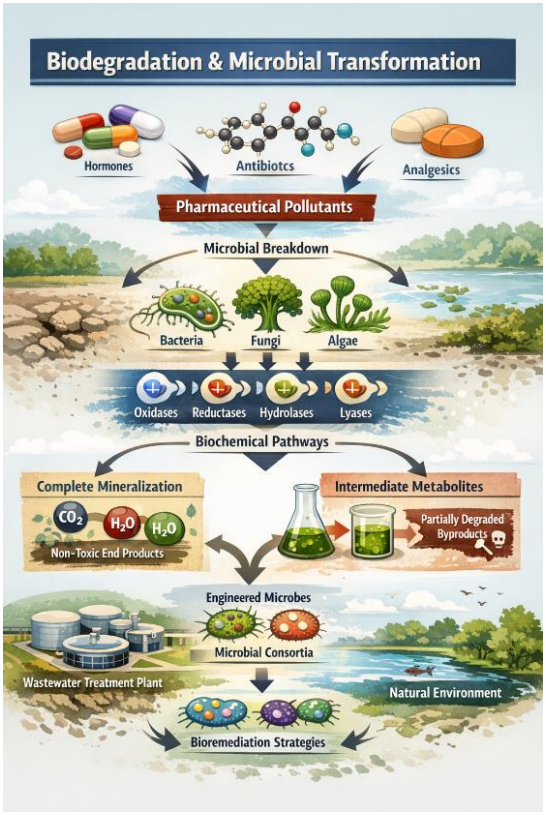

Figure 2: Biodegradation and Microbial Transformation

Mechanisms of Bioaccumulation in Aquatic Organisms

Bioaccumulation refers to the uptake and accumulation of pharmaceutical residues in aquatic organisms over time, resulting in concentrations higher than those in the surrounding environment. This process is influenced by factors such as the physicochemical properties of the compound, including lipophilicity, molecular size, and stability, as well as biological factors such as metabolic capacity and feeding behavior of the organism. Pharmaceuticals can enter aquatic organisms through multiple pathways, including direct absorption from water across gill membranes, ingestion of contaminated food or sediment, and dermal uptake. Lipophilic compounds tend to accumulate in fatty tissues, while hydrophilic compounds may be distributed in other tissues or rapidly excreted. The rate of bioaccumulation depends on the balance between uptake and elimination processes[13]. Some pharmaceuticals may undergo biotransformation within organisms, leading to metabolites that may also accumulate. Bioaccumulation can have significant ecological implications, particularly when compounds are transferred through the food chain, leading to bio magnification. Chronic exposure to accumulated pharmaceuticals can affect physiological functions, including growth, reproduction, and immune response. The presence of multiple contaminants can further complicate these effects through combined toxicity. Monitoring bioaccumulation is essential for assessing ecological risks and understanding the long-term impact of pharmaceutical pollution on aquatic ecosystems[14].

Development of Antimicrobial Resistance in the Environment

The presence of antibiotic residues in the environment is a major contributor to the development of antimicrobial resistance (AMR), a global public health concern. Sub-therapeutic concentrations of antibiotics in water, soil, and sediments create selective pressure that promotes the survival and proliferation of resistant microorganisms. These conditions facilitate the evolution of resistance mechanisms, such as enzymatic degradation of antibiotics, modification of target sites, and efflux pump activity. Environmental reservoirs, including wastewater treatment plants, agricultural fields, and natural water bodies, serve as hotspots for the emergence and spread of resistant bacteria. The widespread use of antibiotics in human medicine, veterinary practices, and agriculture has intensified this problem. Resistant bacteria can be transferred between environmental compartments and may eventually reach humans through water, food, or direct contact[15]. The persistence of antibiotic residues and resistant microorganisms in the environment poses significant challenges for infection control and treatment. Addressing AMR requires integrated approaches, including reducing antibiotic usage, improving waste management, and developing alternative therapies. Environmental monitoring and risk assessment are

essential for understanding the extent of AMR and implementing effective mitigation strategies.

Role of Pharmaceutical Residues in Resistance Gene Spread

Pharmaceutical residues, particularly antibiotics, play a crucial role in the spread of resistance genes in the environment by creating selective conditions that favor resistant microorganisms. These residues can promote horizontal gene transfer mechanisms, such as conjugation, transformation, and transduction, which enable the exchange of genetic material between different bacterial species. Resistance genes are often carried on mobile genetic elements, including plasmids, transposons, and integrin's, facilitating their rapid dissemination across microbial communities. Environmental compartments such as wastewater treatment plants, agricultural soils, and aquatic systems serve as reservoirs for these genes, increasing the risk of their spread to pathogenic bacteria[16]. The presence of multiple contaminants can further enhance gene transfer by inducing stress responses in microorganisms. The spread of resistance genes poses a significant threat to public health, as it can compromise the effectiveness of existing antibiotics. Monitoring and controlling the spread of resistance genes require comprehensive strategies, including reducing environmental contamination, improving wastewater treatment, and implementing strict regulatory measures. Understanding the role of pharmaceutical residues in resistance gene dynamics is essential for developing effective interventions to combat antimicrobial resistance [17].

Challenges in Environmental Monitoring

Environmental monitoring of pharmaceutical residues presents several challenges due to the complexity of environmental matrices, low concentrations of contaminants, and the diversity of compounds present. Detecting pharmaceuticals at trace levels requires highly sensitive and selective analytical techniques, such as liquid chromatography-mass spectrometry, which can be costly and require specialized expertise. Sample preparation and extraction methods must be carefully optimized to isolate target compounds from complex matrices such as water, soil, and sediments. The presence of multiple pharmaceuticals and their transformation products complicates analysis and interpretation of results. Additionally, variability in environmental conditions, such as seasonal changes and geographical differences, can affect the distribution and concentration of contaminants[18]. Lack of standardized methods and protocols further hinders the comparability of data across studies. Continuous monitoring is necessary to assess temporal trends and evaluate the effectiveness of mitigation strategies. Advances in biosensor technologies and remote sensing offer potential solutions for real-time monitoring, but challenges related to sensitivity and reliability remain. Addressing these challenges requires the development of cost-effective, robust, and standardized monitoring approaches to improve environmental assessment and management[19].

Environmental Risk Assessment Models

Environmental risk assessment models are essential tools for evaluating the potential impact of pharmaceutical residues on ecosystems and human health. These models integrate data on exposure, toxicity, and environmental fate to estimate the likelihood and severity of adverse effects. The risk assessment process typically involves hazard identification, dose-response assessment, exposure assessment, and risk characterization. Advanced modeling approaches, such as quantitative structure-activity relationship models and ecological risk indices, are used to predict the behavior and toxicity of pharmaceuticals. However, the complexity of environmental systems and the presence of multiple contaminants pose challenges in accurately assessing risks [20]. Data gaps, particularly for chronic exposure and mixture effects, add to the uncertainty of model predictions. Regulatory frameworks are increasingly incorporating risk assessment into decision-making processes, but there is a need for standardized methodologies and improved data availability. Integrating monitoring data with modeling approaches can enhance the accuracy and reliability of risk assessments. Developing robust risk assessment models is critical for informing regulatory policies and guiding environmental management strategies.

Advanced Wastewater Treatment Technologies

Advanced wastewater treatment technologies have been developed to address the limitations of conventional treatment systems in removing pharmaceutical residues from water. These technologies include advanced oxidation processes, membrane filtration, adsorption, and hybrid systems that combine multiple treatment methods. Advanced oxidation processes, such as zonation and photo catalysis, generate reactive species capable of degrading complex pharmaceutical compounds into simpler molecules. Membrane technologies, including Nano filtration and reverse osmosis, effectively remove contaminants based on size exclusion and charge interactions [21]. Adsorption using activated carbon or novel materials provides an efficient method for capturing pharmaceuticals from water. Hybrid systems that integrate biological and physicochemical processes offer enhanced removal efficiency. Despite their effectiveness, these technologies can be energy-intensive and costly, limiting their widespread application. Ongoing research focuses on improving efficiency, reducing costs, and developing sustainable treatment solutions.

Bioremediation and Phytoremediation

Bioremediation and phytoremediation are eco-friendly and sustainable approaches for removing pharmaceutical residues from the environment by utilizing biological systems such as microorganisms and

plants. In bioremediation, bacteria, fungi, and algae degrade pharmaceutical compounds through enzymatic processes, converting them into less toxic or non-toxic substances. This approach can be applied in situ or in controlled environments such as bioreactors. Phytoremediation involves the use of plants to absorb, accumulate, and metabolize contaminants from soil and water. Certain plant species have the ability to take up pharmaceutical residues and transform them through metabolic processes [22]. These methods are cost-effective and environmentally sustainable compared to conventional treatment technologies. However, their efficiency depends on factors such as contaminant concentration, environmental conditions, and species selection. Combining bioremediation and phytoremediation with other treatment methods can enhance overall effectiveness. Continued research and development are essential to optimize these approaches for large-scale applications and to address the challenges associated with pharmaceutical pollution.

CONCLUSION

The Eco toxicological assessment of pharmaceutical residues in aquatic and terrestrial ecosystems highlights a growing environmental and public health concern driven by the continuous release and persistence of biologically active compounds. Pharmaceuticals, including antibiotics, hormones, analgesics, and anticancer agents, are increasingly detected in diverse environmental compartments at trace levels, yet their potential to exert significant biological effects even at low concentrations underscores their ecological relevance. The complexity of their environmental behavior, governed by factors such as physicochemical properties, environmental conditions, and microbial activity, contributes to their pseudo-persistence and widespread distribution. In aquatic ecosystems, pharmaceutical residues have been shown to affect fish, invertebrates, algae, and microbial communities, leading to alterations in growth, reproduction, and behavior, while in terrestrial systems, they can disrupt soil microbial diversity, plant health, and nutrient cycling processes. The processes of bioaccumulation and biomagnification further amplify their impact across trophic levels, posing long-term risks to ecosystem stability and biodiversity. Of particular concern is the role of antibiotic residues in the development and spread of antimicrobial resistance, which not only affects environmental health but also has profound implications for human medicine. Despite advances in analytical techniques and monitoring tools, significant challenges remain in accurately assessing the ecological risks associated with pharmaceutical mixtures, transformation products, and chronic exposure scenarios. Current environmental risk assessment models, although useful, require refinement to address the unique characteristics and combined effects of these contaminants. Additionally, conventional wastewater treatment systems are often insufficient for the complete removal of pharmaceutical residues, necessitating the adoption of advanced treatment technologies and innovative approaches such as bioremediation and phytoremediation. Effective management of pharmaceutical pollution requires a holistic and interdisciplinary approach that integrates scientific research, regulatory frameworks, and sustainable practices. Strengthening environmental monitoring systems, standardizing assessment methodologies, and enhancing data availability are essential for informed decision-making. Furthermore, the implementation of green pharmacy principles, responsible drug use, and proper disposal practices can help reduce the environmental burden at the source. Collaboration among scientists, policymakers, industry stakeholders, and the public is critical to developing and implementing effective mitigation strategies. In conclusion, addressing the Eco toxicological impacts of pharmaceutical residues is imperative for protecting ecosystem integrity, preserving biodiversity, and safeguarding public health, and requires coordinated global efforts supported by innovation, regulation, and environmental stewardship.

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