Pharmaceuticals in Water

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The presence of pharmaceuticals in the aquatic environment presents a challenge to modern science. The most significant impact this can induce is the emergence of antibiotic resistance, which can lead to a global health emergency. It is important to note that the impact of pharmaceuticals in the aquatic environment is not limited to antibiotic resistance. Pharmaceuticals can also affect the behaviour and reproductive systems of aquatic organisms, with cascading effects on entire ecosystems.

pharmaceuticals aquatic ecosystems hydrobiology phytoremediation

advance oxidative processes

1. Introduction

Hydrobiology is a branch of ecology that studies living organisms in aquatic habitats. It focuses on the interactions between aquatic organisms and the physical and chemical environment, as well as their interactions with each other [1]. Emerging pollutants are substances that have recently been identified as environmental contaminants and that have the capacity to induce deleterious impacts on the health of ecosystems and humans [2]. Pharmaceutical products are one example of emerging pollutants as they are found in various aquatic systems around the globe. They are emerging pollutants due to their continuous and widespread usage [3]. When these pharmaceutical products enter water bodies, they can have a significant impact on aquatic organisms, including altering their behaviour and causing reproductive problems and even death. Additionally, these substances are persistent and xenobiotics in the environment, leading to chronic exposure of aquatic organisms and humans who consume contaminated water [2][4].

Recent reports highlight the urgency of understanding the emerging pollutants' impacts on aquatic habitats and their inhabitants, including the field of hydrobiology [3][4][5]. For instance, research by Li et al. [6] explored the incidence and ecological risk of pharmaceuticals present in a drinking water reservoir source in China (mainland). The examination found that various pharmaceutical compounds and products were present in the water and posed ecological risks to the aquatic organisms in the reservoir. Similarly, a study by Li et al. [3] and Mastrángelo et al. [7] evaluated the impact of emerging pollutants, including pharmaceuticals, on the microbial composition nexus in an urban river. The study found that the microbial community composition was significantly altered in the presence of these pollutants. These studies demonstrate the need for continued research and management strategies to minimize the effects of emerging pollutants on water ecosystems and human health.

Pharmaceutical products have been increasingly detected in water bodies due to various pathways, including direct discharge of treated and untreated wastewater, surface runoff, and agricultural and industrial runoff [8]. The presence of these products in water bodies poses a significant risk to aquatic organisms and human health. The discharge of treated and untreated wastewater containing pharmaceuticals into rivers and streams is one of the major paths and routes for the introduction of these products into aquatic systems [8]. In addition, agricultural activities and livestock farming were identified as potential sources of contamination, as drugs such as antibiotics and hormones are often used in these practices [9]. The existence of pharmaceutical products in environmental matrices, especially water systems, highlights the need for improved waste management practices, increased public awareness, and the development of more effective technologies related to wastewater treatment to reduce the impact of emerging pollutants on the environment and human health [10][11].

2. Routes of Pharmaceutical Product Entry into Water Bodies and Their Detection

Pharmaceutical products can enter aquatic systems through various pathways [12]. A general route that presents the channels through which the pharmaceutics can enter aquatic systems is presented in **Figure 1**. One of the primary sources is direct discharge from wastewater treatment plants [9][11].

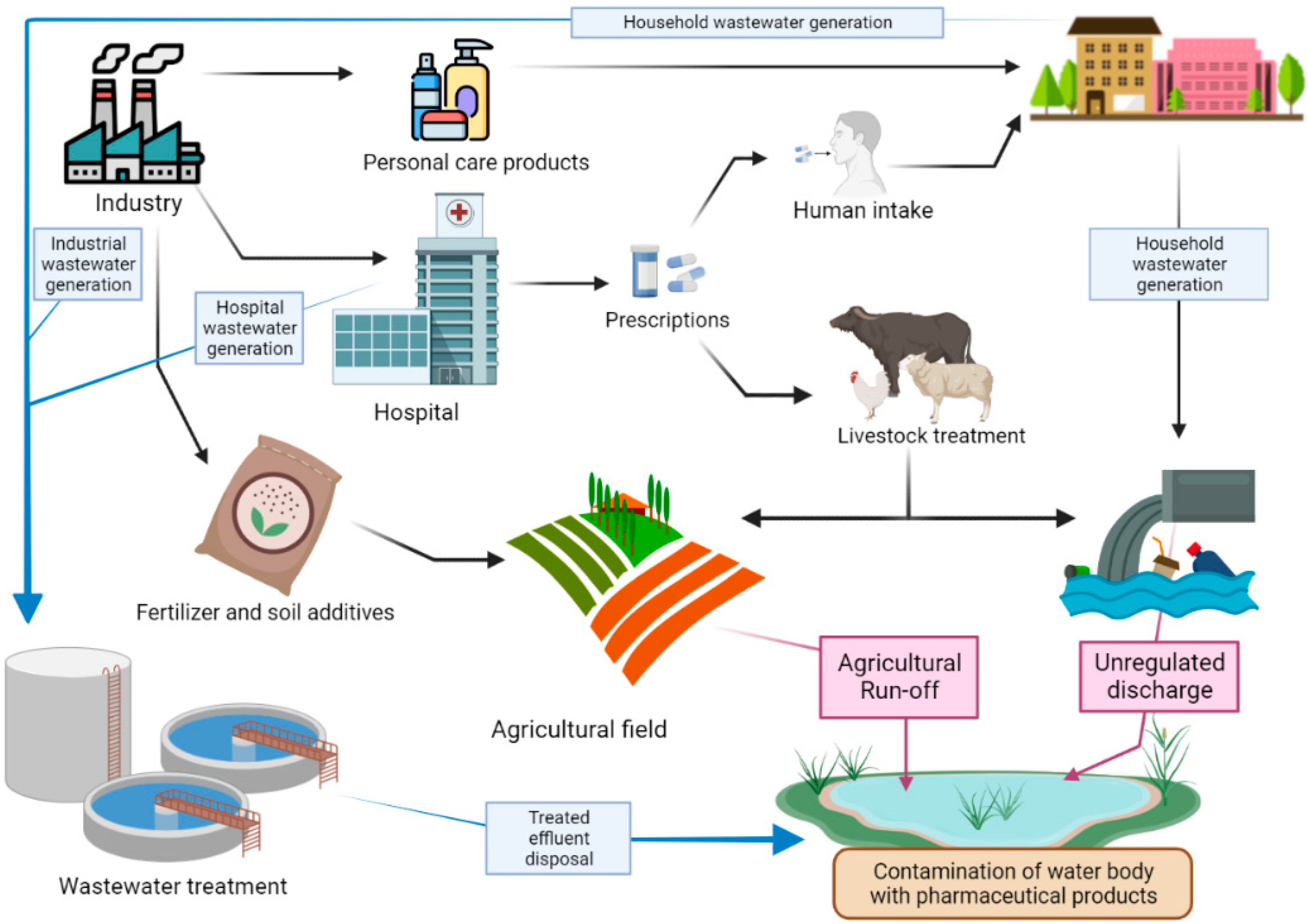

Figure 1. Pathways through which pharmaceutical contaminants can enter aquatic systems [12].

Pharmaceutical products are often excreted by humans and animals, and they can pass through wastewater treatment plants without being fully removed [13][14]. There are numerous studies that have reported the presence of pharmaceutical products in wastewater. An extensive review of the presence of pharmaceuticals in domestic wastewater was presented by Petal et al. [15] and Falahi et al. [16]. If the wastewater remains untreated, this can lead to bioaccumulation in aquatic animals. For instance, Carrizo et al. [9] conducted a study in Argentina on pacu fish (*Piaractus mesopotamicus*) and reported the presence of pharmaceuticals and their metabolites (including 1,7-dimethylxanthine, benzoylecgonine, bis(2-ethylhexyl) phthalate, caffeine, carbendazim, cyclamate, dodecanedioic acid, ethylparaben, xanthine, methylparaben, metolachlor, salicylic acid, and saccharin) in all analysed samples. Similarly, in another study conducted by Mastrángelo et al. [7], the presence of acetaminophen, atenolol, carbamazepine, ciprofloxacin, hydrochlorothiazide, sulfamethoxazole, valsartan, and venlafaxine in surface water, ciprofloxacin in the biofilm, and *Lemma gibba*, were reported. It clearly indicates the importance of effective treatment for the removal of pharmaceutical products, as having them in wastewater and water streams can exacerbate the menace of antibiotic resistance in opportunistic pathogens [5][17]. The presence of pharmaceutical products, including antibiotics, in wastewater can lead to the selection and proliferation of antibiotic-resistant bacteria [18]. These resistant bacteria can then be released into the environment, potentially infecting humans and animals. In addition, the discharge of untreated wastewater into water bodies can provide a reservoir for the exchange of resistance genes between different bacterial species [6]. Effective wastewater treatment is therefore essential to prevent the spread of antibiotic resistance and protect public health [14]. Treated wastewater can also contain residual pharmaceuticals that are released into rivers, lakes, and oceans, potentially affecting aquatic organisms [10]. Another source of pharmaceutical products in aquatic systems is leakage from landfills [12].

When pharmaceuticals are disposed of in landfills, they can leach into the surrounding groundwater and surface water. This can happen when rainwater percolates through the landfill and carries dissolved pharmaceuticals with it [19]. Over time, the leached pharmaceuticals can find their way into streams, rivers, and other aquatic systems. Agricultural runoff is another potential pathway for pharmaceutical products to enter aquatic systems. Livestock farms and agricultural fields often use pharmaceuticals such as antibiotics and hormones to prevent disease and promote growth in animals [9]. These chemicals can be excreted in animal waste and washed off fields by rainwater or irrigation. The runoff can then enter streams and rivers, carrying with it residual pharmaceuticals that can potentially harm aquatic organisms [20]. Overall, the presence of pharmaceutical products in aquatic systems can have significant ecological impacts. It is important to understand the sources and pathways of pharmaceuticals to minimize their impact on the environment and ensure the safety of aquatic ecosystems.

A comprehensive review of the literature focusing on methods for monitoring and assessing the levels of pharmaceutical products in water is presented by Rathi et al. [21]. These methods can be classified based on underlying working principles (Analytical Chemistry Techniques or biological methods) and monitoring methodology statutes (active and passive techniques). **Table 1** summarizes those methods used for the detection of pharmaceutical products in aquatic environments. Passive sampling involves the use of devices or materials to absorb or adsorb chemicals from water over time, while active sampling requires physically collecting water samples. Laboratory techniques such as high-performance liquid chromatography (HPLC), mass spectrometry (MS), enzyme-linked immunosorbent assay (ELISA), and polymerase chain reaction (PCR) can be used to detect and quantify specific pharmaceutical products in water samples [22][23]. Similarly, biological methods can be used to assess the potential effects of pharmaceutical products on living organisms in the aquatic system [23][24][25][26][27][28]. Using a combination of these methods, researchers and regulatory agencies can better understand the presence and potential impacts of pharmaceutical products in water and take appropriate actions to protect public health and the environment.

Table 1. Methods used for the detection of pharmaceutical products in aquatic systems.

Methods		Description	Monitoring Status	Usage	References
Analytical Chemistry Techniques: Pharmaceutical products can be detected and quantified using various analytical chemistry techniques	High-Performance Liquid Chromatography (HPLC)	Separates and identifies individual components in a sample based on their chemical properties.	Active	Commonly used methods (individually and in combination) for the detection of pharmaceutical contaminants	[29]
	Gas Chromatography (GC)	Separates and analyzes volatile compounds in a sample.	Active		
	Mass Spectrometry (MS)	Measures the mass-to-charge ratio of ions to identify and quantify compounds in a sample.	Active		
	Diffusive Gradients in Thin Films (DGT)	Uses a resin gel that binds to the pharmaceuticals, allowing for their detection after	Passive	Antiviral agent, hypoglycemic, blood lipid regulator, anticonvulsant drug, anti-inflammatory drug, antidepressant,	[30]

Methods		Description	Monitoring Status	Usage	References
		being collected on the resin.		antiplatyhelmintic drug, antirheumatic drug, β-lactams, macrolides, fluoroquinolones, sulfonamide, tetracyclines, and other antibiotics	
	Polar Organic Chemical Integrative Samplers (POCIS)	Uses a sorbent material to collect pharmaceuticals over time.	Passive	Carbamazepine, Ibuprofen, Gemfibrozil, Triclosan, Octocrylene, Caffeine, Ketoprofen, Naproxen, Diclofenac, Mefenamic acid	[22]
	Solid Phase Microextraction (SPME)	Uses a small fiber coated with a sorbent material to extract pharmaceuticals from the water over time.	Passive	Nifedipine, furosemide, hydrochlorothiazide, valsartan, pravastatin sodium, rosuvastatin calcium salt, and gemfibrozil	[23]
Biological Methods. Living organisms or biological origin products that can be used to monitor the effects of pharmaceutical products on	Bioassays	Measures the biological response of an organism or cell to a pharmaceutical product. (Growth, reproduction, and survival—*Caenorhabditis elegan*, germination assay—*Lactuca sativa*, and bio-	Active	Ibuprofen	[27]

Methods		Description	Monitoring Status	Usage	References
aquatic ecosystems		luminance assay-*Vibrio fischeri*)			
	Biomarkers	Measures the presence or levels of specific molecules or genes in an organism that indicate exposure to a pharmaceutical product. (Enzymatic profiling for Fish—invasive, Hemolymph for carb—Noninvasive)	Passive	Triclosan and 17α-Ethynylestradiol	[26][28]
	Ecotoxicology	Examines the effects of pharmaceutical products on the behavior, reproduction, growth, and survival of aquatic organisms. (Mortality (LC50) and reproduction inhibition (NOEC) in *Daphnia magna*	Passive	Diclofenac, ibuprofen, clofibric acid, carbamazepine, salicylic acid, gemfibrozil, acetaminophen, bezafibrate, tolfenamic acid	[25]
	Enzyme-Linked Immunosorbent Assay (ELISA)	A type of immunoassay that detects and measures specific molecules, including	Active	Amoxicillin, caffeine, chloramphenicol, ciprofloxacin, dexamethasone, diclofenac,	[24]

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...ques. The ... [31]. This is ...graphy. It is also important to assess the bioavailability and toxicity of the pharmaceuticals, as this can help inform risk assessments. This can be done by measuring the aquatic concentration of the compound, as well as its rate of degradation in the environment [32]. The next step is to study the direct and indirect effects of pharmaceuticals on

[5][33] Methods	Description	Monitoring Status	Usage	References
	pharmaceuticals, in a sample.		nitrofurazone, sulfamethoxazole, and triclosan	

ounds by e, studies e [34]. It is er quality e [35]. The rganisms, antibiotic resistance development, and endocrine disruption [36]. These products can also affect the food chain, with the potential to harm the health of fish and other aquatic life that humans consume [17]. Additionally, pharmaceutical products can lead to the growth of harmful algae and bacteria in the water, which can harm aquatic life and make the water unsuitable for human use. The accumulation of pharmaceutical products in the environment can also have unknown long-term effects on the ecosystem, making it crucial to monitor and regulate the use and disposal of these products. These risks posed by pharmaceutical products to hydrobiology have been highlighted in several studies. For instance, Tambosi et al. [37] and Patel et al. [15] pointed out that pharmaceutical products can introduce new or higher concentrations of various chemicals into the environment, disrupting the balance of aquatic ecosystems.

These pollutants include antibiotics, hormones, and antifouling agents, among others. Similarly, a study by Kayode-Afolayan et al. [33] highlighted the impact of pharmaceuticals on nitrogen and phosphorus levels in water bodies, as well as their effects on the health and behaviour of aquatic species. This work also proposed that some pharmaceuticals can act as endocrine-disrupting compounds, causing serious biological effects on aquatic organisms.

These findings demonstrate the importance of continued research and management efforts to minimize the impact of pharmaceutical products on aquatic ecosystems. Pharmaceuticals in water bodies can accumulate in sediments, potentially leading to long-term exposure to aquatic organisms [33][38]. Another study by Foster et al. [39] highlighted the potential of fluoxetine to cause changes in the metabolism and gene expression of *Rana pipiens*, potentially leading to negative impacts on their growth, development, and survival. Additionally, a recent study by Leonardo et al. [40] showed that the presence of pharmaceuticals in water bodies can lead to the development of antibiotic-resistant bacteria, posing potential risks to human health. In another study, Bereketoglu et al. [41] observed various effects in zebrafish embryos and larvae caused by nonsteroidal anti-inflammatory drugs (NSAIDs). These effects included malformations and mortality in the embryos, apoptosis in the larvae, downregulation of genes that are biased towards females, and an increase in the proportion of males. The effects were particularly significant in areas with high concentrations of the drug. It demonstrates the harmful impact that pharmaceutical products can have on aquatic ecosystems and the need for effective management practices to mitigate these effects.

4. Methods of Choice for the Management of Pharmaceutical Pollution in Water

There are several pharmaceutical remediation methods currently in use for treating pharmaceutical products in aquatic environments. These methods include biological treatments such as activated sludge, bioremediation, phytoremediation, and nutrient removal [42]. Other physical remediation methods include adsorption, absorption, and membrane filtration [43]. Chemical treatments such as oxidation, chlorination, and ozonation may also be used [44]. New research is also being conducted to develop novel remediation technologies, such as engineered nanomaterials and biosystems used for the adsorption of antibiotics, which hold promise for treating contaminated waters [45][46]. At present, a few of these systems are in the research stage and need thorough evaluation before commercial application. Biological treatments are often preferred for the treatment of pharmaceutical products in aquatic environments because they can be more cost-effective compared with physical or chemical treatments, and they typically result in lower residual impact. Bioremediation uses bacteria, fungi, algae, or plants to degrade or transform toxins in the environment [47][48][49][50]. However, the risk of antibiotic resistance and the emergence of super tolerant microbial bugs are among the most prominent obstacles to the use of microbial-based bioremediation technologies. Other biological treatments include oyster culture, marsh wetlands, and constructed wetlands, which use plants and animals to filter out contaminants. Such treatments must be carefully managed to ensure that the water is safe for human and aquatic life.

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