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Regulations and treatment strategies for pharmaceutical wastewater – A review

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Abstract. Pharmaceutical residues are recognized as emerging micropollutants that are predominantly present in the environment, mainly due to direct discharge or inefficiently treated effluents from wastewater treatment plants. Although conventional treatment partially removes pharmaceuticals (less than 50% for most pharmaceutical compounds), it is incapable of completely eliminating pharmaceuticals from wastewater due to the complexity of the compounds and inappropriate operational conditions. However, advanced treatment technology demonstrated a removal rate of over 90%, but cost and energy requirements are considered important aspects. Additionally, a legal and regulatory system needs to be implemented to control pharmaceutical discharge. Herein, a comprehensive review of global consumption and pathways, as well as guidelines for the efficient removal of pharmaceuticals. Additionally, a legal and regulatory framework needs to be implemented to control the discharge of pharmaceuticals. Finally, we discuss the future outlook for developing new approaches and innovative treatment technologies to reduce pharmaceutical residues in the environment.

Keywords: Aquatic environment, Emerging contaminants, Hospital Wastewater, Regulation, Public Health.

1. Introduction

In the 1970s, pharmaceutical compounds were first detected in sewage. By 1972, out of 20 studies, only two articles concerning pharmaceutical compounds were published, with more focus on risk assessments of drugs and profitability considerations rather than environmental issues (Elias, 1973). As of now, there are over hundreds of pharmaceutically active compounds (PhACs) and metabolites released from potential sources such as untreated/partially treated sewage from hospitals (Khan et al., 2020), wastewater treatment plants (WWTP's), septic systems (Phillips et al., 2015), and pharmaceutical industries effluents (Khan et al., 2021), animal livestock's (Ramirez-Morales et al., 2021) and aquaculture sites, thereby polluting environmental matrices such as surface water (Wilkinson et al., 2022), underground water (Lapworth et al., 2012), soil (Aydın et al., 2022), etc. (see Table 1). Among these, hospitals are a major source of pollution, and even conventional WWTPs fail to eliminate complex contaminants effectively. These conventional WWTPs are not designed to remove these complex contaminants found in hospital wastewater (HWW). However, it is not always possible to determine the primary pathway in a specific site, especially for surface waters.

A recent investigation shows the presence of 61 pharmaceuticals in 258 rivers from 104 countries, representing the pharmaceutical footprint towards 471.4 million population across 137 regions (Wilkinson et al., 2022). The widespread occurrence of these compounds poses potential risks to

humans and the environment, as 30–90% of consumed pharmaceuticals are excreted as active substances, and fecal matter often enters sewer systems untreated (BIO Intelligence Service, 2013; Khan et al., 2021).

The detection of pharmaceuticals in the environment mainly depends on the effluent source, the facility at WWTP, environmental characteristics, weather patterns, dilution, dispersion, and the presence of transformation products (Lapworth et al., 2012; dos Santos et al., 2021). As discussed above, the conventional WWTPs are not equipped to efficiently eliminate these emerging contaminants (EC). This inefficiency arises not only from the design limitations of conventional treatment systems but also from the insufficient understanding of the ecotoxicity and complex behavior of these contaminants in aquatic environments (Petrie et al., 2015). This complex nature of pharmaceutical residues is characterized by at least five dimensions of major concerns:

- Present in trace concentration ranges in the environment, i.e., ng/L to μg/L (Verlicchi, 2021).
- Several pharmaceuticals and their metabolites or conjugates with various chemical compositions are excreted from the HWW effluents and often washed into sewage systems (Kanama et al., 2018).
- Various pharmaceuticals have been shown to adsorb onto polyethylene microplastics in wastewater environments (McDougall et al., 2022).
- Pharmaceutical compounds with large Kow values (i.e., very lipophilic substances) are of great concern since they can be adsorbed in soil/sediment and living organisms (Zhang et al., 2021).
- Pharmaceutical residues posed a threat to their persistence (pseudo-persistent), antibiotic-resistant bacterial development, and mobility in the environment (Patel et al., 2019).

Other hindrances associated with emerging contaminants are the water dilution and the metabolite process in WWTP (Diwan et al., 2009; Verlicchi et al., 2010, 2015). However, the extent of pharmaceutical removal in conventional WWTPs depends on chemical characteristics such as solubility, volatility, lipophilicity, and biodegradability (Verlicchi et al., 2010; 2012). In addition, operational parameters including hydraulic retention time, sludge age, temperature, and pH also play a crucial role in determining removal efficiency. Furthermore, the complex interactions between parent compounds and their transformation products can lead to incomplete degradation or even the formation of more persistent and toxic by-products. Therefore, optimizing treatment conditions and incorporating advanced processes are essential to enhance the elimination of these contaminants from wastewater. By comparison, advanced treatments—such as advanced oxidation processes (AOPs), adsorption, and membrane filtration, and hybrid treatments—are typically necessary to achieve effective elimination (Dolar et al., 2012; Patel et al., 2019; McDougall et al., 2022).

Table 1. Maximum detected concentrations (ng/L) of pharmaceutical residues in water matrices in different countries

Environmental matrix		Max. detected concentrations (ng/L)	Country	Reference
Surface water	River/ Canal	70700	Pakistan	Wilkinson et al. (2022)
	Lake	5,600	Uganda	Nantaba et al. (2021)
	Sea or Ocean	66400	Tunisia	Tahrani et al. (2017)
	Aquaculture	91,150	Portugal	Pereira et al. (2020)
	Lagoon/ Ponds	175	Italy, Venice	Pojana et al. (2007)
Groundwater	Aquifer	650 x10^6	United Kingdom	Bennett et al. (2017)
Well water (untreated)		6490	Nigeria	Ebele et al. (2020)
Sub-watersheds		5660	Cameroon	Branchet et al. (2019)
Tap / Drinking Water		564	China	Leung et al. (2013)

In this review, the recent research trend on (1) the global consumption and pathways of PWW in the environment; (2) an overview of treatment scenario for HWW around the world is discussed; (3) highlights the current regulation, policy, and legislation towards pharmaceutical effluents routes to the environment and its controlling and managing approaches and (4) Lastly, the review provides a critical evaluation of recent research developments and outlines potential avenues for future studies.

2. Review Methodology

The primary objective of this study is to critically review the status of the regulation and treatment of HWW around the world and summarize available information on regulatory strategies by the international organization. Accordingly, we have identified original and reviewed articles using databases like Web of Science, PubMed, Google Scholar, Scopus, and NIH. The adapted keywords were "hospital wastewater" and "pharmaceutical wastewater", hospital wastewater regulations keywords such as "pharmaceutically active compounds", "regulations" "legislation" "policy" "law" and other strings like "conventional and primary treatment",

"advanced and tertiary treatment" and "pathways and sources" etc. Besides, we accessed the websites of the world health organizations (WHO), European Commission (EC), Environmental Protection Agency (EPA), International Atomic Energy Agency (IAEA), Organization for Economic Co-operation and Development (OECD), Pan American Health Organization (PAHO), National Association of Clean Water Agencies (NACWA), Association of Metropolitan Water Agencies (AMWA), Safe Drinking Water Act (SDWA), Network of reference laboratories (NORMAN), Society of Environmental Toxicology and Chemistry (SETAC), Oslo and Paris Commission for the protection of the Marine Environment of the North East Atlantic (OSPAR), National Pollutant Discharge Elimination System (NPDES) and various health ministry's information on pharmaceutical/ hospital wastewater (PWW/HWW). Furthermore, we have selected specific searches based on regions (such as continents /specific countries) in order to gather information around the world.

3. Global consumption and pathways

3.1. Consumption pattern

Significant pharmaceutical discharge has been documented across the world, and hospitals are the primary contributors to pharmaceutical residues entering the sewerage system. In 2013, 54,000 t of antibiotics were consumed equally by humans and animals in China, and almost (99%) 53800 tons entered the environment via various wastewater treatments (Zhang et al., 2015). According to the U.S. Food and Drug Administration (FDA) fact sheet, more than 20,000 prescription drug products have been approved for marketing in the United States. These products contain thousands of active and inactive ingredients that are regularly used in human health applications. The exact number of unique active ingredients is smaller than the total number of approved products, as many formulations share the same active substances but differ in dosage form or manufacturer (FDA, 2021). However, around 22% of global active pharmaceutical ingredient manufacturers are located in the United States, followed by Europe, highlighting the significant role these regions play in the global pharmaceutical supply chain. This concentration of manufacturing capacity underscores the dependence of global healthcare systems on a limited number of regions for essential drug components and emphasizes the need for diversified and sustainable API production worldwide.

Recently, a 200% increase was estimated as a result of rapidly growing pharmaceutical markets in developing nations, particularly *BRICS*- Brazil, Russia, India, China, South Africa and *MIST*- Mexico, Indonesia, South Korea, and Turkey (Tannoury & Attieh, 2017). This widespread manufacture of pharmaceuticals has resulted in substantial releases of treated or untreated pharmaceutical chemicals into water streams. Consequently, the persistence of pharmaceutical residues in the environment threatens ecological balance across marine and terrestrial systems and represents a growing concern for human and environmental health (Lunghi et al., 2025; Emmanuel et al., 2009; Carter et al., 2019).

The pharmaceutical compounds which are often found in HWW are categorized as (a) anti-inflammatories and analgesics (Diclofenac, Ibuprofen, Ketoprofen, Naproxen paracetamol, etc.); (b) antibiotics (Erythromycin, Ofloxacin, Azithromycin, Ciprofloxacin, Clarithromycin, Sulfamethoxazole, Norfloxacin, Tetracyclines); (c) Anti-diabetics (Glibenclamide); (d) Psychiatric drugs (carbamazepine, Diazepam, Fluoxetine); (e) Lipid regulators (Simvastatin, Gemfibrozil, Pravastatin); (f) Antihistamines (Famotidine, Ranitidine); (g) Cytotoxic drug (Sorafenib); (h) Diuretics (Furosemide) and (i) β-blockers (metoprolol, atenolol, propranolol), etc. The PhACs are pseudo-persistent that typically released continuously from HWW and the pharmaceutical industries to the environment.

Table 2 shows the summary of the range of concentrations of typical parameters (apart from pharmaceuticals) detected in hospitals and WWTP's effluents around the globe. It is worth noting the presence of several complex compounds in the hospital units, whether in the parent state or as metabolites that are released directly or indirectly to the environment (Manaia et al., 2018; Pan & Chu, 2018; Hanna et al., 2018).

Recently, Wilkinson et al. (2022) studied the highest mean cumulative concentration of pharmaceutical residues detected globally. The most polluted region was Asia (Pakistan: 70,700 ng/L), followed by Africa (Ethiopia: 51,300 ng/L) (Wilkinson et al., 2022). The maximum concentration of pharmaceuticals was detected in North American samples was detected in Costa Rica (mean 25,800 ng/L, maximum 63,100 ng/L). In Europe, the most contaminated samples were recorded in Spain, showing mean concentrations of 17,100 ng/L and peak values reaching 59,500 ng/L. However, the Oceania samples' concentration was comparatively low compared to other regions and found to be maximum in Australia (mean 577 ng/L, maximum 750 ng/L) (Wilkinson et al., 2022).

In India, PhACs are detected in industrial effluents, WWTPs' influents and effluents, HWW, surface water, and groundwater (Patel et al., 2019). In a recent study, 19 out of 102 samples tested positive for PhACs in tap water loaded from Danube river-derived water situated in Hungary (Kondor et al., 2021). Similar results reported the presence of twenty-eight PhACs in surface and drinking water sources in

Table 2. Summary of the typical parameters detected in hospital wastewater (HWW) and urban wastewater (UWW) around the globe

Parameter	Units	Origin	HWW	UWW	Reference
			Range	Range	
Flow	m^3/day	French research facility Site Pilote de Bellecombe (SIPIBEL)	98–277	2598–6549	Wiest et al. (2018)
pH	-	Hospital and Domestic wastewater	6-9.18	6.3–7.8	
Conductivity	mS cm^{-1}	-	750–1000	420–1340	Khan et al. (2020), Hocaoglu et al. (2021)
BOD_5	mg/L	Microbiology laboratory sterilization and disinfection equipment, anesthetic agents, and culture nutrient solutions. SIPIBEL	101–1906	70–488	
COD	mg/L		199–3344	180–1698	Achak et al. (2021)
TOC	mg/L		79–332	63–264	
TSS	mg/L		11–1183	41–608	Khan et al. (2020), Hocaoglu et al., (2021)
Chlorides	mg/L		80–400	30–100	
NH_4-N	mgNH_4/L		10–55	12–45	Khan et al. (2020), Hocaoglu et al. (2021)
TKN	mg N/L		5–100	20–102	
TP	mgP-PO_4/L		7.3–104	4–18	Wiest et al. (2018)
AOX	mg/L	Sterilization of surgical tools, cleaning activities	0.2–10	0.1	
Phenols	mg/L	Cleaning and building maintenance	0.4–8.4	0.02–0.1	Hocaoglu et al. (2021)
Detergents	mg/L	Hospital laundry/	3–7.2	4–8	
E. coli	MPN/100 mL	Fecal matter from infected persons -	10^3–10^6	10^6–10^7	Khan et al. (2020), Hocaoglu et al. (2021)
FC	MPN/100 mL	-	10^3–10^7	10^6–10^7	
TC	MPN/100 mL	-	10^6–10^9	10^7–10^8	Achak et al. (2021)

AOX: Halogenated Organic Compounds, BOD: Biochemical oxygen demand, COD: Chemical oxygen demand, FC: Faecal coliform, E. Coli: Escherichia coli, TC: Total coliform, TOC: Total organic carbon, TP: Total Phosphorus, TSS: Total Suspended Solids

Brazil. Further, the study highlighted the presence of PhACs in water that largely depend on climatic factors, people's behavior, and socioeconomic characteristics of the particular area (Santos et al., 2020).

3.2. Source Control

The hospital wastewater (HWW) represents a significant driver of pharmaceuticals being flushed (>80%) via human excretion, as shown in Figure 1. It can only be expected to rise over time as the demand to develop newer and more potent pharmaceuticals increases (Jia, et al., 2018). Due to this lack of treatment capabilities, it is critical to manage the pharmaceuticals entering these facilities using source control measures in order to effectively minimize the environmental load. As a result, prevention becomes a long-term control imperative. Any long-term strategy for controlling pharmaceuticals in the environment must, however, be holistic and comprehensive, emphasizing pollution prevention and incorporating rigorous source-control measures.

3.3. Pathways

An extensive literature is available on pharmaceutical residues in the United States, many European countries, and China, whereas limited data is available for the rest of the world. In spite of data for some countries, information is rarely investigated for more than twenty pharmaceuticals in a single method (aus der Beek et al., 2016). Mostly lower-income nations (due to high population density) tend to have poorer sanitation and hygiene, urbanization, and sewer connectivity, treatment, and lack of regulation (Kookana et al., 2014).

According to health community statistics, the level of CIP pollution detected in surface water and underground water was within the concentration range of 1 $g.L^{-1}$, respectively. However, the level of CIP reported in the hospitals and pharmaceutical industries' effluents is substantially greater, ranging from 150-50 $mg.L^{-1}$, respectively, which is exceedingly toxic to the environment and human health (El-Shafey et al., 2012).

4. Development or upgrading treatment units

Conventional WWTPs are frequently incapable of completely degrading ECs because they are not intended to handle such complex compounds (Fig. 2). Although physicochemical treatment was utilized before the on-site treatment of WWTPs (Khan et al., 2021). Biological wastewater treatment processes (constructed wetlands, activated sludge process

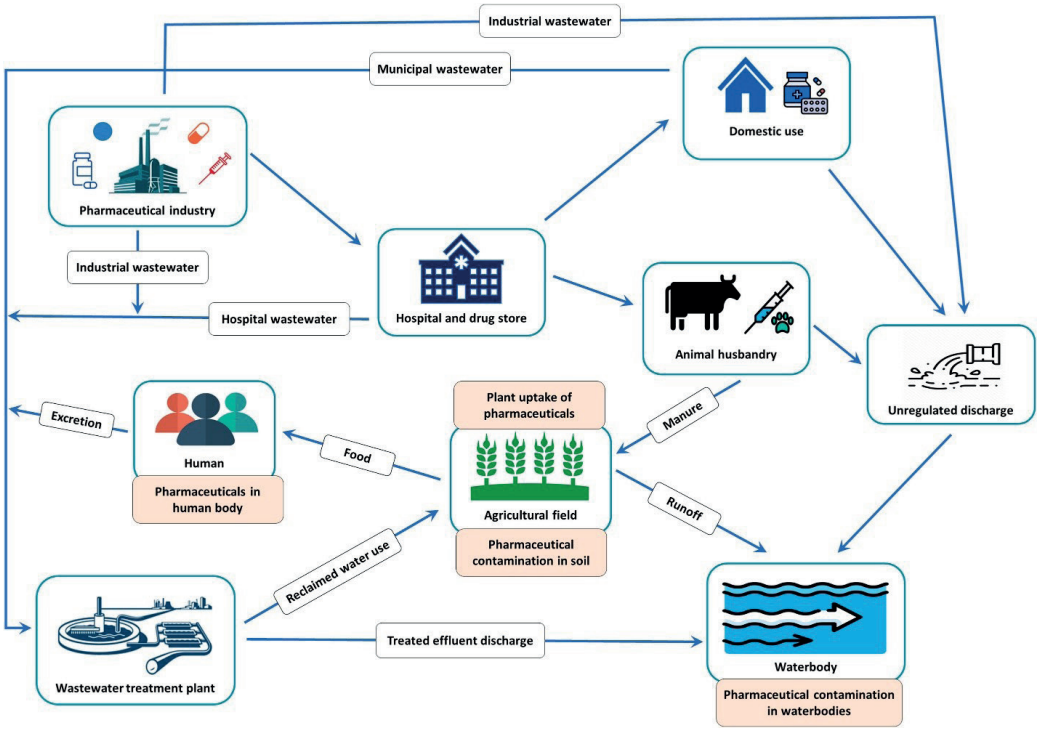

Figure 1. The pharmaceutical pathways eventually make their way into the environment; the route includes pharmaceutical industries, hospital wastewater, domestic wastewater, WWTP's effluents, Agricultural fields etc (Mosharaf et al., 2024)

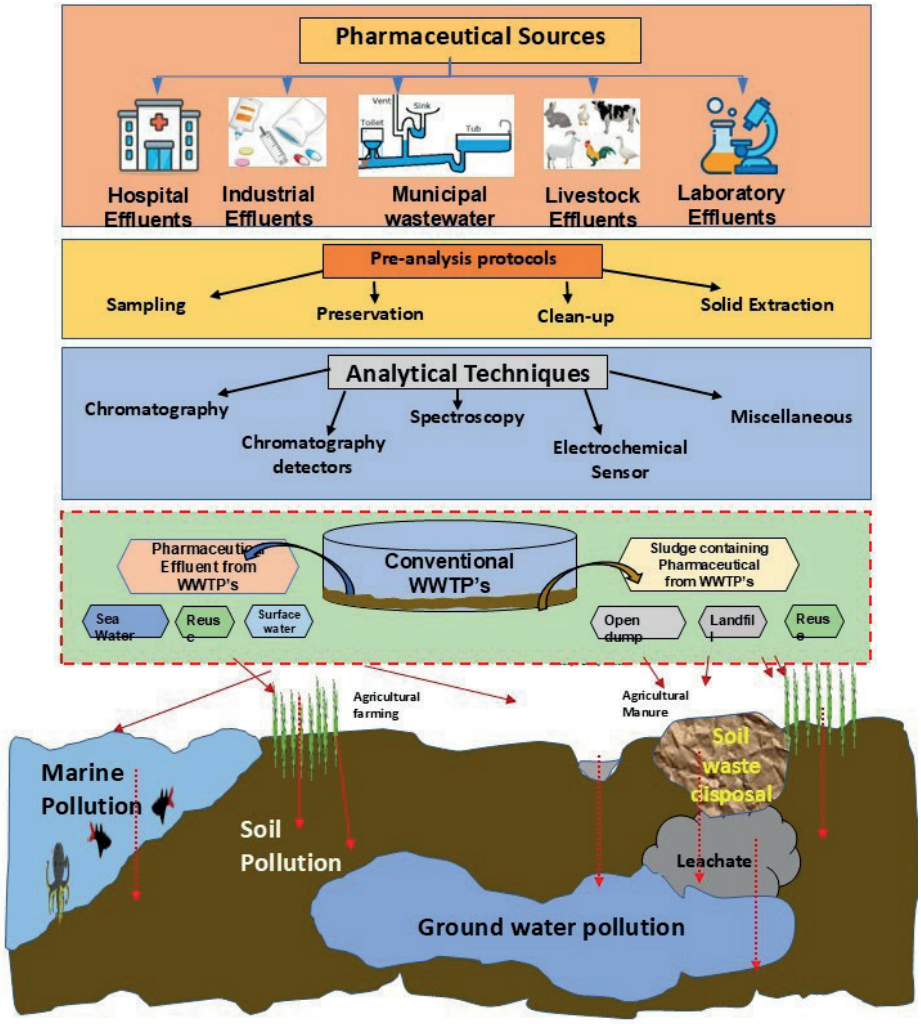

Figure 2. The diagram illustrates the journey and detection of pharmaceuticals in the environment, from their sources to their eventual impact, and the methods used for their analysis

(ASP), membrane bioreactors (MBBR) (Khan et al., 2022a; Dolar et al., 2012), and microbial treatment) are commonly suggested as a substitute for HWW treatment. AOPs have been studied to remove various pharmaceuticals from hospital wastewater (Patel et al., 2019; Khan et al., 2021). Several research works have reported adsorption-based processes (Ghosh et al., 2023; Singh et al., 2023; Khan et al., 2022b). However, these treatment methods successfully degrade various ECs; their high operating costs and complexity inhibit them from being employed at full-scale treatment plants.

5. Current guidelines to control Pharmaceutical pollution

Currently, there are no specific guidelines in place to control the concentrations of pharmaceutical compounds in the environment (Fig. 3). Several researchers, international organizations, and government authorities have acknowledged that there is a need to set strict guidelines or strengthen existing laws for the treatment and monitoring of effluent from hospitals and pharmaceutical industries. However, it can only be possible by mutual collaboration between governments and industries to encourage and support a tough attitude towards law enforcement, especially in developing countries. This section provides a detailed discussion of several international guidelines/regulations/policies/legislation/ recommendations, as well as highlights the difficulties and suggests amendments concerning pharmaceutical pollution.

5.1. WHO guidelines

The WHO published several guidelines in 1958 based on drinking-water quality. In 2004 (3rd edition of WHO Guidelines for Drinking-Water Quality), the decision was made after several editions to seek further expansion of the guidelines addressing health-based issues on water quality, neglecting micropollutants concern (WHO, 2003). However, the 4th edition of the WHO guidelines introduces concern over pharmaceuticals in wastewater excreted via humans, direct disposal, and agricultural runoff that have the potential risk to drinking water (WHO, 2004). The WHO released a study in 2011 that evaluated the presence of pharmaceuticals in drinking water (WHO, 2011). This WHO document comes to the conclusion that there is relatively little risk, even though limited data makes analysis challenging. This recent edition reviews assessments of pharmaceuticals in drinking water through the acceptable daily intake (ADI), exposed as the point of departure (PoD) (WHO, 2017). As drafted in the WHO Guidelines, the ADI scrutinizes the subsequent measures needed to mitigate risk factors. As a result, uncertainties exist, notably concerning the molecule's highly active nature, mixing effects, and long-term chronic impacts at lower concentrations. These issues should be looked into further to see if the current exposure poses a potential risk.

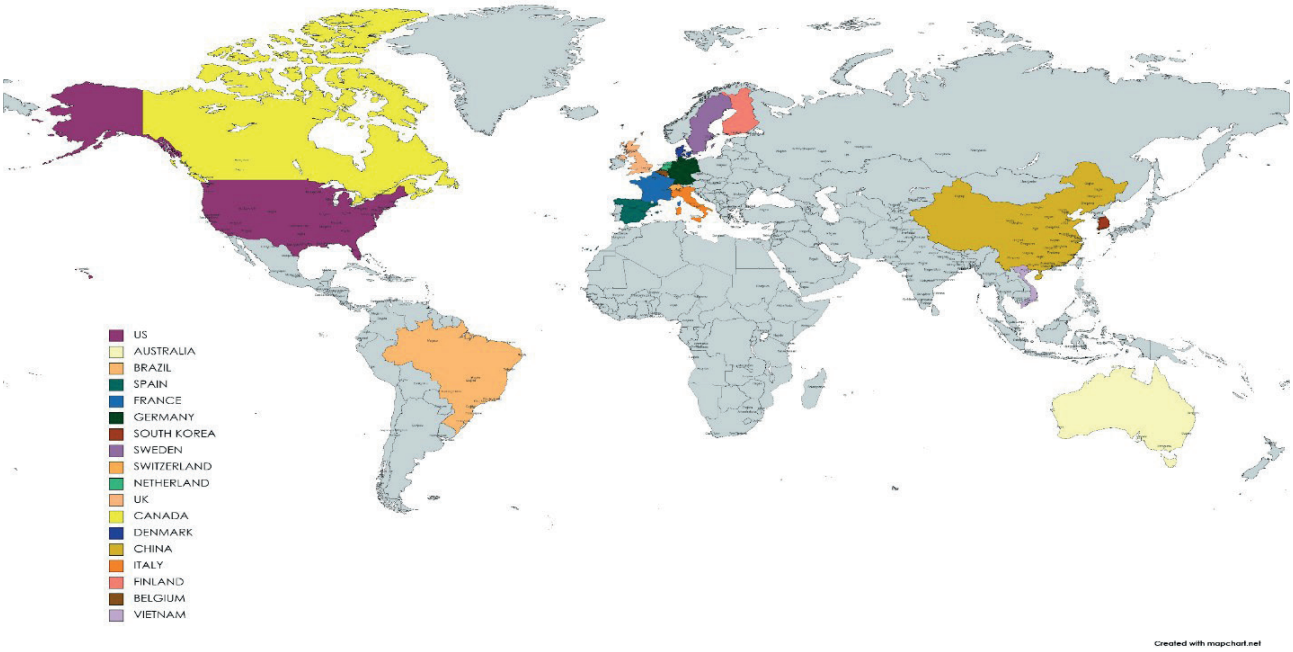

Figure 3. Worldwide Implementation of Legislation/ Law for HWW and availability of on-site treatment facilities in different countries of the world (NWQMS, 2008; OECD, 2019; Gagnon, 2009; Kleywegt et al., 2007; Carraro et al., 2018; UBA, 2015; EEA, 2010; EU, 2007; SR, 2016; FOEN, 2015; Miarov et al., 2020; EPA, 1995, 2010; Snyder et al., 2007). Custom map courtesy of mapchart.net (www.mapchart.net)

5.2. EPA guidelines

The United States Environmental Protection Agency (USEPA) enacted a series of environmental laws: the Safe Drinking Water Act of 1974, the Toxic Substances Control Act of 1976, and the Clean Water Act (CWA) of 1972. These laws were made as a foundation for regulatory decision-making in order to analyze hazards to public health and the environment. On June 11, 2003, the EPA took provisions of the effluent guidelines and pre-treatment standards for the Pharmaceutical industries (EPA, 2003). The CWA requires the EPA to establish pretreatment regulations to limit pollutant emissions from WWTPs that release wastewater indirectly through sewers (EPA, 2006).

The EPA develops recommendations and regulations for effluent limits in order to impose the lowest degree of treatment for effluents released from industries. The EPA draws its effluent standards and regulations from the demonstrated model plant and treatment technologies that are performed efficiently and economically viable for industries. However, EPA does not require the adoption of specific technology. To meet the criteria, dischargers are permitted to employ any applicable control approach.

5.3. EU guidelines

The European Union (EU) has established numerous directives and regulations addressing water management and the control of emerging pollutants (EPs) within its water policies. Among these, the Water Framework Directive (WFD) represents the cornerstone of EU water legislation, aiming to achieve and maintain good water quality across all member states. Implemented in 2002, the WFD set progressive targets for attaining 'good' ecological and chemical status of surface and groundwater bodies by 2015, 2021, and 2027. The directive outlines specific objectives and provides methodological frameworks for assessing and improving water quality, with a particular focus on rivers and other surface waters. Furthermore, the latest amendment (Directive 2013/39/EU) introduced updated priority substances and strengthened measures for monitoring and controlling chemical pollution in aquatic environments. Several crucial regulations imposed by European legislation in water politics in the current scenario are as follows:

1. EU Water Framework Directive (2000/60/EC)
   (1) (2008/105/EC) (EC, 2020)
   (2) (2013/39/EC)
2. Marine Strategy Framework Directive (2008/57/EC)
3. Drinking Water Directive (98/83/EC)
4. Groundwater Directive (GWD) 2006/118/EC
5. Urban Wastewater Directive (91/271/EC)
6. Surface water Directive (75/440/EEC)
7. Pharmaceutical products for human use Directive No. 2004/27/EC
8. Veterinary pharmaceutical products Directive No. 2004/28/EC
9. Industrial Chemicals Directive (REACH)
10. Industrial Emission Directive (2010/75/EU)

In addition, several legislative measures regulate the marketing and use of chemical substances, which play a crucial role in achieving good water quality and safeguarding environmental and human health. Figure 4 provides some EU open data sources engaged with ECs.

5.4. Australian guidelines

The Australian Guidelines for Water Reuse were established to provide a reliable standard for utilizing reused sewage, grey water, and stormwater to supplement sources of drinking water. These guidelines were developed in two phases, viz, Phase 1: guidance for water reuse other than drinking and environmental flows, and Phase 2: an extension of Phase 1 guidelines for the Augmentation of Drinking Water Supplies. These guidelines are concerned with water sources, pre-treatment, and augmenting drinking water sources. In addition, set up guidelines to screen reused water against microbiological and chemical hazards, including pharmaceuticals (NWQMS, 2006; NWQMS, 2008).

5.5. OECD recommendations

According to the OECD (2019) report presents policy guidelines for reducing pharmaceuticals in freshwater, thereby minimizing the threats it pose to human and environmental health (OECD, 2019). Several actions and strategies also contribute to achieving the objectives outlined in the *Strategic Approach to Pharmaceuticals in the Environment*. The OECD has set the following four proactive measures for managing pharmaceuticals in the environment at a low cost. For these initiatives to be successfully carried out, all parties involved and decision-makers must work together in conjunction with a complete life-cycle system. This life-cycle system encompasses the whole pharmaceutical chain, and includes the phases of design, authorization, manufacturing, prescribing, retail distribution, patient and farmer consumption, collection, disposal, and wastewater treatment (OECD, 2019).

6. Challenges

Based on the above discussions, it is clear that many developing countries lack strict regulations. Even many devel-

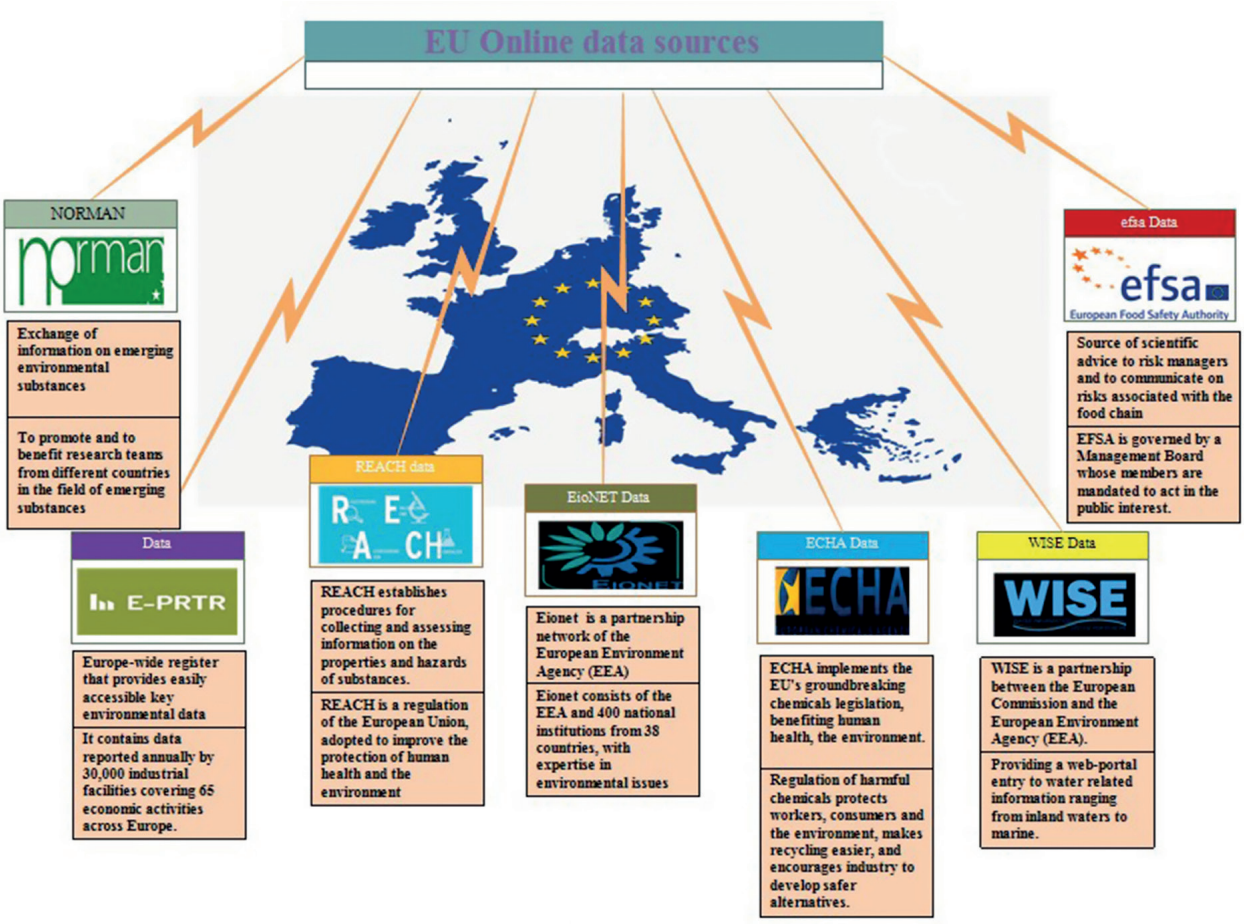

Figure 4. Illustration of major EU open data sources and information dealing with emerging pollutants (Logos are displayed for identification and referential purposes only)

oped countries still have not implemented any regulations for pharmaceutical residues. However, the EU, EPA, and WHO initiated many regulations, particularly regarding HWW effluents. Despite these encouraging efforts, strict legislation/laws remain missing for the on-site treatment of pharmaceutical residues and are only limited to monitoring and treatment on urban-scale WWTP's systems.

Furthermore, analytical analysis of pharmaceutical pollutants is a challenging task due to a pool of pharmaceutical compounds; their identification is difficult due to their derivatives and metabolites; occurrences in water matrices, and their derivatives with varying contamination loads. In addition, the absence of established procedures, guidelines, and reference materials only adds to the complexity of the analysis, particularly regarding the possible interferences of different components with similar physicochemical properties in varying concentrations.

A conceptual approach proposed by Ayres & Braithwaite (1992), regarding responsive regulation that triggers a regulatory response. The authors proposed that regulation be sensitive to industrial structure since different phases will support varying degrees of control (Ayres & Braithwaite, 1992).

7. Conclusion and Future Outlook

The detection of pharmaceuticals in the environment, even at very low concentrations, indicates a very likely risk to human health. The current advances and future research could pave the way for efficient treatment procedures (such as pre-treatment at point sources) for pharmaceutical effluents. However, the implementation of strict guidelines concerning effluent standards can reduce the pharmaceutical residues entering the aquatic environment. In addition, encouraging takeback programs, guidance, and comprehensive consumer instruction will enhance efforts for the proper discharge of pharmaceuticals and minimize the impact on our environment.

Although the literature on the occurrences, treatments, and guidelines for pharmaceutical wastewater is growing,

notable development has already been attained. The following future needs so far are essential:

- Treatment efficiency is a major concern for pharmaceutical pollutants. Future studies should explore innovative or upgraded conventional treatment units or the application of hybrid treatment, considering economic and environmental costs.
- The lack of legislation or legislation implementation, and the lack of information/understanding regarding the behavior and ecotoxicology of all the transformation products (Fent et al., 2006).
- It should be emphasized that wastewater treatment in centralized sewage plants requires upgrading. Moreover, it should be made mandatory and legally binding for hospitals to implement on-site or pre-treatment facilities.

Conflicts of interest

No potential conflicts of interest associated with this present study.

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