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Review Article

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A Review on Occurrence, Risk Assessment and Removal of Pharmaceuticals in Hospital Effluents

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Abstract Hospital effluents contribute to pharmaceutical contamination in the environment, a global issue of grave concern because of the hazards it poses to organisms. Insights about the occurrence, risk and remediation of such contaminants will set the stage to combat this menace. This paper therefore provides review on the occurrence of pharmaceuticals in hospital effluents, the environmental risks they pose, and their remediation. It highlights the occurrence and fate of pharmaceuticals in hospital effluents, analytical determination of pharmaceuticals in effluents samples and the removal of pharmaceuticals in hospital effluents as proposed in 156 scholarly sites and databases within the years 2013 to 2024 using keywords like hospital effluents, pharmaceuticals, analytical determination, environmental risk assessment and treatment. The pathways of pharmaceuticals to and from the hospital effluents have been established. There are diverse and evolving methods for determination of pharmaceuticals in effluents; the choice depends on objective for analysis and availability. The concentrations of pharmaceuticals in hospital effluents are minute and depend on their properties, season and ecological processes. Risk levels of pharmaceuticals depend on type of effluent, seasonal variation, organism and its use. Certain single secondary or tertiary treatment options or their combination are capable of removing pharmaceuticals in hospital effluents. Non-conventional treatment options are cost effective, eco-friendly and sustainable. Studies to ascertain the risk posed by pharmaceuticals in hospital effluents are required to inform policies necessary to regulate the management of hospital effluents.

Keywords Pharmaceuticals · Hospital effluents · Analytical determination · Treatment · Environmental risk assessment

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Introduction

Pharmaceuticals occur in the environment posing as threats to the ecosystem, wildlife and humans. Reports have been made about their adverse effects on growth, behaviour and reproduction of some aquatic species; though such effects are related to the class of pharmaceutical (European Commission, 2019; OECD, 2019; Gencer Balkis et al., 2024). There is the possibility of bioaccumulation and bio concentration of certain pharmaceuticals along the food chain. The long-term effect on humans may be the development of drug intolerance and pathogenic antibiotic resistance aside toxicity. They have therefore been tagged as chemical contaminants of emerging environmental concern which demand prompt or immediate attention because their pharmacological effect at low concentrations, stability and persistence (Kusturica et al., 2022; Shahid et al., 2021; Yadav et al., 2020; Deryal et al., 2024, 2025). Report on monitoring, occurrence, fate, environmental risk, and safe disposal are some of the proactive measures outlined by European Commission (2019) and OECD (2019) to deal with the menace. Thus, identifying the risk posed by pharmaceuticals and preventing their entry into the environment are possible ways of addressing this issue. Treatment of pharmaceutical waste at the source or site of contamination before disposal can be a way of preventing its entry into the environment.

Hospital effluents have been identified as sources of pharmaceutical contamination in the environment (BUND, 2020; Niemi et al., 2020; Stenuick, 2021; Vaudreuil et al., 2022). Pharmaceuticals and their metabolites get into hospital effluents mainly through excretion after consumption, and disposal; and subsequently contaminate water bodies when untreated or when treatment is not aimed at the constituents' pharmaceuticals (Niemi et al., 2020; Serna-Galvis et al., 2022). Since hospital effluents serve as sources of pharmaceutical residues in the environment, determination of their pharmaceutical contaminants, the risk they pose, and their treatment can be pragmatic ways of management. Subsequently, there has been suggestions of such studies on hospital effluents for in-depth knowledge (Munzhelele et al., 2024; Serna-Galvis et al., 2022). When hospital effluents are not discharged according to the guidelines and standards by environmental regulatory bodies, they become a worrying issue (Kumari et al., 2020). Thus, this review focuses on studies on the determination of pharmaceuticals in hospital effluents, their environmental risk assessment and remediation.

Materials and Methods

The study reviews the occurrence and fate of pharmaceuticals in hospital effluents, analytical determination of pharmaceuticals in environmental matrices such as hospital effluents, and the possible means of their remediation since pharmaceuticals are regarded as emerging contaminants. Information was sourced from about 156 articles, guidelines, and reports within the years 2013 to 2024 using keywords like pharmaceuticals, hospital effluents, analytical determination, environmental risk assessment, treatment of hospital effluents, and removal of pharmaceuticals. Databases and scholarly sites that were searched for relevant information included Elsevier, Springer, Hindawi, PubMed, Google Scholar, ResearchGate, Academia, Scopus, and other sources such as institutional repositories, books, etc.

Occurrence and Fate of Pharmaceuticals in Hospital Effluents

Occurrence of Pharmaceuticals in Hospital Effluents

Effluent simply means wastewater, and is defined by the United States Environmental Protection Agency (US EPA, 2018) as treated or untreated wastewater often discharged into aquatic environments; hence hospital effluent connotes wastewater from hospitals. Hospital effluent or wastewater is the residual collection from medical and non-medical activities or services like diagnosis, first-aid, surgery, laboratory examinations, laundry, and drug dispensing (Orias, 2015), which involve the use of water in a hospital. It is considered as toxic liquid discharges composed of micro-pollutants (microorganisms, radioactive elements, and toxic chemicals); and macro-pollutants (Biochemical Oxygen Demand, Chemical Oxygen Demand, Total Nitrogen, Total Organic Concentration, carbonates, and phosphorus); thereby presenting biological, chemical, and physical risks or danger (Carraro et al., 2016; Fatimazahra et al., 2023). Pharmaceuticals are micro-pollutants, as they are considered as chemicals detected at concentrations of ng/L to µg/L (Azuma et al., 2016). Comparatively, hospital effluents have higher concentrations of pharmaceutically active compounds (PhACs) and their metabolites (Balakrishna et al., 2017; Chonova et al., 2016; Prabhasnkar et al., 2016; Souza & Féris, 2016; Vieira et al., 2021). Additionally, Health Care Without Harm, Europe (2021) points out that hospital effluents rather add to the concentrations of specialized pharmaceuticals like cytostatic drugs, certain antibiotics, and X-ray contrast media, which bear higher environmental risk.

As shown in Figure 1, pharmaceuticals get into hospital effluents through excretion (urine and faeces) after consumption as confirmed by Al Aukidy et al. (2014) and Moratalla et al. (2022); and disposal from hospital services. Hospital services also contribute to the pharmaceutical contaminants of hospital effluents (Orias and Perrodin, 2014)

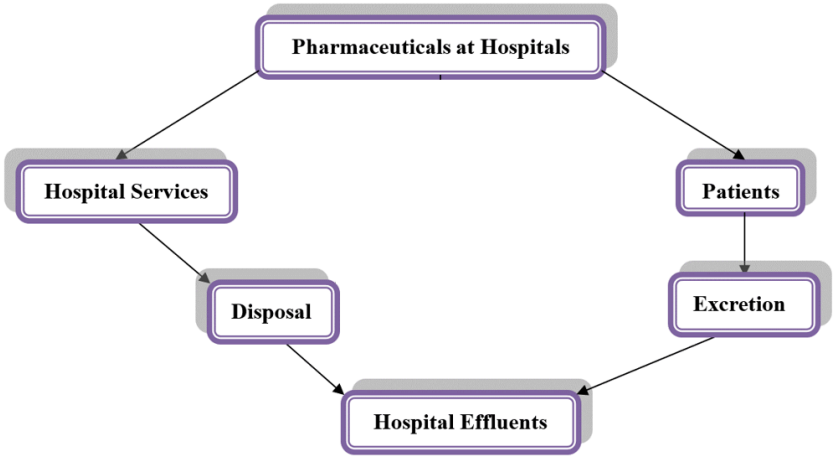

Figure 1. Pathway of pharmaceuticals from hospitals to effluents Source: Authors' Construct, 2022

as a study by Akin (2016) revealed that wastewater generated from laboratory service increases the pharmaceutical contamination of hospital effluent. This has deepened concerns about the presence of pharmaceuticals and their derivatives in aquatic environments as they serve as sinks or reservoirs for hospital wastewater. Concentrations of pharmaceuticals in hospital effluents depend on the population and the size of the hospital (Al Aukidy et al., 2017); the type and the use of drugs prescribed, the range of activities, season of year, and time of day (Fedaku et al., 2019). Thus, big hospitals produce more and wider range of pharmaceutical residues as they have a number of specialized wards like maternity, psychiatric, paediatric wards, confirming a report by Oliveira et al. (2017) that the occurrence of classes of pharmaceuticals depends on the healthcare services available at the hospital.

Different classes of pharmaceuticals have been detected in hospital effluents. Mendoza et al. (2015) identified the presence of acetaminophen, diclofenac, ibuprofen, and naproxen (non-steroidal antic-inflammatory drugs-NSAIDs); furosemide (diuretic); clarithromycin, ofloxacin, and trimethoprim (antibiotics); propranolol (β-blocker) and prophyphenazone (anti-inflammatory) in hospital wastewater from a medium-size hospital in Spain (DrugBank, 2006; MedlinePlus, 2021). In Greece, Papageorgiou et al. (2019) reported on the occurrence of diclofenac, ibuprofen, and paracetamol (NSAIDs), salicylic acid (analgesic derivative); amoxicillin, ampicillin, azithromycin, and clarithromycin (antibiotics); irbesartan, telmisartan, and valsartan (anti-hypertensives); atenolol, metoprolol and pindolol (beta blockers); furosemide (diuretic); carbamazepine (anticonvulsant); citalopram, and venlafaxine (antidepressant drugs); and caffeine (stimulant) in hospital effluent (DrugBank, 2006; MedlinePlus, 2021).

A comparison of the two reports shows that the occurrence of pharmaceutical residues in hospital effluent is increasing rendering hospital effluents more toxic. However, some classes seem to be more rampant in hospital effluents than others as Santos et al. (2013) have shown that analgesics and antibiotics are the most detected pharmaceuticals in hospital effluents and Kosma et al. (2020) have declared antibiotics as the most identified class of pharmaceuticals in hospital effluents. Consequently, in their review, Majumder et al. (2021) declared analgesics and antibiotics as the most prevalent pharmaceuticals in hospital effluents. This is evident in Table 1 which shows the maximum concentrations of commonly used pharmaceuticals detected in hospital effluents. Carbamazepine had the highest concentration, followed by acetaminophen, atenolol, caffeine, sulfamethoxazole, ciprofloxacin and then naproxen, all of which were detected above 100 µg/L.

The occurrence of pharmaceuticals in hospital effluents has been identified in a number of developed and developing countries (Amoaei et al., 2015; Beek et al., 2016); making the issue a global concern. In their review, Fekadu et al. (2019) identified diclofenac, ibuprofen, paracetamol (analgesics); naproxen (anti-inflammatory); venlafaxine, clarithromycin (antibiotics); sulfamethoxazole, carbamazepine, trimothoprim and ketoprofen as the ten most frequently detected pharmaceuticals in Africa and Europe. Hospital effluents, therefore, serve as major sources of pharmaceutical contamination of the environment.

Fate of Pharmaceuticals in Hospital Effluents

Pharmaceuticals occur in hospital effluents at very low concentrations with varied dissolubility, stability, and degradation properties (Akin, 2016). They can be broken down by sunlight (photo-degradation) (Paíga et al., 2019;

Reis et al., 2019); or by high temperatures or removed by geological environment (Rozman et al., 2015); or degraded by hydrolysis or ultraviolet radiation (Caban et al., 2015); and their concentrations can be reduced through dilution

Table 1. Maximum occurrence of pharmaceuticals in hospital effluents

Pharmaceuticals		Concentration (µg/L)
Class	Compound	
NSAIDs	Caffeine	902.00
	Ibuprofen	71.30
	Acetaminophen	1510.00
	Diclofenac	3.59
	Phenazone	0.82
	Naproxen	123.00
	Ketoprofen	20.00
Analgesic (opioid)	Tramadol	16.63
β-blockers	Atenolol	919.00
	Metoprolol	4.59
	Propranolol	3.80
Antibiotics	Azithromycin	11.63
	Ciprofloxacin	179.00
	Clindamycin	32.09
	Erythromycin	15.00
	Metronidazole	1.14
	Norfloxacin	3.85
	Sulfadiazine	13.00
	Sulfamethoxazole	198.53
	Trimethoprim	50.00
	Clarithromycin	17.00
	Rexithromycin	7.50
	Oxolinic acid	3.00
	Ofloxacin	78.85
	Enoxacin	2.00
	Sulfamerazine	18.00
	Tetracycline	3.00
	Amoxycillin	1.00
	Penicillin G	1.00
	Oxacillin	1.00
	Trimethoprim	22.50
	Vancomycin	7.40
Antifungal	Econazole	0.02
Anesthetics	Lidocaine	0.16
Proton pump inhibitor (GERD)	Omeprazole	5.06
Short-acting β2-agonist (SABA)	Salbutamol	0.78
Anticonvulsants/ benzodiazepines	Carbamazepine	7008.00
	Gabapentin	17.83
	Lorazepam	5.11
	Primidone	0.02
	Oxcarbazepine	1.59

Pharmaceuticals		Concentration (µg/L)
Class	Compound	
Angiotensin-converting enzyme/receptor blocker/ HMG-CoA reductase inhibitor/ Calcium channel blocker/Crestor	Enalapril	0.56
	Atorvastatin	6.79
	Irbesartan	0.05
	Losartan	34.81
	Valsartan	0.16
	Amlodipine	0.30
	Rosuvastatin	0.10
	Fluvastatin	1.85
Antiparasitic	Levamisole	3.09

Source: Afsa et al. (2020), Alkahtani et al. (2024), Al Qarni et al. (2016), Ashfaq et al. (2017), Hernández-Tenorio et al. (2021), Nasri et al. (2024), Olvera-Néstor et al. (2016), Serna-Galvis et al. (2022), Ulvi et al. (2022), Wiest et al. (2018)

by rainfall. Though active pharmaceutical ingredients (APIs) may persist since they are meant to withstand degradation (Alfonso-Muniozguren et al., 2021; Maghear, 2018); the primary contaminants can occur as they are or breakdown at different rates to form their derivatives or metabolites depending on seasonal factors like light, rainfall and temperature as well as their nature and processes of the earth. Consequently, Reis et al. (2019) have reported on seasonal variations of concentrations of pharmaceuticals while Kosma et al. (2020) in their study showed the occurrence of antibiotics in their original state or broken down to their derivatives in hospital effluents. Similarly, salicylic acid being a derivative of aspirin has been detected in hospital wastewater (Kosma et al., 2014). Such derivatives or transformation products can also persist (Lumbaque et al., 2020). A study by Guerra et al. (2014) showed that while antibiotics are very stable and persist, anti-inflammatory drugs easily get biodegraded.

Ulvi et al. (2022) reported of a higher contribution of pharmaceuticals by hospital effluents to municipal wastewaters in winter than summer; an indication of a possible degradation as a result of chemical reactions caused by certain factors as enumerated (Bhangare et al., 2022). The degradation of pharmaceuticals seems to be a complex interaction of factors. One factor of controversy is pharmaceutical structure which may be linked to its properties (Alfonso-Muniozguren, et al, 2021). Thus Verlicchi et al. (2016) reported that some therapeutic groups like sulfonamides and trimethoprim mostly occur in hospital effluents because they are broad spectrum and stable.

Prior to being discharged to the environment (mainly aquatic), hospital effluents are channeled to wastewater treatment plants for removal of contaminants, as shown in Figure 2, in developed countries; whiles in developing countries, treatment is rarely done due to lack of law enforcement and weak institutional policies (Al Aukidy et al., 2017; Esseku, 2016). Most treatment plants cannot effectively remove the pharmaceutical contaminants (Reis et al., 2019; Wu et al., 2015; Ulvi et al., 2022) and thus, they end up in aquatic environment, mainly surface water and subsequently in drinking and groundwater (Reis et al., 2019; Rozman et al., 2015). While some pharmaceutical compounds like diclofenac, naproxen, and propylparaben remain in solution, others like ibuprofen, methylparaben, salicylic acid, and tetra hydrocannabinol get adsorbed to sediments (Carmona and Picó, 2014). As depicted in Figure 2, pharmaceuticals in hospital effluents get into aquatic environments directly or through wastewater treatment plants (Al Aukidy et al., 2017), and then to ground and drinking water or adsorbed on soils (Balakrishna et al., 2017; Gyesi et al., 2022; Kies et al., 2019; Simazaki et al., 2015).

When hospital effluents are discharged directly into an aquatic or soil environment, the constituent pharmaceuticals persist or get transformed depending on the prevailing physico-chemical processes of the recipient environment. Thus, hospital effluents affect the state of ground water and the wholesomeness of drinking water whether treated and untreated (Ma et al., 2018). When absorbed by plants or ingested by animals through food or water (Figure 2), they can be digested and metabolized to degradable forms but the fat-soluble ones can bioaccumulate in fatty tissues and biomagnification along food chains (Eapen et al., 2024; Maghear, 2018).

Determination of Pharmaceuticals in Effluent Samples

The steps involved in determination of pharmaceuticals in environmental samples are sample preparation (clean-up and extraction) and instrumental analysis of which sample preparation is of utmost importance because it aids in

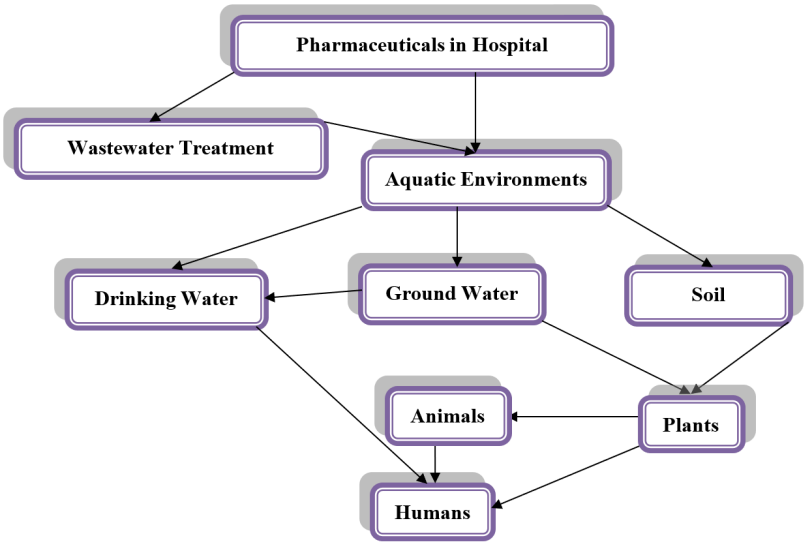

Figure 2. Pathway of pharmaceuticals in hospital effluents Source: Authors' Construct, 2022

extraction of analyte in the most possible high concentrated form and preservation of the stationary phase (Majors, 2015; Sadutto and Picó, 2020).

Sample preparation is also vital in situations where analyte occurs in traces that make detection difficult, thus Pérez-Lemus et al. (2019) emphasize sample preparation as the most critical because of the occurrence of pharmaceuticals at very low concentrations. The aim of sample preparation is to obtain a homogeneous solution which is representative of collected sample for analysis (Agilent Technologies Inc., 2013) and minimize matrix suppression (Pérez-Lemus et al., 2019). There are simple techniques like centrifugation, dilution, filtration and precipitation; little more complex ones like liquid-liquid extraction (LLE) and its miniaturized form, liquid phase micro extraction (LPME), solid phase extraction (SPE); and more complex ones like size exclusion, homogenizing and accelerated solvent extraction among others (Bardsley, 2016). In their review, Pérez-Lemus et al. (2019) specified liquid, microwave, ultrasound, matrix solid-phase dispersion and quick, easy, cheap, effective, rugged and safe as examples of extraction techniques with the two latter ones being very new extraction techniques. Hoi et al. (2020) itemized accelerated solvent, liquid, microwave and solid phase as extraction techniques with the latter being the commonest.

Selection of method for sample preparation is dependent on the physical state of the sample – solid, liquid or suspension as well as their solubility and volatility (Agilent Technologies Inc., 2013). In contemporary times, there is the search for high-speed automated methods of sample preparation as they are estimated to reduce errors during analysis by 50%, duration of analysis and labour in order to achieve quick and precise measurements (Majors, 2015; Poole et al., 2017; Sadutto and Picó, 2020).

Sample preparation is followed by actual analysis which involves method development and validation. The development of method is crucial with regard to pharmaceuticals and involves choosing and optimizing analytical components and conditions (ICH, 2015). The consistency and suitability of the method is achieved by validation which addresses issues of quality and effectiveness of methods like accuracy, precision, linearity, robustness, limit of detection and limit of quantitation (ICH, 2015). Validation ensures that the developed method is reliable and reproducible; and guidelines needed for it are International Council on Harmonization (ICH) guidelines.

Due to the existence of pharmaceuticals in minute quantities, their determination and quantification require very sensitive analytical methods or techniques (Caban et al., 2015). There are a number of analytical methods or techniques used for the determination of pharmaceuticals in environmental matrices. Table 2 presents majority of such techniques. These include titrimetry, chromatography, spectrometry, spectroscopy, capillary electrophoresis among others, and hyphenated (combination of) techniques (Montaseri & Forbes, 2018; Modebrlu & Baby, 2019; Thakur et al., (2021); Wang, 2023; Youssef et al., 2019). Each of these techniques have their advantages and disadvantages. In the quest for efficiency regarding sensitivity, selectivity, time and labour, new analytical methods are developed by reducing sample manipulation and solvent consumption as well employing simultaneous multiple identification (Boulard et al., 2018; Kim et al., 2018; Wu et al., 2021).

Table 2. Analytical methods for determination of pharmaceuticals in environmental samples

Method	Applicability	Advantage	Disadvantage
Titrimetry	Estimation of pharmaceuticals and their metabolites	High precision and robust Saves time and labour Inexpensive No need for reference standard and calibration	Non selective High quantities of samples and reagents Quick and complete reaction of analyte and standard solution needed Lack specificity
Enzyme-linked Immunosorbent Assay (ELISA)	Routine pharmaceutical analysis in environmental samples	Simultaneous screening, saves time, low cost	Determination of one analyte at a time
Chromatography	Pharmaceutical analysis	Versatile, accuracy of separation and detection	Expensive
Gas chromatography	Detection of impurities; Detection of volatile organic compounds; Used in formulation of high-molecular mass compounds like polypeptides and thermally unstable antibiotics Analyzing non polar substances	Accurate detection Quantification of complex mixtures	Comparative non-volatility Derivatization
(GC) Liquid chromatography (LC)	Analyzing polar substances Separation of mixtures	Versatile, sensitive Applicable for very complex mixtures	Matrix effects and insufficient selectivity Several analytical steps needed, time-consuming, and expensive instrumentation
High Performance Liquid Chromatography (HPLC)	Drug formulation Screening and identification of unknown substances and impurities in pharmaceuticals; Quality control and assurance in pharmaceutical industry; Separation of complex mixtures of molecules in chemicals and biological systems for specific role identification	Wide range of mobile phases to choose Flexible for analysis of wide variety of samples Quick separation Short time for analysis Improved reliability High accuracy, precision and specificity	Very expensive (cost of columns and solvents) Lack of long-term reproducibility
Thin layer Chromatography (TLC)	Hydrophilic Interaction Chromatography (HILIC)	Qualitative analysis, forensic use Detection of impuritiesIdentification and separation of components of mixture Improved separation and quantitative measurement Separation of small polar molecules	Small quantities of analyte can be used Minimum sample clean-up High specificity and sample loading capacity Robust, simplistic, fast and versatile High resolution and highly reproducible Good retention
High Performance Thin Layer Chromatography (HPTLC)	Improved separation and quantitative measurement	Robust, simplistic, fast and versatile High resolution and highly reproducible	Sophisticated, time consuming
Hydrophilic Interaction Chromatography (HILIC)	Separation of small polar molecules	Good retention	Complex (involves many reactions)
Spectroscopy	Pharmaceutical Analysis Assay of pharmaceuticals	Fast, inexpensive, non-invasive/non-destructive and applicable both off-line and in-/at-/on-line.	Complexity of interpretation
Ultra violet visible (UV-Vis)	Identification and Non-destructive, chea Small samples required Minimal data processing quantification of molecules	Versatile Non-destructive, no sample preparation required selective	Interference from multiple absorbing species pH and temperature dependent
IR			
Nuclear Magnetic Resonance (NMR)	Qualitative and quantitative determination of molecules Quantitative technique		Expensive, specificity, concentration dependent

Method	Applicability	Advantage	Disadvantage
Mass Spectrometry (MS)	Chemical analysis in food and industries Quantitative pharmaceutical analysis	Sensitivity and specificity of detection Provides structural information and unambiguous detection and quantitation of analytes, high resolution Basis for development of new methods	Expensive
Time of Flight (TOF)MS Spectrophotometry	Structural and composition determination Pharmaceutical formulations	Simple, rugged and high scan speed Unlimited mass range and very high resolution	
Derivative Spectrophotometry	Clinical, forensic and biomedical analysis	Simple, rapid, accurate and high precision Less time and labour consumption, easily adapted and reproducible Popular, cost effective and sensitive	Derivative methods for specific situations
Difference Spectrophotometry	Clinical, forensic and biomedical analysis	Improve sensitivity and selectivity by resolving challenges encountered in combination, stability, degradation, impurity and interference during drug analysis and in biological systems	Spectral Interference
Colorimetry	Clinical, forensic and biomedical analysis	Improved accuracy and selectivity Stability, simple Determination of minute quantities	Dependent on functional groups Specific criteria and time management required
Chromatography with Spectrometry			Very expensive, involves tedious multiple extraction steps and time-consuming
GC/MS		Cost effective	
LC/MS	Pharmaceutical Analysis	Suitable for analysis of polar compounds Rapid analysis, mostly employed High sensitivity, selectivity and robustness	High cost
LC-MS/MS LC-MS/MS HPLC-MS/MS HPLC-HRMS HPLC/UV HPLC/NMR HPLC-TOFMS HILIC-ESI-MS/MS	Extremely polar pharmaceuticals	High sensitivity and retention time	Limited number of compounds
UHPLC-MS/MS	Determination of pharmaceuticals in environmental matrices	High sensitivity and selectivity	
UPLC-MS/MS	Determination of pharmaceuticals in environmental matrices		
UPLC-QqLIT UHPLC-	Determination of pharmaceuticals in environmental matrices		
ESI-QTOF-MS/MS	Determination of pharmaceuticals in environmental matrices	Wide scope target screenining	
Electrochemical	Quantification of specific pharmaceutical using electrochemical modes	Quicker time scale Requires minute quantities (nano liters) of analyte	Sophisticated instrumentation
Voltammetry		Aqueous condition	
Capillary electrophoresis (CE)	Detection of pharmaceuticals in aqueous condition Analysis of small inorganic ions Low molecular weight and chiral analysis of large biomolecules	Quicker time scale, cost effective, Miniaturzed approach Requires minute quantities (nano liters) of analyte Separate a wide range of molecules Versatility, high resolution	Sophisticated instrumentation Poor sensitivity.

Method	Applicability	Advantage	Disadvantage
Capillary zone electrophoresis (CZE)	Separation based on size to charge ratio	Commonly used	
Micellar electrokinetic chromatography (MEKC)	Separation of neutral species	Commonly used	
Capillary gel electrophoresis	Separation of large molecules		
Capillary isoelectric focusing (CIEF)	Separation based on isoelectric points		
Capillary isotachophoresis	Separation based on electrophoretic mobilities		Not commonly used
Diffusive Gradient in Thin film technique (DGT) PEP-2-DGT	In-situ analysis	Accurate and convenient	

Source: Abdulrahman et al. (2021), Abdulrahman et al. (2016), Arvaniti et al. (2023), Basavaiah et al. (2016), Basicmedicalkey (2016), Bernado-Bermejo et al. (2020), Biancolillo and Marini (2018), Elimam et al. (2015), Kaklamanos et al. (2020), Kim et al. (2018), Kim et al. (2018), Li et al. (2020), O'Sullivan-Carroll et al. (2022), Qarah and El-Maaiden (2023), Qarah et al. (2020), Qarah et al. (2016), Qarah et al. (2015), Selim et al. (2016), Shantier (2020), Shantier and Gadkariem (2014), Shantier and Gadkariem (2014), Siddiqui et al. (2017), Tobolkina and Rudaz (2021), Vaudreuil et al. (2022), Voeten et al. (2018), Vumazonke et al. (2020), Wang (2023), Zhu et al. (2022)

Pérez-Lemus et al. (2019) point out that a new efficient way for the determination of pharmaceuticals and personal care products in environmental matrices involves miniaturization and automation of analytical techniques; due to their improved efficiency to determine constituents in environmental samples (Chisvert *et al.*, 2018). Thus new analytical techniques will keep evolving, and the choice of method depends on one's own basis.

Environmental Risk Assessment of Pharmaceuticals

According to the European Medicines Agency (2015), environmental risk assessment (ERA) of pharmaceuticals is the study of the potential effects of pharmaceuticals on the environment and the precautionary measures to be taken. Contemporary ERA procedures have led to the acquisition of more insight into environmental issues and aid in protecting environmental health (Lee and Choi, 2019); thus, managing the environment and making decisions with respect to pharmaceuticals depends on their ERA (He et al., 2020). Though ERA, which includes the ranking of drugs for subsequent monitoring and control measures in the environment, is needed for the management of pharmaceuticals (Oelkers and Floeter, 2019); information on the potential risk of most pharmaceuticals for humans is non-existent because they occur in low concentrations (Gunnarsson et al., 2019; Kusturica et al., 2022). Consequently, Zhu et al. (2019) in their study revealed that the environmental risks of most APIs are not known. Lee and Choi (2019) suggest that risk assessment of active ingredients of drugs should be a preferred option while Han and Lee (2017) add that the metabolites of pharmaceuticals should be considered in the ERA of APIs as they bear equal or higher risk. Again, the ERA of pharmaceuticals should be carried out periodically at intervals of five years as indicated by Pereira et al. (2017).

There are various guidelines or frameworks for assessing the risk of pharmaceuticals; the commonly used one is the European Medicinal Agency (Lee and Choi, 2019; Walter and Mitkidis, 2018). In their review, Berkner et al. (2016) considered the risk assessment of nanopharmaceuticals using the guidelines of the European Union which are based on API though Ågerstrand et al. (2015) had proposed recommendations for improvement of the guidelines. While Pereira et al. (2017) suggest the inclusion of consumption and excretion data for improvement, Lee and Choi (2019) point out that the focus should be on active ingredients instead of the product. Thus, some researchers like Arvaniti et al (2023) used the former proposal. The estimation of the environmental risk of pharmaceuticals is based on aquatic concentrations; as well as the Persistence, Bioaccumulation and Toxicity (PBT) of the pharmaceutical in the EU (EU EMEA, 2024).

Pharmaceuticals depict various levels of environmental risk depending on certain factors like the type of effluent, seasonal variation and organism; with the level of risk being an indication of the degree of attention to be given to a particular pharmaceutical (Aydin et al., 2018; Ulvi et al., 2022). A case in point is the report of a high risk level exhibited by azithromycin and clarithromycin detected in

hospital effluent for algae and fish in winter Aydin et al. (2018) and that of medium and high risk levels shown by atenolol detected in hospital effluents for fish in summer and winter respectively by Ulvi et al. (2022). Risk levels of atenolol detected in municipal wastewater for fish differed. Analgesics and NSAIDs like paracetamol, naproxen, ibuprofen, diclofenac and amlodipine detected in hospital effluents have been found to pose various levels of risk to daphnia, fish and algae (Ashfaq et al., 2017). With the exception of amlodipine, all the afore mentioned analgesics and NSAIDs together with the following antibiotics - clarithromycin, ofloxacin and trimethoprim and the β-blocker, propranolol found in hospital effluents showed high risk (Mendoza et al., 2015). Even when risk of pharmaceutical detected is negligible, precautionary measures need to be taken since risk can rise as a result of continuous or increased use. Thus, there is a relationship among the use, occurrence and risk of pharmaceuticals. According to Carvalho et al. (2014), caution should be taken when assessing the risk of a number of chemicals occurring at a time due to the cocktail effect and synergistic interaction, though the latter is regarded as less important (Cedergreen, 2014). Though Claessens et al. (2013) have reported on the non-existence of risk posed by pharmaceutical mixtures, recent study by Spilsbury et al. (2024) revealed that such mixtures can exhibit considerable environmental risk.

Removal of Pharmaceuticals in Hospital Effluents

Hospital effluents are subjected to co-treatment, special treatment and/or direct disposal into the environment (Al Aukidy et al., 2017). The strategies used in managing hospital effluents include segregation, collection, handling, transportation, treatment, and disposal; and treatment technologies employed can be off-site or on-site conventional treatment (Wiafe et al., 2016). On-site treatment seems preferable for treatment of hospital effluents since the constituent contaminants including PhACs can be removed before the effluents get into the environment (Al Aukidy et al., 2017). Timraz et al. (2017) have suggested on-site treatment for the management of emerging contaminants and Paulus et al. (2019) reported on its efficiency in the removal of antibiotics and reduction of antibiotic resistance genes.

Diverse technologies which may be physical, biological and chemical processes or their combinations have been employed for the treatment of hospital effluent with the aim of removing the constituent pharmaceuticals (Ghime and Ghosh, 2020; Kanakaraju et al., 2018). Physical processes include grit removal, sedimentation and skimming (Crini and Lichtfouse, 2018; Gangaraju et al., 2021). Sludge obtained can be taken through processes like aerobic or anaerobic digestion (biological processes like biofiltration, activated sludge, or oxidation pond), and disposed (by incineration or as leachate at land filled) or reused as fertilizer, or recycled to obtain other products (as in the concept of circular economy (Gangaraju et al., 2021; Marin and Rusănescu, 2023; Nguyen et al., 2022). Chemical processes include the use of chemicals for treatment such as adsorption, chemical precipitation, neutralization and disinfection by chlorination as tertiary wastewater treatment options (AOS Treatment Solutions (2018).

Majumder et al, (2021) and Stanbury et al. (2017) recommend tertiary (chemical and disinfection) treatment which involves adsorption, ozone treatment, UV treatment for treatment of hospital effluents due to the nature of their constituents. Advanced oxidation processes (AOPs) are regarded as efficient for the removal of a number of classes of pharmaceuticals (Mansouri et al., 2021; Verlicchi et al., 2015). Among such processes are photo-Fenton process, ozonation and reverse osmosis have been confirmed as efficient for the removal of various pharmaceuticals and the reduction of antibiotic gene resistance (Khan et al., 2023; Paulus et al., 2019; Rodríguez-Serin et al., 2022; Verlicchi et al., 2015). Additionally, Khan et al. (2023), Rodríguez-Serin et al. (2022) and Verlicchi et al. (2015) have indicated membrane bio-reactors (MBR) and activated sludge as the suitable secondary treatment options for removing pharmaceuticals from effluents. Electrochemical process has shown partial removal (Ensano et al., 2017). Some researchers like Khan et al. (2023) and Mahtab and Farooqi (2022) have emphasized the need for an integrated method for optimum removal. There are advanced technological means of total removal of pharmaceuticals in effluents like dielectric barrier discharges proposed by Mouele et al. (2021) and countercurrent extraction column suggested Rodríguez-Llorente et al. (2023).

The fore-mentioned means of treatment are difficult to manage especially in developing countries due to high cost of capital and maintenance aside the expertise required. Non-conventional treatment is a low-cost and less mechanized form of treatment that relies on naturally occurring processes, and is therefore eco-friendly (Fahad et al. 2019). Examples are constructed wetlands, oxidation ditches, and waste stabilization ponds. A review by García et al. (2020) indicated that constructed wetlands are capable of removing emerging contaminants like pharmaceuticals and their derivatives. It requires low capital investment and running cost in addition to being sustainable and environmentally friendly (Almuktar et al., 2018; Stanbury et al., 2017). The conclusion drawn by Dires et al. (2018) in their study showed that constructed

wetland is a cost-effective way of disposing of hospital effluents that can be considered in developing countries.

Conclusion

Pathways of pharmaceuticals into the environment via hospital effluents have been established. Once in the environment, their eventual negative impact on ecosystem and human cannot be overemphasized though there are processes that reduce their negative impact. Dealing with this menace involves assessing the risk posed by such pharmaceuticals in the environment and appropriate management of hospital effluents. Estimation of environmental risks of pharmaceuticals involves their quantification. There are diverse and evolving methods for determination and quantification of pharmaceuticals; the choice depends on the objective for the analysis and availability. Concentration of pharmaceuticals occur in minute concentrations and is affected by properties of the pharmaceuticals, seasonal conditions, ecological and geological processes.

Environmental risk assessment is a legal requirement with frameworks and procedure for its estimation to ascertain the risk level of pharmaceuticals as high, moderate and low. The level of risk depends on the type of effluent, seasonal variation, the organism and its use. Management of hospital effluents may be offsite (centralized) involving conventional or non-conventional wastewater treatment or on-site (decentralized) system. It has been established that certain single secondary or tertiary treatment options or their combination or integration are capable of removing pharmaceuticals in hospital effluents. Non-conventional treatment options should be considered since they are cost effective, eco-friendly and sustainable. Studies to ascertain the risk posed by pharmaceuticals in hospital effluents are required to inform policies necessary to regulate the management of hospital effluents.

Developing countries struggle with pharmaceutical pollution from hospital effluents due to weak infrastructure and regulations. Cost-effective, decentralized treatment systems and improved risk assessment can help mitigate environmental and health risks. Non-conventional methods like nature-based solutions and advanced oxidation should be integrated for sustainability. Policymakers must invest in wastewater treatment, enforce regulations, and raise awareness to protect ecosystems and public health.

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