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Impacts of pharmaceutical effluents on aquatic ecosystems

Shola D. Kayode-Afolayan, Eze F. Ahuekwe, Obinna C. Nwinyi*

Department of Biological Sciences, College of Sciences and Technology, Covenant University, Ota, Ogun state, Nigeria

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ABSTRACT

The discharge of raw, contaminated, and inadequately treated pharmaceutical wastewater into water supplies and river channels contribute to short, medium, and long- term environmental and human health impacts. The deterioration and depletion of natural resources exemplified in recipient surface water systems, entirely account for the poor quality of pharmaceutical wastewater effluent. Consequently, to ensure the safety of communities from polluted environments, this review outlines the different anticipated exposure routes to the environment, situates the impact and fate of some pharmaceutical wastes on the aquatic environment. We highlighted some of the current measures for detecting pharmaceutical effluents and the future trends in the treatment of pharmaceutical effluents.

Introduction

Water has found diverse use in domestic, industrial, and agricultural purposes. These have resulted in the release of several unwanted compounds and contaminants into wastewaters [1]. The challenges are commonly observed in agricultural practices where leaching and erosion of topsoils, most of which contain recalcitrant compounds such as polychlorinated biphenyls, glyphosate, organochlorines, and organophosphates are released into the aquatic environment. In addition, industrial discharges of active ingredients from various industries and the disposal of inorganic nutrients and non-degradable organic matter have immensely contributed to the pollution of surface water [2]. These activities have impaired the water cycle, thus, establishing a global concern attributed to their potential long-term impacts on the ecosystems, wildlife, and human health. The occurrence of novel compounds which have been termed as “emerging contaminants" in aquatic ecosystems and wastewaters have been documented. However, there is paucity of knowledge about the existence and fate of these contaminants in the environment [3].

Pharmaceuticals and personal care products comprise of compounds used for therapeutic and esthetic purposes by consumers. Also, these products are utilized for veterinary purposes to improve the health and growth of animals. This has however, amounted to the production of millions of tons of pharmaceutical products on a yearly basis [4].

In recent decades, the presence of pharmaceutical residues in water bodies have been reported around the world [5]. The need to determine the impacts of their bioavailability, persistence, and bioaccumulation across trophic levels in the environment has necessitated the need for more studies. However, existing research indicate that these contaminants pose threats, albeit in substantial concentrations on the environment, animals, and humans [6]. Also, the ease of access to prescription

* Corresponding author.
E-mail address: obinna.nwinyi@covenantuniversity.edu.ng (O.C. Nwinyi).

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drugs, particularly in Europe, has increased significantly over a period of only about 15 years (2000–2015) and this confirms an assertion of significant consumption, mainly due to the enormous growth of the global population, technological advancements, and scientific developments. [7]. Owing to this increase in the consumption of drugs, there is a need for the retrospective analysis of possible environmental impacts when in large quantities.

Drug administration is an important component of animal and human lives. These pharmaceutical products are formulated to exact specific effects on host organisms. These drugs contain organic ingredients that have been historically employed in veterinary and human medicines [8]. When these medicines are unused or become spent and expired, they are disposed-off indiscriminately especially in sinks and lavatories which subsequently end up in leachates, landfills, sludges, and wastewater treatment plants where they pollute aquatic ecosystems and receiving water bodies [9]. The occurrence of antibiotics and their concentrations in the ecosystem affects microbial communities by enhancing proliferation of microorganisms and contributing to the growth of pathogen-resistant antibiotics [10].

In water and soil environments, the presence of these pharmaceutical residues (antibiotics) in the environment distorts the functions and structures of microbial species [11]. The ecotoxicological human health implications as a result of the occurrence and accumulation of these contaminants in water sources are the principal dangers associated with these emerging pollutants [12]. Drug residues and their derivatives can permeate the aquifers, rendering water hazardous for plants, aquatic organisms and even humans [13]. These polluted waters are often employed for irrigational purposes [14]. When these contaminated water sources are used for agricultural purposes, they may contain significant amounts of nutrients and harmful contaminants that are responsible for effecting damage and harm to agricultural products [15].

The appropriate determination and quantification of pharmaceuticals, particularly in environmental samples has proved to be a challenging issue where the analytical methods have not been in existence for many years [16]. Thus, this review paper focuses on the presence of pharmaceutical residues in the environment, its impact on plants, animal and human and the associated fate.

Overview of aquatic ecosystems

The aquatic ecosystem serves as a habitat to communities of organisms that are dependent on each other and their environment. This ecosystem is broadly divided into two; marine ecosystems and freshwater ecosystems [17].

Marine

The marine ecosystem is the largest of all ecosystems [18], and encompasses an approximate of about 70% of the earth's surface and contains about 96% of the world's water. They are responsible for 32% of the world's net primary production [18]. They are distinct from the freshwater ecosystems due to increased levels of dissolved compounds and high salt concentrations in the water. An approximated 84% of dissolved compounds found in the marine ecosystem are composed of salt- sodium and chlorine [19]. Marine ecosystems are divided into zones such as the oceanic, benthic, and intertidal zones and these are depending on their shoreline features and water depth [20]. The oceanic zone is the broad part of the ocean where whales, sharks, and tuna live. The benthic zone is the type of marine ecosystem that is made up of substrates below water where diverse invertebrates live. The regions between high and low tides are the intertidal zones and can also be referred to as the littoral zone [21]. Other zones are the salt marshes, coral reefs, mangrove swamps, estuaries and the lagoons. Hydrothermal vents may occur in the deep water where the base of the food web is formed from chemosynthetic sulfur bacteria [22].

Freshwater

Freshwater comprises of lakes, ponds, rivers, streams, springs, wetlands, and bogs. They are different from the marine ecosystems because of the minimal amount of salt concentration [23]. They include Wetlands, Lotic and Lentic zones.

Wetlands

A wetland is a region where land is covered by water, fresh water, salt water or in-between. Examples of wetlands are areas that are always easily flooded, edges of lakes, and delta mouths of a river. Organic matter, dead trees accumulate in this zone. Aggregates of wood debris serve as habitats for fish, birds and also help in protection of shorelines from leaching and erosion [24]. Wetlands are divided into two subclasses which are the ponds and water reservoirs.

Lotic

The lotic ecosystem also referred to as the riverine ecosystem deals with flowing water ecosystems. They can be any form of constantly moving water, such as rivers, brooks, springs, or streams. Atmospheric gasses, turbidity, dissolved compounds are components of a lotic ecosystem.

This ecosystem consists of two zones: the pools and rapids. The pools are the deep areas of water with aggregates of silt and slower currents, while the rapids are areas where the water moves fast enough to not allow deposition of materials [25].

Lentic

The lentic ecosystem is also referred to as the lacustrine ecosystem and deals with still water ecosystem. Examples are seeps, lakes.

Pharmaceuticals, active pharmaceutical ingredients and effluents

Human therapeutics originated from the utilization of natural products for the treatment of common conditions, the earliest of which came from roots, shrubs, plants, and some fungi [26].

There has been an unprecedented increase of pharmaceutical consumption since its advent in early the 1900′s. The rate at which pharmaceuticals are used is considerably dependent on the pharmaceutical class [27]. Some pharmaceuticals are purchased over the counter, such as painkillers and antibiotics and as a result their usage is likely to be higher compared to prescription drugs.

Novel drugs are perpetually being developed to reduce side effects, improve effectiveness, and enhance specificity [28]. For example, progestins which are used in treating embryogenesis and controlling menstrual cycles were observed to cause masculinization effects which included growth of facial hair in women. This made it necessary for the generation of more effective medications with little or no adverse effects [29].

Pharmaceuticals and active pharmaceutical ingredients

Pharmaceuticals are substances or combination of substances that are administered to animals or human for the purposes of modifying metabolic and physiological functions by applications of immunological and pharmacological actions.

Active pharmaceutical ingredients on the other hand are defined as the active components in a drug and they can also be composed of other ingredients that are biologically active. There are mostly referred to as excipients and are incorporated into many medications to help in absorption and augment solubility [30].

Essentially, pharmaceuticals and APIs are substances that produce biological effects when administered [31]. They are designed to instigate changes in biological functions in humans and animals. Pharmaceuticals are mainly composed of organic molecules that contain hydrocarbon groups, and their molecular structures are made up of hydrophobic and hydrophilic molecules [32].

Pharmaceutical effluent

These are residual by-products generated by pharmaceutical industries during drug production processes. Pharmaceutical effluents are difficult to treat because they are mostly composed of recalcitrant substances such as organic matter (pharmaceutical actives), and inorganic nutrients (phosphates, nitrates, sulphates). Thus, there is no definite treatment technique for the efficient removal of pharmaceuticals, and this contributes to why a cocktail of treatment techniques are recommended [33].

Ecopharmacology

Ecopharmacology is a novel study and an evolving field that deals with environmental pharmaceuticals, and the deleterious environmental impacts posed by lipophilic pharmaceutical actives and their metabolites [34]. Pharmaceuticals may have various impacts on certain organisms in the environment. Up until now, there has been limited information based on the potential of pharmaceutical residues to bioaccumulate in ecosystems and food webs [35]. It has been observed that if certain compounds and actives are distributed within the food web in the ecosystem, it may result in various deleterious effects. For instance, Diclofenac is the most extensively investigated pharmaceutical globally and have been found to accumulate in the prey of vultures [36]. The presence of other studied pharmaceuticals such as phenelzine, venlafaxine and the norfluoxetine and naltrexone metabolites have been detected in fish [37]. Residues of diclofenac and hepatic disease were experimentally replicated by exposing gray-backed vultures to direct-oral feeding of diclofenac-treated livestock [38].

Exposure routes of pharmaceutical residues to aquatic environments

Sewage and hospitals

Effluent from sewage is regarded as a significant source of various pharmaceutical products and their metabolites into the aquatic ecosystem. Degradation efficiency for pharmaceuticals in wastewater treatment plants vary between < 10 to ≤ 100 percent and this is dependent on the physicochemical characteristics and the treatment technology employed [39]. Human pharmaceuticals found in sewage can come from indiscriminate disposal by patients, discharge from hospitals, and in most cases, disposal of wastewater used for production of pharmaceuticals [40]. Sewage can be deposited into marine environments through coastal and estuarine outflows for wastewater treatment plants combined with sewer overflows through rivers that collect the effluents from the wastewater treatment plants [41]. For example, China's Yangtze River carries sewage from 450 million people into the sea and discharges an approximate 172 tons of pharmaceuticals each year [42].

Also, sewage can be disposed from vessels into the coastal waters. Commercial ships can be employed to discharge already treated sewage into large waterbodies (oceans and seas) 5 nautical miles from the nearest land, and untreated sewage can be discharged at approximately 15 nautical miles away from any terrestrial settlement [43]. Since small boats may not undergo any treatment before discharge, they may be implicative as a point source of antibiotics in waterbodies.

One of the major problems posed by the discharge of pharmaceuticals is the reliance of some individuals especially in rural settlements on these water sources for drinking and domestic purposes [44]. For instance, in Spain, there has been the problem of reuse of reclaimed wastewater for irrigational purposes that resulted in pharmaceutical contamination in some parts of Spain [45]. The contamination of these waterbodies can lead to debilitating health effects, and sometimes, death.

Rural and a small percentage of urban areas worldwide rely on sewer systems or decentralized sewage treatment disposal facilities [46]. These systems are probable sources of pharmaceuticals in coastal waters through seepage to groundwater and surface waters, depending on the efficiency of their treatment and the soil capacity [47].

Expectedly, the pharmaceutical actives and metabolites present in hospital wastewater are significantly greater compared to those from municipal effluents. Nevertheless, due to the much lower proportion of wastewater from hospitals in these municipal effluents especially in developed countries, the overall substance flow is much lower [48].

Aquaculture

Universally, seafood production via aquaculture is growing exponentially, with more than 80% of aquaculture based in the Asian continent [49]. A variety of veterinary drugs such as antibiotics, are licensed for human use, and are also employed prophylactically in marine aquaculture to prevent disease outbreaks [50]. A veterinary medicine can lose as much as 70% of the administered therapeutic dose to the immediate environment [51]. Mechanisms in which these drugs are lost include drug excretion from the gills and kidneys of fish, fecal expulsion of drug metabolites, and dispersal of non-ingested pellets [52]. Other aquatic species in the environment such as bigger fishes and sea mammals feed on leftover food and fecal matter from aquatic aquaculture, which inadvertently further distributes pharmaceuticals and their transformation products [53].

In Vietnamese mangroves, unusually high levels of antibiotics of up to 2.5 mg/L were observed in samples collected from shrimp ponds [54]. Practices in aquaculture such as the use of antibiotics differ significantly among countries [55].

Animal husbandry and horticulture

Horticulture and animal husbandry can as well lead to the presence of pharmaceuticals in coastal waters along estuaries and in coastal zones [56]. Antibiotics are incorporated into the drinking water and animal feeds for treating diseases especially in farms where considerable numbers of animals are reared. Although, prohibited in Europe, the use of antibiotics in feed as feed supplements albeit in low doses, still exists in some parts of the world [57]. Some countries encourage the use of antibiotics on crops including rifampicin and trimethoprim [58].

Private households

Expired drugs and their residues are commonly discarded off by means of sewerage from households and may be a prominent route that requires rather urgent attention [59]. This has necessitated the need for legislations across the globe against the disposal of unused or expired drugs [60].

Availability and fate of pharmaceutical substances in the environment

In the aquatic (freshwater and marine) ecosystems, different mechanisms regulate the deposition of active ingredients. Transformation by abiotic approaches such as UV-light degradation, sorption, hydrolysis, sediment solubility, anaerobic and aerobic biodegradation are some of the most principal methods [61].

Depending on the characteristics and composition of the compound used in manufacturing the pharmaceutical product and the characteristics of the environment, it is possible to establish which of the approaches will be the most effective. Aerobic and anaerobic biodegradation, nonetheless, are efficient methods of eliminating pharmaceuticals from polluted sources of water [62]. Diclofenac, for example, has been found in subsequent surveys to biodegrade after 10 days following absorption into sludge. Sedimentation, hydrolysis, and photolysis are strategies that enable drug transformations to take place in wastewater or water treatment plants and sometimes, in surface water [63].

Direct and indirect photolysis is also a primary option for the conversion of pharmaceutical microcontaminants in surface water. Primary photolysis results from direct absorption of sunlight, while natural photosensitizers are necessary for indirect photolysis [64].

Pharmaceuticals can be divided into three principal potential fates:

i The substance is mineralized to water and carbon dioxide, as observed in aspirin [65].
ii The substances are metabolized but still exist in water-soluble forms of the parent compound, and therefore, passes through the wastewater treatment plant and ends up in receiving water bodies and can subsequently impact aquatic organisms if the metabolites are biologically active [66].
iii The polymer is lipid-soluble and not rapidly degradable, so the sludge will sustain a portion of it.

Provided the sludge is spread on fields of farmlands, the compounds contained in the sludge will be able to impact the proliferation of a myriad of microorganisms [67]. Also, the compounds employed for the production of therapeutic drugs and growth promoters in animal husbandry would most likely accumulate and be integrated in animal wastes and ultimately end up as manure [68].

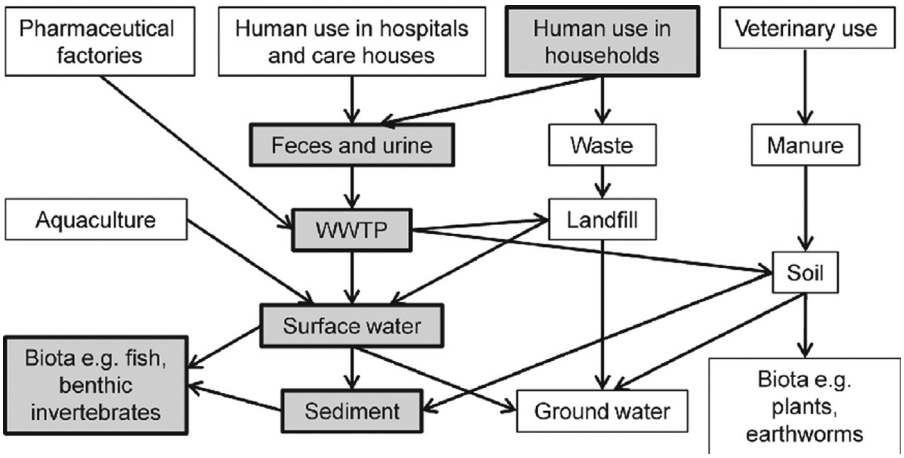

Fig. 1. Exposure of pharmaceuticals in the environment [74].

Across decades, the aquatic environment has accounted for an estimate of about 300 various drugs at levels ranging from trace to relatively substantial concentrations [69]. Moreover, since pharmaceuticals are constantly released into the environment, many of these substances and their metabolites are likely to be accessible to animals and even humans during their entire lifetime [43]. In the aquatic and terrestrial ecosystem, therefore, it is conceivable that pharmaceuticals will also have effects on non-target organisms.

Some pharmaceuticals have previously been closely associated with adverse effects on marine ecosystems and have also been shown to exact specific adverse effects on the health of humans. As they are detected in relatively insignificant concentrations coupled with their low toxicity, it has now been established that other pharmaceuticals, including synthetic and natural hormone products, pose major threats to the aquatic environment [62]. Furthermore, pharmaceutical compounds found in surface and groundwater have also been observed due to the direct or indirect effect of the wastewater [70]. The presence of these contaminants has also been recorded in fish and algae in varying concentrations all over the world [71,72].

There is also widespread concern regarding possible bioavailability, bioaccumulation, and persistence of discharged pharmaceuticals. In addition, pharmaceuticals discharged as combinations also pose serious concerns, since the cumulative health and environmental impacts of pharmaceuticals have remained unknown for a long time [73].

In addition to the potential ecological risks, the long-term consumption of drinking water containing trace amounts of pharmaceuticals can also affect the health of humans. As the chemical compounds in drinkable water are at levels well below those used in therapy, thresholds for the toxicity of most pharmaceutical residues have not yet been defined.

Approximately 180 different drugs from wastewater treatment plants, sludges, surface, and groundwater around the world have been reported (Fig. 1). Ironically, in remote areas in the Arctic, these pharmaceutical compounds have also been detected and quantified [74,75].

The data collected on the concentration levels of pharmaceutical products have been reported for different ecological compartments and various countries [76,77], revealed that psychotropic and control substances such as tramadol, hydrocodone, amphetamine, cocaine (benzoylecgonine), morphine, and methadone (amphetamine) have only in recent time been discovered in surface and wastewaters [71]. Regular and seasonal variations were evaluated and fluctuations in paraxanthine, cocaine, amphetamine and nicotine concentrations were reported, where estimates of intake were established using the total concentrations detected in wastewaters [77].

Case studies of occurrences of pharmaceutical effluents

Sweden has been reported to be one of the leading countries in which large quantities of pharmaceutical residues have been detected in their water sources in modern times, and this was partially due to the existence of a multitude of pharmaceutical institutions [78]. Host to some of the world's best medical research facilities, Sweden's generation of environmental pharmaceuticals has been a big concern for aquatic life (freshwater and marine) and human health for decades, as most of the veterinary pharmaceuticals that were estimated in waterbodies (surface water and ground water) were recorded in Sweden between 1988 and 1994 [79].

The aggregate use of antibiotics persisted in Sweden at estimates of about 40 tons of active substance per year. In 1985 antibiotic use was banned for growth-promoting purposes and was only legislated to be used strictly for veterinary purposes. In 1997, the total amount of antiparasitic drugs was estimated to be approximately 15 tons annually [78]. Before being expelled from the body with urine, medical compounds are initially metabolized to phase I or phase II metabolites and may be exposed to the environment [80]. Phase I reactions primarily involve oxidation, hydrolysis, and sometimes, their metabolites are more hazardous and deleterious than the parent compound. For phase II reactions, conjugation is involved, and it usually leads to the inactivation of compounds [81].

Impacts on aquatic ecosystem

The impacts of pharmaceutical actives on aquatic ecosystems can be divided into two:

i Based on the composition of the pharmaceutical effluent.
ii Based on the toxic effects on aquatic fauna.

Based on the composition of the pharmaceutical effluent

These include the following:

- High content of organic matter (alcohols, acetone)
- Inhibiting and toxic compounds (antibiotics)
- Slowly biodegradable organic compounds and recalcitrant molecules (aromatic compounds, chlorinated hydrocarbons)
- Soaps and detergents with surfactants [82].

High content of organic matter.

Oxygen depletion. Lakes experience more vulnerability to pollutants than rivers and this is due to the fact that rivers have self-purification mechanisms. In minute quantities of these wastewater discharge, there are little or no effects and may even be valuable as sources of organic pollutants that helps in providing nutrients for aquatic life in rivers. When these pollutants are deposited in massive amounts, they can result in damage to the ecosystem at large, by reduction of oxygen content of water [83], and the reduction of light available for photosynthesis [84].

Eutrophication (algal bloom). Eutrophication occurs when a body of water becomes excessively enriched by nitrogen and phosphorus compounds and leads to escalated growth of plants and algae [85]. Pharmaceutical effluents contain organic compounds like acetone and alcohols that are used as solvents and denaturant in denatured alcohol.

Inhibiting and toxic compounds (antibiotics).

Antibiotic resistance. Discharge of pharmaceutical wastewater contributes to increased resistance to antibiotics [86]. Pharmaceutical pollutants are responsible for increase in resistant bacteria but the increasing rate at which anti-microbial drugs are being administered and used has contributed to the increase of pharmaceuticals in freshwater and has resulted in consequential effects on human health [87].

Active pharmaceutical ingredients when discharged into waterways have effects on naturally occurring microbes and have culminated in drug resistance. Drug resistance can be caused by resistant strains when released in wastewater, coupled with possible gene transfers due to constant exposure to antimicrobial compounds.

Hematological and hormonal imbalances in fish. Steroidal pharmaceuticals, progestins, glucocorticoids and estrogen have been found albeit in small concentrations in the aquatic environment. Incessant exposure to synthetic estrogen has resulted in endocrine and hormonal disruption in fish [88].

This has resulted in the feminization of male fish which are exposed to these effluents. This is a situation in which the male fish begins to exhibit intersex and impaired reproduction [89]. Scientists have elucidated that exposure to steroidal estrogen (EE 2) has resulted in impaired breeding of juvenile and male fish. Other examples are feminization of male fishes exposed to estrogen and this can significantly disrupt population of fish [90]. Oxazepam (anxiety-treatment drug) can also influence fish behavior in aquatic ecosystems and significantly impair the behavior and rates of food consumption in fishes even in lower concentrations.

Asides the hormonal and hematological effects posed to fishes in pharmaceutical-infested waters, oxygen depletion of these waterbodies as a result of pharmaceutical by-products has also been discovered. The presence of recalcitrant molecules results in the depletion of oxygen in an aquatic biocoenosis. Aggregates of suspended solids result in the inaccessibility of sunlight to algae and cyanobacteria that are responsible for the production of food for the ecosystem. This affects the health of the normal flora and fauna of the ecosystem [91].

Slow biodegradable organic compounds and their recalcitrant molecules.

Disruption of immune responses in aquatic fauna. These classes of pollutants are referred to as immunotoxic or carcinogenic. They are responsible for the effects caused on the innate and acquired immunity of fish. They have been found to affect the macrophage activities and lymphocyte proliferation in fish upon continual exposure [92]. Immunotoxicological assessment studies have revealed that xenobiotic-mediated suppression of innate responses may have more effect on pathogen resistance than suppression that results from acquired immune responses [93].

Soaps and detergents with surfactants. Surfactants are amphiphilic monomers made up of hydrophobic heads and hydrophilic tails. Residual surfactants find their way into wastewater either due to the fact that they are not treated or are partially treated due to inadequacies in employing only one treatment procedure and are distributed in various environmental compartments from water to soils [94]. Due to their unique functional properties, surfactants have found common use in pharmaceutical industries in varying range of uses which include clean-up of equipment and machinery after drug manufacturing processes, improving drug solubility and stability, stabilizing texture of semisolid preparations, aiding processing, and improving physical and chemical drug formulations [95].

Based on the toxic effects on aquatic fauna

Microorganisms. It was reported by [96], that ibuprofen (an anti-inflammatory analgesic) is orally administered to relieve musculoskeletal conditions, and rheumatic pain. This brings to attention possible antimicrobial activities against bacteria and pathogenic fungi. Also, it was deduced that ibuprofen was susceptible to methicillin-resistant staphylococcus aureus (MRSA).

Phytoplankton. Pharmaceutical residues have been reported to distort the growth of phytoplanktons. It was reported by [97], that streptomycin prevented the growth of blue-green algal species at concentrations (0.05 to 0.93 mg/L). Likewise, *Scenedesmus obliquus* and *Chlorella vulgaris* were found to have grown luxuriously in streptomycin concentrations of 0.66 mg/L.

Plants. The impacts of oxytetracycline and chlortetracycline on plants differ between species [98]. Researchers reported that pinto beans were the most sensitive plant species when cultivated on clay-loam soils. Also, low toxicity of erythromycin and lincomycin used in industrial agriculture as feed additives was documented on Daphnia magna straus [99].

Amphipods- invertebrates. The negative impacts associated with ocean-dumped pharmaceutical residues on marine amphipods, *Amphitoe valida* were succinctly studied by [100], and the toxic effects were found to significantly increase when the duration of exposure to waste concentrations was increased. The survival rates of *Amphitoe valida* when exposed to pharmaceutical residues above 1% were found to be lower when compared to the control groups.

The uptake of three pharmaceutical compounds by aquatic invertebrates (ramshorn snail, damselfly larvae, and waterlouse) were detected, and the propensity for bioaccumulation of these actives among these species were also ascertained [101]. The calanoid copepods *Temora turbinata* were observed to lead to decreased egg development, lower adult size lower adult size, decreased egg development and irregular growth patterns when increased in pharmaceutical waste concentrations above 1 ppm [102].

Analytical approaches used for the determination of pharmaceutical residues in environmental samples

The advent of commercially accessible interfaces for linking Liquid Chromatography (LC) with Mass Spectrometry (MS) and indications of chemical compounds as environmental contaminants has helped in the identification of drug metabolites in pharmaceutical effluents.

For the detection of drug compounds, the traditional 'gold standard' GC–MS approach is not adequately viable because it increases the degree of uncertainty of the process and also because derivatization techniques do not identify the potential of multiple peaks for a single analyte with many functional group variations, rendering it almost impossible to measure.

The strategies developed to date for the detection and classification of bioactive compounds in the environment have centered on the use of a three-step approach that includes: enhancement of process sensitivity through sample preconcentration, use of liquid chromatography (LC) as an analytical detection process, and ultimately, effective detection with the aid of mass spectrometry.

Sample preparation

Considerations for sample preparation

It is important that the process used to prepare the results of the sample in the analyte be optimized to a level that is more suitable to detect the analytical technique being used. As such, generating lower overall system detection limits is rather the first requirement for the integration of a sample preparation method in the analytical phase [103].

The need to purify the sample by processing the matrix before testing using analytical techniques is another justification for preparing samples before testing, so as to eliminate contaminants from the environmental samples to be analyzed. Consequently, environmental samples have large quantities of dissolved organic matter caused by physical and biological processes, and these can affect analytical evaluation. For instance, in spectrophotometric processes, dissolved organic matter can disrupt and disturb chromatography columns or enable the analytes to vaporize at the similar wavelength ranges [104]. As a result, the analyte to be identified must always be fully removed from the matrix, and optimize the selectivity, specificity, and precision of the method [105].

Different techniques such as nuclear magnetic resonance imaging (NMR), infrared spectroscopy (IR) and Gas Chromatography (GC) require that the analytes be conditioned prior to examination in specific states. This facilitates the acclimatization of the samples to be analyzed. Usually, the method of sample preparation is supposed to be inexpensive, convenient, and easy to perform. Also, regardless of the techniques utilized, sample loss should be at the lowest, there should be maximum analyte selectivity, and the methods used should not lead to the formation of factors that may contribute to or negatively impact analytical evaluation. For example, highly alkaline and acidic extracts may cause damage to chromatography columns [106].

Solid phase extraction (SPE)

Liquid-liquid extraction process (LLE) involves the transfer of analytes between specific immiscible liquid phases, which are typically water and either hexane or ether as they are the most used organic solvents for LLE, and this is effectively achieved by agitating the analytes to promote mixing and mass transport, thereby allowing the immiscible liquids to coalesce and disperse [107].

The small preconcentration variables that are attainable are yet another major issue with using LLE. The efficiency of LLE to optimize sample components is determined by the composition of the two liquid phases and it is thus, nearly difficult, and burdensome to extract sufficient sample volumes frequently required for analyte enrichment with the limited volumes of organic solvent [108]. Owing to the reduced expenses associated with both instruments and their solvents, and the simplicity in which the process could be conducted or even automated, the transition from LLE to SPE-dependent sample preparation techniques became necessary [109].

The three steps of SPE

The conventional SPE protocol usually comprises of three fundamental stages irrespective of the proposed application:

i Conditioning and sample adsorption;
ii Washing;
iii Elution

In order to establish the functional surface groups, conditioning requires transferring a liquid phase solvent such as ether or isopropanol through the sorbent pad [110].

To extract unwanted matrix constituents or residual compounds and nutrients from the sorbent, a washing technique is then implemented. The measures of the wash solvent are normally designed to extract most matrix constituents without compromising the preservation of the analyte of interest [111]. The last stage involved in the SPE process is the elution step. The analyte of interest is eluted with the use of a compatible solvent. In order to ascertain that all residual analytes are eluted, the velocity of the elution solvent is normally, relatively slower compared to the movement of the sample via the sorbent pad. The flowrate of elution solvent available should be limited in order to optimize the preconcentration factor [112].

In order to guarantee optimal recovery, it is beneficial that the intended analytes to be determined have a retention factor (k) with a close proximity to zero under elution standards.

For the examination of pharmaceuticals, capillary electrophoresis (CE) is sometimes also employed since they provide limits of detection in the range of micrograms per liter (μg/L), but they are more flexible, less sensitive, and much less costly than the liquid chromatography (LC) and gas chromatography (GC). CE approaches are often more suitable for the study of samples of wastewater as opposed to samples from surface and groundwater. Also, numerous advancements have actually been developed in instrumentation and preparation of samples, clean-up techniques, and derivatization in a continual attempt to maximize analytical techniques [113].

A clean-up phase is deemed essential to resolve such analytical challenges especially when both LC and GC analytical procedures are employed and is applied even before the final extract is analyzed.

For the study of pharmaceutical compounds, both GC and LC are relevant. For the study of polar molecules and reactive compounds, GC is more favourable, but it can be used for the evaluation of low pharmaceutical levels by incorporating a derivatization phase [114]. This phase is very significant, and many optimization attempts have been developed, due to the probability of losses of analytes that can arise as it can negatively impact the precision of the process. Some of the benefits of using the GC comprises of its good specificity, high sensitivity and resolution, excellent precision and accuracy, and a broad dynamic range [88].

In environmental studies, GC-GC has recently been implemented, offering even improved separation, identification, detection, and recognition of chemical compounds in complex environmental samples [115]. LC is the best suitable separation technique for polar organic contaminants and has the benefit of reduced evaluation time available for studies to be monitored. A major limitation of using HPLC analysis in the evaluation of pharmaceutical components in environmental samples is due to the reduced precision, specificity, and linearity.

Current studies and remedies

The current approaches that have been applied for wastewater treatment have been facilitated by employing bioremediation techniques for the effectual treatment of non-degrading compounds that are readily present in wastewaters from trace levels to rather significant amounts [116]. One of such approach is the utilization of microalgal biomass for waste degradation and water reclamation.

Microalgae has increasingly been considered as a substitute for conventional wastewater treatment approaches. This is mainly attributable to the fact that microalgae enable the recovery of nutrients whilst conserving costs and minimizing greenhouse gas emissions [117].

By contrast, microalgae-based technologies consume slightly less energy (0.2 kWh / m3), which helps to conserve more than half the energy presently used for conventional wastewater treatment by minimizing the amount of energy expended

[118]. Subsequently, the ability of microalgae to yield and generate an abundance of biomass that can be incorporated in wastewater treatment plants is a function of photosynthetic efficiency and an abundance of solar energy [119]. However, some of the challenges associated with employing this technology for water reclamation especially in the African continent is that only a few companies have successfully been able to utilize this technology for operation worldwide. This may be due to the fact that there still has not been a comprehensive understanding of how the process can be replicated on an industrial scale. Owing to this, the approach has not yet found extensive use despite the numerous advantages involved. Another challenge, however, is that the generation of microalgae needs long hydraulic retention periods of up to 8–11 days, but the strive for removing pollutants at an even shorter retention time has obligated the need for further research.

Conclusion

The presence of pharmaceutical by-products and their active ingredients in the environment, especially in aquatic ecosystems cannot be efficiently ameliorated, mostly due to the ever-increasing presence of pharmaceutical industries. However, deleterious effects on aquatic flora and fauna can be controlled by the avoidance of indiscriminate discarding of hazardous pharmaceutical waste in waterbodies from industrial processes and individuals alike. It is recommended that waste programs should be implemented by industries, with proper legislation, guidelines, and control on how hospitals and pharmaceutical industries can manage their disposable hazardous wastes. In addition, health professionals should display educational materials in drug stores, and community takeback schemes for unused and expired drugs should be encouraged.

Declaration of Competing Interest

Authors declare that no competing interest exists.

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