Effects of Pharmaceutical Waste in Aquatic Life

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Abstract

The waste from pharmaceutical products may cause harm to the aquatic life when it get washed into the environment through erosion or when it is discharged untreated into drinking water, underground water and into the aquatic environment which usually cause adverse effects to targeted and nontargeted aquatic organisms and indirectly affect the public health. The sources of pharmaceutical wastewater effluent which are mainly from point and nonpoints are noted to emanate from hospitals, municipal waste, domestics and industrials sources. Unfortunately, most of the pharmaceutical active ingredients are not properly removed, using most wastewater treatment methods before they get into aquatic environment where they cause toxic effects to living organisms. Different types of pharmaceutical wastes from groups of pharmaceuticals including antibiotics, analgesic, hormones, antidepressant, antihypertensive, contraceptive and steroids have been identified and reported to cause physiological dysfunctions, ranging from reproductive, haematological, behavioural, mutagenic, carcinogenic to physiological and enzymological effects. However, there is a need for proper monitoring and documentation of the potential health hazards/or implications, caused by these pharmaceutical wastes to the environment as well as aquatic life for possible mitigation.

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25.1 Introduction

Different types of pharmaceuticals including antibiotics, antihypertensive, contraceptive hormones, anti-inflammatory drugs, analgesic, and antiepileptic drugs are used to prevent, cure and in the treatment of different illness or diseases both in humans and animals. Continuous increase in the usage of pharmaceuticals to treat illness, for disease prevention, influx of wastewaters which are not treated enter into the environment, may increase the availability of drugs in the water body (Fekadu et al. 2019; Williams et al. 2019). Discharges from pharmaceutical industries, hospital effluents, animal and human excretion, improper discarding of unused or expired medicines, contaminated pharmaceutical products, waste released from research foundations and drugs development establishments could also increase the availability of pharmaceuticals and their metabolites into the environment. The residues and the metabolites from the pharmaceuticals usually find their ways into the aquatic ecosystem untreated, especially through effluents from treatment plant where they directly cause ecological impact on the aquatic organisms and indirectly on human health. In the process, most of the pharmaceutical wastes are not adequately broken down during the treatment and consequently, an appreciable part is discharged into the aquatic environment through wastewater effluent. The study shows that the traditional method of wastewater treatment does not naturally remove the targeted pharmaceuticals. The presence and persistence of pharmaceutical wastes in aquatic ecosystem could be deleterious owing to their reaction with other potential contaminants as well as newly emerging xenobiotics.

Further, the continuous influx of the pharmaceuticals and their metabolites may bioaccumulate into aquatic organisms and result in long term chronic effects as well as bio-magnify through food chain, thereby, militating against the survival of the organisms that inhabit such an environment. The effect of pharmaceuticals residues are usually not adequately monitored within aquatic wildlife, indicating the knowledge gap in determining the extent of exposure as well as the route of the chemicals in the organism (Miller et al. 2018). Usually, pharmaceutical wastes are designed to cross biological membranes. However, the rate of assimilation and internal concentrations of the compound are paramount. The availability and concentration of pharmaceutical waste entering or present in aquatic environment depend largely on the quantity of drugs, used by patients, the extent at which the sewage is being treated as well as the efficiency of the wastewater treatment plants. Understanding the potentials for pharmaceutical waste to cause adverse effects to the aquatic ecosystem, requires the ability to evaluate the occurrence or composition of these wastes to entire group of organisms that constitute the aquatic biota such as fish, invertebrates, plants and algae. However, there is a positive relationship that exists

among the most regularly consumed groups of pharmaceutical products and their occurrence in the aquatic ecosystem.

In general, concentrations of pharmaceuticals and their metabolites, found in waste water treatment work (WWTW) effluent, range from ng L^{-1} to μg L range, in contrast, pharmaceuticals hardly supersedes 100 ng L in surface waters (Trudeau et al. 2005). Level of transformation of pharmaceuticals that develop in the body of a patient who takes drugs, the rate of degradation in the waste water system that receives water and the manner the compound partitions into column body, to a large extent determines the concentration of pharmaceuticals that can be found in an aquatic environment (Winker et al. 2008).

Metabolism of drugs, that occurs, can vary appreciably between compounds in such a way that some compounds are excreted completely either through urine or faeces from the parent compound without undergoing metabolism whereas other undergo complete metabolism.

In general, pharmaceutical wastes can be hazardous, readily inflammable, abrasive, or extremely unstable and could cause irritation to body cells. Some pharmaceuticals are genotoxic or mutagenic as well as harmful when discharged into the aquatic environment and can cause tumours and reproductive abnormalities to inhabitant aquatic organisms. The potential effects of pharmaceuticals waste in aquatic environment, especially in fish and other aquatic organisms, are explored in this paper.

25.2 Sources of Pharmaceutical Wastes

The main pathway of pharmaceutical wastes or products to aquatic ecosystem is through sewage treatment plant (STP) effluent or urban waste water treatment plants (WWTP) after voiding as a consequence of patient consumption (Corcoran et al. 2010). Drugs and their metabolites can be detected in domestic waste, effluents from hospitals and farming waste due to the fact that they are used by human beings. However, point and diffuse sources are the major pathways in which pharmaceuticals are discharged into the aquatic environment.

Therefore, sources of pharmaceuticals can be classified into two major groups, namely point and nonpoint or diffused sources.

25.2.1 Point Source Pharmaceutical Wastes

Point source is said to be a singular, noticeable origin of contaminant such as a canal or a drainage system which is usually emptied into an aquatic ecosystem. Usually, pharmaceutical and industrial wastes and hospital effluents are major point source of pollution which is normally released into water bodies.

Majority of the waste water is released into the sewage treatment plants through the sewage system. Improper human transformation of drug and excretion into waste drainage system are also some of source of discharging pharmaceuticals wastes into

the aquatic ecosystem. Hospital and industrial waste water as well as domestic pathway through sewage treatment plants has been the major channel of pharmaceutical waste that usually enters into the aquatic ecosystem (Ternes 1998).

Some studies have investigated the occurrence of pharmaceuticals in the sewage treatment plants and found that the removal of the pharmaceuticals usually undergo incomplete processes. Besides water bodies, soil zone could be adversely affected by the discharges from waste water. The application of the waste water in farming activities can give room to the availability of some pharmaceutical products and other pollutant in the soils through irrigation processes (Chen et al. 2011; Fenet 2012; Durán-Álvarez et al. 2012).

The septic tank is one of the most important sources of the pharmaceuticals such as ibuprofen, paracetamol, salicylic acid, and triclosan that enter into the aquatic environment (Conn et al. 2010). Seepage of septic system could lead to contamination of water reserve by discharging some pharmaceutical wastes into the aquatic ecosystem. Also concentrations which ranged between 0.058 and 0.9μg L^{-1} of verapamil has been detected in aquatic ecosystem (Al-Rifai et al. 2007; Khan and Ongerth 2004).

25.2.2 Nonpoint Source or Diffused Pharmaceutical Waste Pollution

It is difficult to identify the exact location or the source where the nonpoint source pollution originates. Seepage that emanate from waste treatment apparatus, domestic and municipal runoff, wastes from agricultural runoff and individual point source discharges are the examples of nonpoint source pollution. Usually, expired and unused drugs as well as adulterated pharmaceutical materials such as injections and biological products applied for treatments which are deposited by domestic households and health care treatment industries to the environment are also nonpoint source of pharmaceutical waste. According to European Environmental Agency, diffused pollution can be the result of an array of operations or activities that have no precise point of discharge. Farming waste is a major source of diffuse pollution. However, deposits from atmospheric as well as rural habitations can also be a noble source. Organic contaminants include pharmaceutical wastes entering into the soil and water reserve through different pathways, with the important one being sewage sludge. Sewage sludge application onto the land surface is an important diffused source of the pharmaceutical waste entering into the soils as well as the freshwater ecosystem (Lapworth et al. 2012) (Fig. 25.1). High pharmaceuticals concentration can be observed in the biosolids, including thiabendazole and other numerous pharmaceuticals such as caffeine and carbamazepine (Kinney 2008). Owing to high solubility of pharmaceuticals with appreciable concentration in addition to some organic compound in biosolid, groundwater pollution from discharge of biosolid to soil and runoff surface could occur (Lapworth et al. 2012).

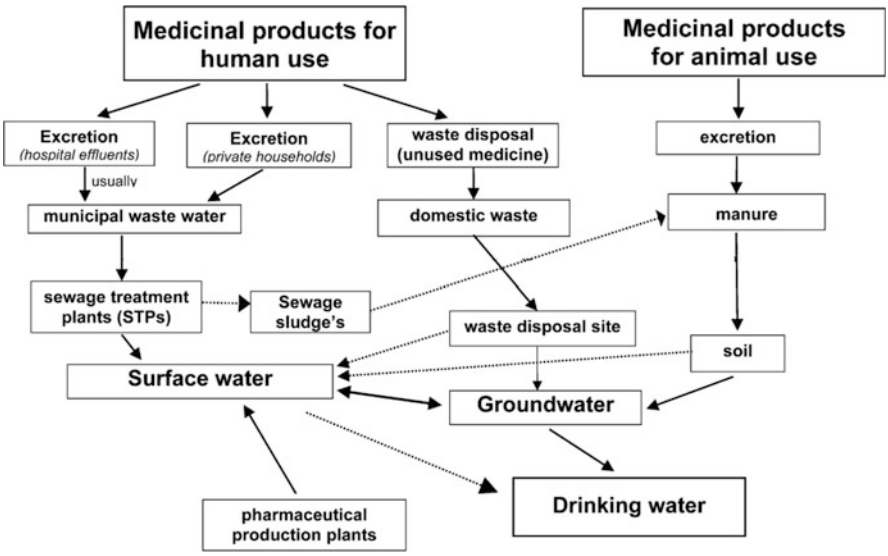

Fig. 25.1 Sources and pathways of pharmaceutical wastes to the aquatic environment as modified from Heberer (2002)

25.3 Effects of Pharmaceutical to Fish

Fish are the most important vertebrate organisms that are vulnerable to pharmaceuticals in aquatic environment, owing to environmental function and similarity of their physiological processes in comparison to mammals. Adverse effects in the populations are usually predicted from laboratory acute and chronic toxicity data in aquatic organisms including algae, crustaceans, and fish (Versteeg et al. 2005). Due to the fact that the primary mode of entry into the aquatic environment for most pharmaceutical waste is through STPs, the environmental risk assessment for the aquatic compartment is paramount. However, in order to understand the concentration that can cause potential effects to aquatic organisms, predicting the concentration is very vital. It is critical to know the effects on organisms across a wide range of concentrations, which will allow us to identify the level of concentrations at which certain compounds can have adverse effects on fish. In general, concentrations of pharmaceutical wastes or metabolites available in the environment are usually too low to illicit any observable direct adverse effects to aquatic organisms, except during chronic and acute laboratory experiments. Some studies reported the effects of certain pharmaceutical waste on natural water bodies that caused certain degrees of abnormalities in fish. Ethinyl estradiol (EE2) which was found to be the main estrogenic contaminant of STP effluents in UK Rivers caused endocrine disruption in fish (Desbrow et al. 1998). High incidences of intersexuality in roach, *Rutilus rutilus*, associated with exposure to sewage treatment

works, that contain estrogens and estrogens waste have been demonstrated (Jobling et al. 1998).

As mentioned above, the most pharmaceuticals in the environment are present at very low concentrations that are unlikely to cause effects in aquatic species. However, relatively little is known about the bioaccumulation potential of pharmaceuticals in nontarget organisms. There is the possibility that some pharmaceuticals could bioaccumulate in aquatic species to the extent that their concentrations may become high enough to initiate an effect.

The occurrence of hormonal compounds in the environment could lead to endocrine-disrupting incidence to most of the aquatic organisms including fishes. However, at environmentally relevant concentrations, EE2 have been reported to induce feminisation in fish as well as induction of the female yolk precursor in males (Örn et al. 2006; Chikae et al. 2003).

Other classes of pharmaceuticals waste such as the NSAIDs have also been reported to cause some notable effects on fish. As such, indomethacin has been shown to disrupt the process of oocyte maturation and ovulation in zebra fish at a concentration of 100 mg L^{-1} (Lister and van der Kraak 2008) while at concentrations of μg L^{-1} of ibuprofen, pattern of spawning in Japanese medaka was altered (Flippin et al. 2007). Diclofenac hinders the stimulation of prostaglandin synthesis in the kidney in brown trout at environmentally relevant concentrations of 0.5–50μg L^{-1} (Hoeger et al. 2005) and caused DNA damage and physiological dysfunction in *Oreochromis niloticus* at sub lethal concentrations (Pandey et al. 2017). Also in rainbow trout, diclofenac induced glomeruloneophritis, necrosis of endothelial cells, and hyaline droplet degeneration in the kidney as well as hyperplasia and hypertrophy in gills at exposure level between 1 and 5μg L^{-1} concentrations (Schwaiger et al. 2004).

Ketoconazole, clotrimazole, and fadrozole pharmaceuticals at 11.1 nM concentration have been found to affect steroidogenesis and reproductive success of fish through the inhibition of steroidogenic enzymes including CYP11a, CYP17, and aromatase (Monteiro et al. 2000; Hinfray et al. 2004). Also a decrease in protein level was observed in *Clarias gariepinus* upon exposure to clotrimazole (Melefa et al. 2020). The potential effects of verapamil, a group of calcium channel blockers pharmaceuticals, have caused DNA damages, neurotic effects, molecular responses as well as oxidative imbalance in various tissues of *O. niloticus* after chronic exposure at sublethal concentrations between 0.14 and 0.57 mg L^{-1} (Ajima et al. 2017, 2020). Further, sublethal concentrations of verapamil significantly altered behavioural potentials, antioxidant biomarkers, haematological parameters and morphological responses in *Oncorhynchus mykiss* (Li et al. 2011). Also the behavioural ability of male Siamese fighting fish was impacted negatively by verapamil on exposure at relatively low concentration (Kania et al. 2015).

25.4 Effects of Pharmaceuticals on Other Aquatic Organisms

Besides fishes, pharmaceutical wastes can cause certain degrees of effects to other aquatic life including algae, mussels and other aquatic organisms. In the aquatic ecosystem, algae are often used as sentinel species in environmental monitoring, as an indicator species, to assess environmental conditions and from geological samples as indicators of past environmental conditions, suggesting that algae can be sensitive to environmental changes, including those caused by pharmaceutical wastes. Adverse effects on algae in aquatic environment might lead to serious ecological results, especially in the food chain. Pharmaceutical wastes can probably affect the algae survival usually by reducing the rate of photosynthesis through impairing the functions of chloroplasts. Availability of pharmaceutical waste in an ecosystem can lead to eutrophication and usually lead to algal mortality in such environment and indirectly affect ecological niche.

Increase in concentration of carbamazepine and diclofenac pharmaceuticals lead to the adverse effects on the chloroplasts in algae (Vannini et al. 2011). Relatively low concentration of sulfamethoxazole pharmaceuticals affected the photosynthetic apparatus of algae (Liu et al. 2011). Pharmaceutical waste products in water can form a mixture of various heavy metals and organic pathogens that are likely to have potential mutagenic and genotoxic effect when living organisms are exposed to it.

Adverse effects of some pharmaceutical drugs on certain aquatic organisms have been explored. In some of the studies, environmental concentration of diclofenac altered stability of lysosomal membrane and cyclooxygenase (COX) reactions as well as DNA damage in *Perna perna* (Fontes et al. 2018), and caused genotoxicity in *Mytilus galloprovincialis* (Mezzelani et al. 2018). Survival and reproduction capacity of *Folsomia candida* were impaired by diclofenac toxicity (Chen et al. 2015) while definitive and toxic effects potentials of diclofenac on developmental stages of Xenopus embryos was reported (Chae et al. 2015). Studies have shown that verapamil induced toxic effects on *Daphnia magna* after the treatment at low concentrations (Villegas-Navarro et al. 2003).

Four drugs, erythromycin, fluoxetine, naproxen and gemfibrozil belonging to different therapeutic classes, were selected by El-Bassat et al. (2012) to examine their toxicity to selected plankton organisms from different trophic levels: algae (*Chlorella vulgaris* and *Ankistrodesmus falcatus*), protozoa (*Paramecium caudatum*), rotifera (*Brachionus calyciflorus*) and cladocera (*Daphnia longispina*). LC_{50} values for three of the drugs were between 12 and 82 mg L^{-1}, with algae and protozoans being most sensitive. Fluoxetine showed LC_{50} values between 40 and 830μg L^{-1}, algae again being most sensitive. The low concentrations of fluoxetine showed enhanced growth rates of *B. calyciflorus* and *D. longispina.* Even at low test concentrations, erythromycin decreased the growth rates of all the test organisms. *Paramecium caudatum* was the species most sensitive to naproxen exposure. After 24 h, gemfibrozil had the least effect on all tested organisms. All the surviving tested organisms underwent oxidative stress to different degrees as a result of drug exposure. Although the test concentrations were above those commonly found in

the environment, the occurrence of sublethal effects at all test concentrations was observed (El-Bassat et al. 2012).

Grabicova et al. (2015) found azithromycin and sertraline as bioaccumulative pharmaceuticals in Hydro-psyche. Even pharmaceuticals present at low levels in water were found in benthic organisms at relatively high concentrations (up to 85 ng g^{-1} w.w. for azithromycin). Consequently, the uptake of pharmaceuticals via the food web could be an important exposure pathway for the wild fish population.

25.5 Management of Pharmaceutical Wastes

Pharmaceutical waste can emanate from many activities and locations in a health care system. A compounding pharmacy on site could generate drug waste. Waste of pharmaceuticals poses an appreciable treatment and management challenges. Small quantities of pharmaceutical waste at households can be thrown away in the municipal waste stream. Large quantities kept at pharmacies, distribution centres, hospitals, etc. must be managed to minimize the risk of release or to exposure to workers and the possible effect it may cause to aquatic biota. Usually, the category of such waste includes expired, unused, and contaminated pharmaceutical products including vaccines and biological products used for therapy. Prescription and over-the-counter drugs end up as pharmaceutical waste including paraphernalia used in pharmacies such as gloves, masks, bottles, etc. Normally, solid pharmaceutical waste is generally easy to handle and package, but liquid waste poses more challenges in confining the waste and minimizing risk of release.

25.6 Treatment of Pharmaceutical Wastes

In the US, the EPA's Land Disposal Restriction requires treatment of pharmaceuticals before disposal. Treatment is aimed at changing the chemical structure of the medicines. The treated medicine should be acceptable for disposal with no worries of it getting into the aquatic ecosystem where it can cause harm to aquatic organism or even harm people. Some methods of treating pharmaceutical wastes are highlighted and discussed as below:

25.6.1 Incineration

Incineration is a high-temperature oxidation process that involves combustion of the organic portion of biomedical waste (BMW) components, producing gaseous emissions including steam, carbon dioxide, nitrogen oxides, particulate matter, and other toxic substances and inorganic solid residues such as ash. Incineration is an appealing option for the waste management with a heterogeneous waste stream, as many streams with pharmaceuticals tend to be included. In addition, under

suboptimal combustion, carbon monoxide and hazardous pollutants such as dioxins and furans may be emitted. Incineration significantly reduces waste volumes, and eliminates pathogens from BMWs. However, it still remains the top used method of medical waste treatment in less developed countries. During the process of incineration, ash from these incinerators must be disposed off in a secured landfill. Other studies have shown that the major and common method of infectious medical waste treatment method in the developed countries is by incineration in which waste is burned to high temperatures (i.e. 1200 °C) and in the process the volume size is reduced and what remains is residual ash. The remaining ash is then dumped at landfill sites and then buried. This process ensures that infectious waste is sterilized and reduced in volume size to ash which in turn reduces cost of transportation to landfill sites.

The challenging issues regarding incineration are the disposal of ash and the treatment of gaseous pollutants, containing furans, dioxins and mercury. In addition, incineration has the advantage of reducing the volume size by 90% of the treated products. Other thermal technologies that have hardly been used for medical waste treatment include gasification, pyrolysis and plasma treatment method.

However, the main disadvantage of incineration of medical waste is the emissions and toxic pollutants dioxins, furans, and mercury arising from burning of the waste. Due to different compositions, burning of infectious waste produces toxic gases into the environment; hence, this method is highly controlled in developed countries as the emitted harmful gases, released into the atmosphere, may affect human health.

25.6.2 Autoclaving

The current known alternative for incineration is autoclaving. This method involves treatment of infectious waste by adding dry heat or steam to elevate the temperature of infectious waste to values sufficient enough to get rid of any microbial contamination. Autoclaving uses saturated steam in direct contact with the BMW in a pressure vessel at time lengths and temperatures sufficient to kill the pathogens. The Biomedical Waste Rules specify the minimum temperature, pressure, and residence time for autoclaves for safe disinfection. The operation requires qualified technicians, and medium investment and operating costs. The BMW is continuously tumbled in the chamber during the process. The advantageous part of the autoclave treatment process is that after waste treatment, the remaining waste can be disposed at the municipal solid waste (MSW) landfill site in the same way as noninfectious waste. Another advantage of autoclave treatment method of infectious medical waste over incineration is that it does not produce pollutants generated from PVC and other products such as mercury, furan and dioxin that are emitted into the environment during incineration.

There are also disadvantage in the use of autoclaving as an infectious waste treatment technology. Autoclave process has heat waste through steam to eliminate the pathogens without direct burning the waste and keeping its appearance like before, the resultant waste after treatment does not distinguish itself from untreated

infectious waste, hence, giving the perception that untreated infectious waste is being dumped on landfill sites.

25.6.3 Microwaving

The application of an electromagnetic field over the BMW trigger the liquid in the waste to vibrate and heat up, eradicating the contagious components by transmission. The equipment is capable only if the ultraviolet radiation touches the waste products. The process of microwaving requires smashing to a satisfactory size and humidification. Microwaving provides debris that can be land loaded with municipal waste. The advantages of this treatment technology are its small electrical energy needs no steam requirement. The disadvantages include the need for qualified technicians and frequent breakdown of shredders.

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