Pharmaceutical waste: Overview, Management, and Impact of improper disposal.

Milcah Njoki Nyaga[1*] David Muriithi Nyagah[2] Aldress Njagi[3]

Abstract

Introduction: Pharmaceutical products are inevitable for human health. Owing to the growing need for pharmaceuticals, pharmaceutical companies introduce drugs annually into the market in addition to the extensive collection of existing pharmaceutical products. Households, farms, health facilities, and pharmaceutical industries release pharmaceutical waste into the environment at low concentrations through routine pharmaceutical use, damage, and expiry. The effects of active pharmaceutical ingredients (API) on non-target species in the environment are not known. Over the years, pharmaceuticals such as diclofenac and ibuprofen in trace amounts have been detected in public water systems, ground and surface water. Unwanted medicines should be safely disposed of at a reduced financial cost to mitigate the public and environmental health risks. Lack of general knowledge of how to dispose of unused pharmaceuticals leads to improper disposal resulting in accidental toxicity, rising healthcare costs, landfills pilfering/scavenging, water supply pollution, anti-microbial resistance, and death. To mitigate such effects, pharmacists should raise public awareness about safe disposal practices. **Objective:** This review aims to examine the sources of pharmaceutical waste, disposal costs, secure disposal methods, the effects of inappropriate disposal, and the role of pharmacists in the disposal. **Method**: The information on the stated objectives was gathered from available sources through a comprehensive literature review. **Conclusion**: Many countries contain tons of pharmaceutical waste that are expensive to destroy. Because of improper disposal, pharmaceutical waste has been found at trace amounts in drinking and surface water. A practical, environmentally sustainable approach to pharmaceutical waste management, with policies and guidelines, and public awareness campaigns, are necessary to address the problem of safe waste disposal. The national drug regulatory bodies should conduct environmental risk assessment resulting from the disposal of unwanted pharmaceuticals. Pharmacists should facilitate extensive training on sustainable drug use and proper pharmaceutical waste disposal at all levels to reduce the risks associated with improper disposal. Reduction of pharmaceutical waste generation at each step of a drug's lifecycle, implementing takeback options, collection at approved sites, and modern technology to treat wastewater are highly recommended to reduce the effects of unwanted pharmaceuticals on human health and the environment.

Keywords: Pharmaceutical waste, Sources, Cost of disposal, Management, Impact, Pharmacists.

Corresponding author contact details: Milcah Njoki Nyaga[1]*, Email: nyaga.milcah@embuni.ac.ke, Cell: +254721325459

Affiliations for all authors

1. School of Education, University of Embu, Kenya. P.O. Box 6-60100, Embu, Kenya, Email: nyaga.milcah@embuni.ac.ke
2. Med-gate Pharmaceuticals, Wang'uru, Kenya. P.O. Box 187 – 10303, Wang'uru, Kenya, Email: davipharm91@gmail.com
3. Tan Pharmacy, Embu, Kenya. P.O. Box 1608-60100, Embu, Kenya, Email: aldinjagi@gmail.com

Introduction

The pharmaceutical industry ranks among the world's wealthiest industries. Owing to a growing need for health care, livestock farming, horticulture, and aquaculture, the pharmaceutical industry has seen more pharmaceutical development in the last few years. With increased usage and degradation of pharmaceutical products and substances, the environment is experiencing high contamination levels. After being burned in home furnaces, the products get disposed of as municipal waste or gaseous waste. [1]

The Pharmacy and Poisons Board (PPB) defines pharmaceutical waste as waste containing medicines expired, contaminated, split, unused, and no longer needed, including items containing or contaminated by pharmaceuticals such as bottles, boxes, vials, ampules, gloves, and masks. [2] Pharmaceutical waste generally includes expired medicine, personal medication discarded by patients, waste material inholding chemotherapeutics and excess medicine, e.g., intravenous (IV) bags and syringes, containers containing hazardous pharmaceuticals and unused drugs, discarded drugs, spill clean-up equipment, and contaminated absorbents and protective gear such as garments. [3] There are three categories of pharmaceutical waste; Hazardous, non-hazardous, and chemo pharmaceutical waste. Hazardous waste includes the Environmental Protection Agency (EPA) coded pharmaceutical waste or pharmaceuticals that are toxic, reactive, corrosive, and ignitable. This waste has detrimental effects on the environment and human health. [3,4] There are two hazardous waste categories: listed and characteristic waste. Listed wastes contain pharmaceutical products for commercial use, while characteristic waste is controlled as they exhibit toxicity, reactivity, corrosivity, and ignitability. [3] Non-Hazardous waste includes expired medicines, manufacturers sample, loose pills, damaged or contaminated patient medication, including packaging. [4] They contain components that have a low threshold of causing harm to human health and the environment. [4] The PPB defines a pharmaceutical waste generator as any person whose actions or actions under his or her supervision generate pharmaceutical waste or, if that person is not identified, the person who owns or regulates the pharmaceutical waste. [2]

In 1999, the World Health Organisation (WHO) developed the guidelines for pharmaceutical waste's safe disposal. The document highlights the methods of disposal, sorting category, and recommended disposal methods. [5] In 2014, the WHO published the second edition of the guidelines for the effective disposal of healthcare waste, highlighting the categories, risks, policy and legislative aspects, minimization, sorting, transport storage, and healthcare waste disposal. [6] In 2015, the WHO and United Nations Children Fund (UNICEF) formed a joint program to ensure healthcare waste's safe management and provided regular updates. [7] The Food and Drug Administration (FDA) requires all manufacturers to provide Environment Assessment reports (E.A.s) backed by scientific data before new drug registration. In 1998, the FDA published guidelines for environmental assessment of new drug applications. The guidelines excluded manufacturers whose pharmaceuticals had an Expected Introduction Concentration (EIC) of < 1 ppb of the active pharmaceutical ingredient (API) in the water bodies from providing E.A.s for new drug applications. Data has shown that APIs of pharmaceutical products with aquatic EIC < 1 ppb have insignificant effects on the environment. These results formed the FDA exclusion criteria in the guidelines. [8]

A Serbian study projected that 74,929 kg of expired drugs is released from households perennially. The study revealed that 97% of households disposed of unwanted pharmaceuticals in trash bins. [9] A South Korean study done to evaluate the environmental risk of drugs in WWTPs found ibuprofen, carbamazepine, ketoprofen, gemfibrozil, acetaminophen, and sulfamethoxazole present at 22.6-8330.9 ng/L, 0.4-35.0 ng/L, 55.4-888.4 ng/L, 16.16-17.1 ng/L, 7.4-12.9 ng/L, 0.1-4.2 ng/L concentrations, respectively. Carbamazepine, ketoprofen, and gemfibrozil posed a high risk to fish, while ibuprofen and sulfamethoxazole posed an increased threat to green algae. [10] A German study reported that 156 pharmaceuticals were present in-ground, surface, and water supply systems. [11] High concentrations of hormones in the aquatic environment have caused the feminization of male fish. [12] An Ethiopian study reported that 55% of the respondents were not aware of the Government's waste management and disposal guidelines. In the survey, 85% and 77% of the respondents opined that waste management policies and focal persons were unavailable. Only 13% of the facilities had a designated person or committee to handle the pharmaceutical waste. Landfill and burning in the open air were the most utilized methods, while respondents never practiced waste immobilization, high-temperature incineration, and manufacturing return. Moreover, 89% of the facilities had not received training in pharmaceutical waste management. Only one industry possessed a wastewater treatment plant (WWTPs); other facilities discharged wastewater directly into the effluent system. [13] On unused opioids, the FDA has implemented takebacks to the Drug Enforcement Administration (DEA) options such as collection at official DEA sites, mail-back, or biannual events. However, if this method is not feasible, the guidelines recommend disposal in the trash and flushing. Flushing has led to trace amounts of opioids in water supply systems. WWTPs are not designed to degrade opioids. APIs have been detected in leachate due to disposing of pharmaceutical waste in the trash. The leachate from landfills enters water sources and wastewater streams, posing a health risk to humans and the environment. [14]

Pharmaceuticals are a vital part of a health framework; therefore, sufficient stocks are required consistently. The human health and veterinary sector receive drugs through donations and procuring. Medicines may be damaged during transport, storage, handling, routine use, and others may expire. During disasters such as famine, war, floods, countries receive large quantities of pharmaceuticals in their supply chain. [2] When treatment guidelines change or new regimens are introduced, other regimens may become obsolete, e.g., antimalaria drug Amodiaquine. Unwanted pharmaceuticals may arise due to insufficient stock control and procurement practices or irrational drug use. Over-prescription, misdiagnosis, and self-medication lead to the accumulation of medications in the environment. Low quality and adulterated medicine are a factor for disposal. Therefore, handling pharmaceutical waste must be done to promote public and environmental health as part of monitoring Sustainable Development Goal 6. [7]

Trends and Sources of pharmaceutical waste

The use of pharmaceuticals is projected to increase due to increased population age and life-span, economic growth in developing countries, new clinical practices, engineering of new medicines, intensification of agricultural practices, and climate change. The United Nations (U.N.) has estimated the pharmaceutical industry's annual growth rate as 6.5%. Furthermore, 10% of manufactured pharmaceutical products are an environmental hazard. The Product Stewardship Council announced in 2019 that one-third of the 4 billion prescription products in the United States of America (USA) had become waste. As a result of climate change, the risk of succumbing to mosquito and tick-borne diseases is projected to increase. The use of antibiotics in livestock is projected to increase by 67% by 2030 in developing countries. In Germany, due to the large aging population, the use of pharmaceuticals is expected to increase by 43% by 2045. APIs are administered globally via over-the-counter, prescription, and veterinary medicines. Animals and humans excrete 30% to 90% of oral pharmaceuticals as active substances via urine and feces. A high concentration of pharmaceuticals has been detected in rivers and industrial effluents in India, China, Korea, the USA, and Israel. Moreover, in the United Kingdom (U.K.), 13% of WWTPs contained high diclofenac, propranolol, ibuprofen, and ethinylestradiol concentrations. [15]

There are six pharmaceutical waste sources, namely pharmaceutical manufacturing plants, hospital, industry, and municipal wastewater treatment plants (MWWTPs), waste management settings such as landfills, agriculture, particularly intensive livestock and crop farming, aquaculture, and septic tanks. [16,17] There are two main pathways to the release of pharmaceuticals: point source such as discharge from WWTPs, and diffuse source, which encompasses surface runoff and leaching of septic tanks to groundwater. The concentration patterns of pharmaceutical waste include continuous, seasonal, and intermittent. The WWTPs have endless concentration patterns, whereas seasonal concentration patterns are linked to water flow, farming practices, temperature, and allergies. Periodic concentration patterns are governed by the overflow of stormwater, pandemics, rainfall, and irrigation designs. The impact of the disposal of pharmaceutical waste depends on the following properties: toxicity, mobility, bioaccumulation, and persistence. Persistence includes transformation products, metabolites, solubility, and half-life. Adverse effects of toxicity may be an individual, population-based, mixture, and additive effects. The sinks of pharmaceutical waste include rivers, oceans, groundwater, soil, lakes, and sediments. [15] Households and hospitals are the primary sources of pharmaceutical chemicals in sewer systems. Health facilities dispose of IV bags and Syringes down the drain. Pharmaceutical waste disposed of in landfills enters sewer systems and groundwater through leaching. [18] A study conducted in the Baltic Sea region to evaluate pharmaceutical waste in the aquatic environment found that the primary source of waste was excreted APIs through feces and urine from humans and animals. Pharmaceuticals entered the marine environment through discharged effluents from MWWTPs. The MWWTPs released approximately 1800 tons of waste annually. Surprisingly, wastewater treatment removed 9 out of 118 pharmaceuticals at 95% efficiency. Drugs detected at high concentrations included analgesics, anti-inflammatory, central nervous system, and cardiovascular agents. [19] A systematic review of pharmaceutical waste disposal found that flushing and discarding pharmaceuticals in the trash bin are the households' main disposal methods. [20]

Impact and concentration of pharmaceutical waste are affected by agricultural, veterinary, medical activities, technology in the WWTPs, illicit drug use, structure of the food web, climate change, consumption rates, waste management practices, drainage, and exposure history, sink type, and water flow variations. [15]

Several studies have described the following as passages of pharmaceutical waste in the environment [7,16,17,21]

1. Release from healthcare waste
2. Improper and direct disposal of expired/unused medicines in the sink or trash or through feces or urine.
3. Disposal by pharmacies

4. Release from low-cost drug companies in economically developing nations like India, Pakistan, Bangladesh, and China.
5. Veterinary medicine or additives in animal food excreted into the soil or surface waters
6. Leaching from faulty landfills
7. Release from pest control drugs and molecular farming
8. Disposal of medicated/euthanized animal carcasses
9. Household sewage or garbage mixed with the excess drug
10. Disposal of dairy waste/slurry
11. Excretion from aquaculture using the medicated feed.
12. Improper disposal of physician samples given for promotional purposes which end up unused or expired.

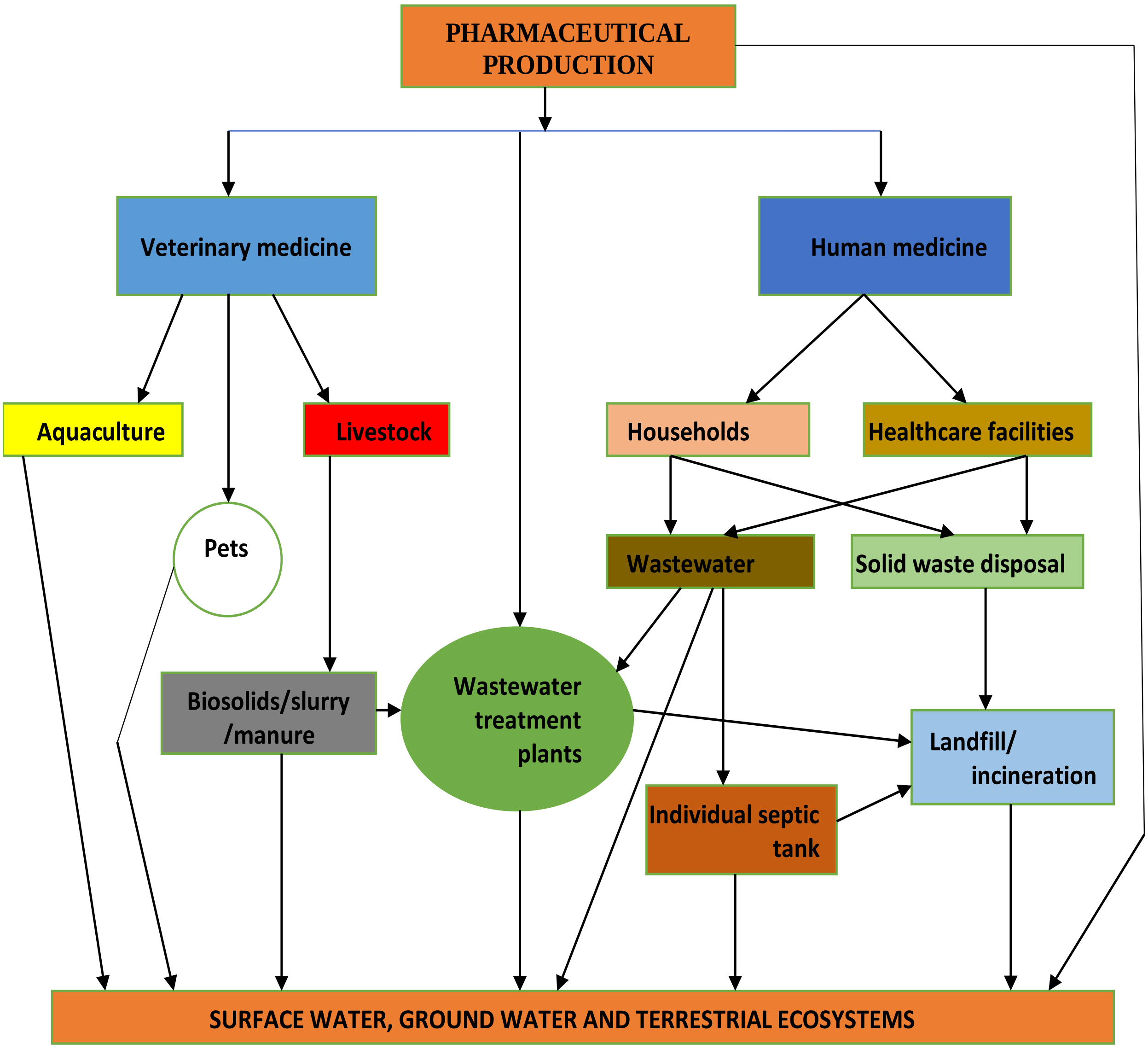

Figure1: Sources and release of pharmaceuticals into the environment

Cost of disposal

Pharmaceuticals are generally disposed of by incineration at high temperatures (above 1200 ° C). Industrialized countries such as Bosnia and Croatia, with efficient incineration facilities and excellent pollution controls, charge $2.2-4.1 per kg. The amount of money needed for pharmaceutical waste disposal in the USA ranges from $4.4-8.2 million. [5] India is using 0.5 to 2% of its pharmaceutical revenue to dispose of pharmaceutical waste. [21] The cost of disposing of one kilogram of pharmaceutical waste in Kenya in the ’90s ranged from Sh200-400. The price now ranges from Sh25-30 / kilogram. In 2017, Kenya disposed of about 65,000 kilograms of pharmaceutical waste worth Sh1.29 million at the Envirosafe Limited incinerator, Athi River. High-temperature incinerators are only available in the Kenya Medical Research and Training Institute (KEMRI) (3000°C) and Kenyatta National Hospital (KNH) (1700°C). Most healthcare facilities in Kenya have brick and motor incinerators that reach 300°C. These incinerators cannot meet the high costs of the incinerators; therefore, they are outsourced. Kenya’s pharmaceutical industries lack incinerators and rely on a return to manufacture method six months before expiry. [22] A Greek study showed that 22900g of cytostatic waste was generated every day, making the production rate 274.8kg annually. The generation rates translated to 140g/patient/day and 210g/bed/day. Such studies are important as they assist in planning the cost of disposal and assessing pharmaceutical waste’s environmental impact. [23]

Measures of disposing of pharmaceutical waste recommended by the WHO

Here are seven main steps to follow when unwanted drugs are disposed of [5]

Decision: The pharmacy company or health care facility should determine when to dispose of accumulated pharmaceutical waste.

Approval: The authorization to dispose of pharmaceutical waste is sought from the authorities concerned. In Kenya, disposal is carried out under the National Environment Management Authority (NEMA) oversight and the PPB. The waste generator should fill out the disposal form appropriately and pay the PPB a fee of 2,500Ksh. The PPB issues a Drug Safe Disposal Certificate upon disposal. [2] In Hong Kong, one has to apply as a chemical waste generator to the Environmental Protection Department (EPD), after which a waste generator number is given to the applicant. The charges are issued to the waste generator within a month after collection. The waste collector issues a trip ticket to the generator upon collection. [24]

Planning: This is crucial if money, human capital, skills, time, equipment, and methods of disposal are to be made available. The volume of pharmaceutical waste should be estimated at this stage and is determined in weights per quantity using 0.2 metric tons per m^3.

Developing working teams: The disposal teams should be composed of pharmacists, pharmacist technicians, and pharmaceutical warehouse staff. Conditions of the worksite, composition, and volume of pharmaceutical waste determine personnel size and ratio.

Safety and health work teams: Protective equipment such as masks, gloves, helmets, boots, and overalls should be given to the groups handling disposal.

Sorting: Pharmaceuticals are available in various pharmacological and dosage forms. Different disposal methods are needed for each of the categories, and some can be safely returned to the supply chain, so it is essential to sort. Pharmaceutical waste should be separated, stored securely, and labeled before disposal.

Disposal: There are several options for waste disposal that should be determined in terms of cost, safety, simplicity, and practicability of the methods. Record: date and location of destruction, disposal method, pharmaceutical name, dosage form and amount, the value of items, reasons for disposal and name and signature of pharmacist disposing of and a witness before destruction.

Security: In dealing with narcotics, psychotropics, and antineoplastics, strict protection and regulation must be maintained to avoid diversion during sorting, scavenging, and pilfering.

Methods of disposing of pharmaceutical waste

There are eight methods of disposal of pharmaceutical waste, namely, return to donor, incineration, immobilization, landfill, sewer, chemical decomposition, burning in open containers, and fast-flowing watercourses. [2,5,16,21]

Return to donor

Large pharmaceuticals that are challenging to dispose of, such as antineoplastics and unwanted/expired donations, should be returned to the manufacturer or donor for disposal. Cross-border transfers can be used to dispose of pharmaceutical waste. This approach involves moving hazardous waste across international boundaries. It is regulated by the Basel Convention on Transboundary Transfers of Hazardous Wastes. However, the procedures around this method take along time to warrant transfer.

Landfill.

Landfilling refers to the direct disposal of untreated pharmaceutical waste in a land disposal site. A landfill is the most used disposal method. There are three categories of landfills.

Open uncontrolled non-engineered dump- It is widely practiced in developing countries. This process should not be used to dispose of untreated waste. After immobilization, it can be used as a last resort. In the event immobilization is not practical, waste should be filled with municipal waste to avoid scavenging. Open dumps should be isolated from watercourses to prevent pollution.

Engineered landfill- this is the second-best method to dispose of immobilized pharmaceutical waste. The technique has features to minimize release into the aquifer.

Heavy-duty sanitary landfill- these sites are well constructed, managed, over the water table, and separated from watercourses. This method is most safe to dispose of waste as it offers protection of the aquifer. Waste is compacted and coated with soil to preserve the conditions for sanitary waste.

Immobilization

There are two methods of waste immobilization, namely; encapsulation and inertization.

Encapsulation- involves immobilizing waste into a concrete block within a drum. The following procedure is used;

1. Clean drums. Do not use drums that previously contained explosive materials.
2. Cut drum lids open and bend them back.
3. Fill drums with solid or semi-solid waste, controlled substances, liquids, powders, or antineoplastics to 75% capacity.
4. Fill the drum with cement, lime, and water in the ratio of 15:15:5. Add a significant quantity of water to achieve consistency.
5. Bend back and weld the lid.
6. Place the drums at the bottom of the landfill and cover with new municipal waste.

Inertization – this method is cheap and can be undertaken using unsophisticated equipment. Materials required include grinder, concrete mixture and cement, lime, and water supply. It is suitable for disposing of solid or semi-solid waste, controlled substances, powders, or antineoplastics. The following procedure is used;

1. Put on protecting clothing such as gloves and masks.
2. Segregate packaging materials such as blister packs, plastics, papers, and cardboards from pharmaceuticals.
3. Mix pharmaceutical waste, water, lime, and cement in the ratio of 65%: 15%: 15%: 5% to form a homogeneous waste.
4. Transport the waste to a landfill using a concrete mixer truck.
5. Decant into urban waste or disperse into municipal waste.

Sewer

Disposing of into drains involves releasing small quantities of diluted waste into sewers. The method is suitable when disposing of liquids, intravenous fluids, and small amounts of disinfectants or antiseptics. This approach should not be used to dispose of undiluted antiseptics or disinfectants and antineoplastics.

Burning in open containers

Should be used for disposal of small amounts of pharmaceutical waste. Pharmaceuticals disposed of by this method should not be burnt at low temperatures to avoid air pollution. It is suitable for medications packed in papers and cupboards. Burning materials that contain Polyvinyl chloride (PVC) should be avoided.

Chemical decomposition

It is only feasible if chemical expertise is available, and disposal by incineration is not possible. It is time consuming, tedious, and chemicals used must always be available. It can be used to dispose of antineoplastics less than 50kg. Should be undertaken following manufactures' recommendations.

Incineration

Incineration can be carried out via two methods, namely, medium and novel high-temperature combustion.

Medium temperature incineration- can be used to dispose of solids, semi-solids, powders, and controlled substances if high-temperature incinerators are unavailable or if less safe methods are available. The incinerator has two chambers that attain 850^{0}C. The second chamber has a combustion retention time of 2 seconds. Pharmaceutical waste should be mixed with municipal waste in the ratio of 1:1000. Medium temperature incinerators should not be used to dispose of halogenated compounds (>1% halogenated compounds) as negligible halogen amounts end up in combustion gases.

Novel high-temperature incineration- can be used to dispose of solids, semi-solids, liquids, powders, controlled substances, and antineoplastics. Such incinerators, e.g., cement kilns, operate at temperatures above 1200^{0}C, have short gas residence time, proper emission controls, long combustion retention time, expensive, and use sophisticated technology. This incinerator disintegrates all organic waste components and absorbs any toxic combustion products. They can be used to dispose of significant volumes of pharmaceutical waste in a short time. Pharmaceuticals should be put in small amounts (5%) in the furnace than fuel feed (95%). Before incineration, remove packaging materials and grind the pharmaceuticals to avoid blockage of fuel feed.

Dangers of improper disposal

Improper habits during storage, handling, and disposal pose serious consequences to the environment, economy, human, and animal life. Pharmaceutical waste finds its way into rivers and lakes or leaches from landfills into aquifers. Households, healthcare facilities, and pharmaceutical industries should not pour down the drain or flush into sewer systems. A study conducted to evaluate disposal practices in South and South-East Asia found that most liquid dosage forms were disposed through the toilet and sink while solid waste was disposed of in trash or bins. The disposal methods highlighted by the study had the potential to cause harmful environmental effects. [25] The following are some of the consequences of improper disposal. [2,4,5,7,21,22,26,27,28,29]

- Contamination of water supplies for wildlife and domestic animals. Uncontrolled sex-drive was observed in sheep after drinking Viagra contaminated water.
- Improper disposal of opioids can lead to drug abuse as teenagers think prescription drugs are safer than other drugs.
- Accidental poisoning of children who come along improperly disposed drugs. Pills are colorful and look like candy; kids may unintentionally take medicine when they aren't cautious and cause overdosing.
- Potential of getting into the wrong hands of the public and pets.
- Improper disposal affects aquatic life. Male fish have turned inter-sex by displaying sexual characteristics due to pollution with Ethinylestradiol. Masculinization of female fish due to androgens. Analgesics have caused reduced hatching and organ damage in fish. Fluoxetine disposed of in watercourses caused frogs to hatch tadpoles with no legs and induced behavior changes, reproduction toxicity, and disruption of hormones in fish. Reduced growth of aquatic plants (artemia, Daphnia) and algae due to antibiotics and antifungals. Data collected by Helsinki Commission (HELCOM) collaborated with Baltic sea states found felodipine, carbamazepine, and tramadol in blue mussels at concentrations >100 µg/kg. Sea birds, e.g., Common eider, contained many of these pharmaceuticals suggesting that they can be transferred in food chains. [30]
- Non-biodegradable disinfectants, antineoplastics, antibiotics kill bacteria in bacteria required for sewage treatment affecting organic degradation processes, nitrification, and denitrification.
- Anti-microbial resistance and development of superbugs due to misuse, overuse, use as a growth promoter in livestock, and release of high quantities of antibiotics in fresh

watercourses. A study conducted among professionals working in pediatric wards at Sau Paulo university hospital found that anti-microbials (22.7%) were the most disposed pharmaceuticals, and the sink drain was the second most utilized method of disposal. Most of the drugs were disposed of in their physical form. Besides, 48% of the disposed of medicines posed a human and environmental health risk. [31]

- Burning pharmaceuticals at low temperatures or in open containers releases airborne toxic carbon emissions that cause pollution.
- Promotion of illegal activities, e.g., scavenging, diversion, and resale of expired pharmaceuticals to the public.
- Damage to the soil. Soil cannot support plant growth, and resulting plants have toxic molecules. Pharmaceutical chemicals in the soil cause phytotoxic effects on plants. 1000 μg/L of amoxicillin, an antibiotic, was observed to affect root growth in carrots and lettuce. Diclofenac, a Nonsteroidal anti-inflammatory reduced viability in Horseradish by 65%. [32]
- Formulation of landfills leads to slow decomposition of waste and leaching, leading to contaminated soil, making it hard for production.
- Infectious blood is disposed of in landfills, syringes being washed up in beaches.
- Heavy use of diclofenac (Cataflam, Voltaren) in cattle caused renal failure in vultures fed in carcasses.
- Increased healthcare costs and unnecessary waste of healthcare costs.
- Loss of reputation, fines, and licensing of the waste generator.

Challenges of managing pharmaceuticals in the environment

Pharmaceuticals are discharged into the environment by manufacturing and ordering pharmaceutical products, agriculture, patient use, improper disposal, consumption, and excretion. Medicines interact with humans and animals to produce a pharmacological effect at low doses. When non-target organisms in the environment are exposed to these pharmaceuticals even at low concentrations, detrimental effects will occur, such as waterborne toxicity in micrograms per liter of the antidepressant fluoxetine has affected spawning in shellfish. [33] Pharmaceuticals are tailored to be stable to reach and interact with target molecules; therefore, they slowly degrade. Constant use of pharmaceuticals leads to their accumulation in the environment at rates higher than their degradation rates. Medicines used in agriculture and aquaculture are released into water bodies directly or via surface runoff. WWTPs are not created to identify or remove pharmaceutical waste from water. For wildlife, exposure to pharmaceuticals is long-term as it occurs via multiple exposure routes such as freshwater bodies and terrestrial ecosystems and involves a mixture of substances. [15] The majority of health facilities have inadequate storage space for waste and cannot destroy waste according to the required standards. Developing countries lack policies, guidelines on waste management, adequate financing, human resource, space, equipment, professional expertise, and time to carry out disposal. [22] A study conducted among hospitals in Basra to evaluate the environmental impact of pharmaceutical waste reported the barriers of safe waste disposal as lack of awareness, handling chemotherapeutic waste like other medical waste, lack of a systematic approach to waste management, and old incinerators that operate at low temperatures, i.e., < 400°C. The incinerators generate toxic emissions and ash that contains a high concentration of heavy metals. The ash ends up in landfills through municipal waste, presenting an increased health risk to the environment and the transfer of diseases. [34] Managing pharmaceutical waste is now a global challenge since several countries lack takeback programs to safely dispose of waste. Public unawareness and irrational medicine use among patients contribute significantly to the accumulation of pharmaceutical waste. [35] An Albanian study found the leading waste management challenges were the high cost of the contract with waste treatment companies, unawareness of waste laws and regulations, decreased inspection visits by the Ministry of Health, and lack of motivators, e.g., incentives. [36] A Nepal study revealed barriers to waste management guidelines, incinerators, sanitary landfills, waste collecting trucks, burial pits, and unawareness of disposal guidelines. [37] Challenges that contributed to the accumulation of pharmaceutical waste in Finland include manual maintenance of expiry dates and stock levels, inconsistent information, infrequent ordering process that ordered large batches, inefficient recycling processes, inaccurate monitoring of waste. [38]

Mitigation options to control pharmaceutical waste in the environment

Studies exploring the harmful effects of pharmaceuticals on the environment are constrained. Pharmaceutical companies focus on patient health, dosage, and effectiveness during clinical trials, and 88% of human medicines do not have data on environmental toxicity. Countries like the Netherlands, France, Germany, and Sweden have developed a strategic approach for tackling environmental pharmaceutical waste. Mitigation options should be geared specifically to the lifecycle of a pharmaceutical to achieve long-term benefits and cost-effectiveness in the following steps; [15,39]

Cross-cutting: The Government should prioritize high-risk APIs, develop monitoring water quality, risk assessment, and modeling together with pharmaceutical and research organizations. Guidelines should be established to define the water and environmental quality standards of pharmaceuticals.

Design: In addition to developing a green pharmacy, pharmaceutical companies should develop customized or effective drugs and biological therapies.

Authorization: Until approving a prescription product, the Government should oversee regulations and determine the environmental risk. Before the market launch, pharmaceuticals with a high ecological risk should face strict conditions. The industry should offer options for risk intervention, Eco-labelling, post-approval monitoring, and mitigation.

Production: The Government and the pharmaceutical sector should develop an environmental criterion describing effluent discharge limits, disclosure of wastewater discharge, and ethical production practices.

Consumption: The health sector should prescribe environmentally friendly pharmaceuticals, individualized medicines, and targeted delivery mechanisms while decreasing inappropriate prescribing. The industry and health sector should improve customer selection and awareness by way of Eco-labelling for self-consumption. The Government should ban high-risk practices such as using antibiotics for prophylaxis in livestock and hormones to enhance livestock growth. Acceptable livestock handling practices, safe management, and improved hygiene and diagnosis are required in health care facilities to prevent emissions.

Collection and disposal: Solid waste utilities should implement anaerobic biogas fermentation and passive manure storage to improve manure management. The industries should introduce schemes for the processing of unused or expired medicines. The public should be told to avoid the dumping of unused or expired drugs in toilets and sinks.

Wastewater treatment: WWTPs should upgrade wastewater utilities to enhance the detection of pharmaceutical traces. The use of photocatalytic-ultrafiltration membranes immobilized by sol-gel in wastewater treatment plants has degraded over 40% and 30% of chlorhexidine digluconate and methylene blue, respectively. [40] A toxicological study showed that a combination of biochemical, Fenton's, and ozone treatment successfully removed 90% of pantoprazole in wastewater. The integrated process is cheap, safe, and consumes less energy. [41] Laccase enzyme extracted from trametes fungus can be used to minimize pharmaceutical chemicals in wastewater. The enzyme causes the degradation of pharmaceuticals such as diclofenac and ibuprofen in wastewater through hydroxylation reaction. [42] Modern anaerobic technologies such as hybrid anaerobic-chemical and anaerobic-aerobic systems are useful in treating wastewater as they have low operation costs, high organic loading, and produce less sludge. The designs have achieved > 90% and 97% removal of amoxicillin and sulfamerazine, respectively. [43] Modern wastewater technology, e.g., the electron-Fenton technique, decreased ibuprofen's concentration from wastewater from 400 ppm to 6.8 ppm when operating at optimum conditions. [44]

Drinking water treatment: Drinking water providers should incorporate water safety planning and upgrade to modern technology treatment plants. Pharmaceutical waste such as ibuprofen detected in surface and groundwater is exceptionally stable. Convectional contaminated water treatment technologies (CCWTTs) are not able to fully degrade such waste, and their application leads to the formation of toxic by-products. Its primary metabolite is present after degradation and poses a risk to human and aquatic life. Modern technology, such as photocatalysts, e.g., Ag_3PO_4 and adsorbent, e.g., halloysite nanotubes, have proven efficient in adsorption of pharmaceutical chemicals such as carbamazepine, ibuprofen, diclofenac, and naproxen. [45] Collaboration between pharmaceutical and water industries should be encouraged to enhance effective water treatment.

A Serbian study showed that assessing the lifecycle of pharmaceuticals is the most effective method of controlling household generated pharmaceutical waste. [9] Waste and inventory reduction projects conducted in Minnesota led to an annual saving of $80,000 and $123,000 in Hennepin County Medical Cente and Falls Memorial Hospital, respectively. The projects led to a significant reduction of pharmaceutical waste by minimizing excess stock, expired medicines, and availing usage reports. [18] A recent study has shown that incorporating a cultural perspective, i.e., understanding pharmaceutical waste disposal from a social, economic, and political context, can tackle the root cause of the problem by explaining why certain medicines are prescribed, consumed, and disposed of by specific populations. The perspective provides insights on how beliefs, perceptions, and values interrelate with waste disposal practices. The study showed that cultural preferences influenced the monitoring and reporting of pharmaceutical waste pollution. [46]

Role of a pharmacist in managing pharmaceutical waste

A pharmacist should be involved during the disposal of unused pharmaceuticals. Pharmacists should be aware of available disposal methods used in their area. They should prohibit disposal by open dumpsites, burning, and destruction in poorly constructed/insecure landfills as these carry a public health risk. They should inform the competent authorities on the cost of disposal, the available disposal options, and where to outsource disposal services. [22] Pharmacists are imperative in the pharmaceutical management cycle to ensure rational drug use to minimize pharmaceuticals' harmful environmental effects. They should be included in the selection, acquisition, usage, delivery and policy mechanism, legislation, and pharmaceutical rules. An Ethiopian study revealed that pharmacists have better knowledge regarding waste disposal practices compared to other cadres. In the survey, 29% and 32% of the respondents indicated that improper storage and receiving short expiry drugs led to medicines damage. [47] The pharmacist should flag up any extravagant or overprescribing to reduce leftovers that end up being disposed of improperly. Pharmacists should promote and track patient adherence and ensure that all prescribed drugs are used. [21] Pharmacists should supervise the ordering of stocks by predicting how much inventory to order and how long it will last to avoid overstocking, which increases the risk of expiring medicines. Proper storage practices should be followed to prevent damage. Pharmacists should establish standard operating procedures for disposing of low quality, expired, damaged, and unwanted pharmaceuticals properly. Being highly resourceful in information about drugs, pharmacists should be at the forefront of recommending the best disposal methods for consumers in households. Physicians should undertake regular patient education, after prescribing, on appropriate means of disposal specific to each dosage type. [48] A Serbian study found that hospital staff in one out of 5 hospitals had not received pharmaceutical waste management training. Moreover, training influenced safe waste management. The study concluded that having waste management specialists and routine training opportunities can enhance pharmaceutical waste management. [49] Healthcare facilities must designate thoroughly trained personnel who can adequately handle waste during emergencies and everyday operations. In the USA, personnel handling waste must undertake hazardous waste disposal training annually. Learning institutions must retain training records of individuals handling pharmaceutical waste. [50] Pharmacists should train stakeholders (prescribers, politicians) and serve as environmental watchdogs at all levels to increase public consciousness of the risks of inappropriate disposal and impact of different pharmaceutical formulations. A Palestine study found a significant relationship ($P<0.001$) between training and improvement in practice and knowledge among healthcare workers handling pharmaceutical waste. The study recommended the hospital administration to conduct healthcare worker-centered training frequently. [51] A Nepal study reported a significant association between knowledge and practices of waste disposal. Knowledgeable respondents practiced safe disposal practices. Participation in continuous medical education and training status influenced safe waste disposal practices clarifying that training waste handlers are essential to achieving safe disposal practices. [37]

The health ministry, drug control agency, environment ministry, waste management experts, pharmacists, and Non-Governmental Organizations (NGOs) should assess, examine, and monitor drug disposal activities. Monitoring can be achieved by creating national legislation and environmentally sustainable disposal strategies to prevent the use and release of toxic pharmaceuticals into the environment. [5] The Organisation for Economic Co-operation and Development (OECD) countries such as the USA, the UK, Sweden, Korea, Germany, Switzerland, and Australia have developed and adopted environmental, pharmaceutical control policy instruments. [15] Finally, higher learning institutions should train pharmacists to work on pharmaceutical waste earlier to practice. The curriculum should be restructured to include sources and risks of pharmaceutical waste, disposal/treatment/removal methods, ways of neutralizing pharmaceutical waste, effects of inappropriate disposal, and removal/treatment guidelines/policies. This program will provide a clear understanding of medicines' interaction with nature, critical in achieving future safe disposal practices. [21]

Conclusion

A large volume of pharmaceutical waste amasses yearly as a result of consumption, overproduction, and over-prescription. Numerous studies have shown trace amounts of pharmaceuticals in waterways, water supply systems, and soil. Due to improper disposal, these active pharmaceutical ingredients enter the food chain and are transferred back to humans, animals, and plants. Safe disposal of pharmaceutical waste is critical if public and environmental safety are to be sustained. The essential shortcomings of pharmaceutical waste disposal are inadequate storage space, insufficient funds, weak infrastructure, low awareness among health care staff, patients, and the public. All stakeholders, such as the Government, pharmaceutical companies, media, healthcare workers, patients, the public, and NGOs should pursue and implement safe waste management practices. Multidisciplinary cooperation and coordination at the household, healthcare, and industrial levels must enforce safe disposal. The introduction of national guidelines, cost-effective solutions to disposal, training personnel, and educating the public are crucial to reducing pharmaceutical waste-related hazards. Legislation dealing with expired medicine needs to be developed to control the large volumes of expired pharmaceuticals that negatively affect the environment. To reduce stockpile accumulation, the Government should invest in public collection schemes, high-temperature incinerators with controlled emissions, and fenced burial places. Regular inspection by regulatory bodies is necessary at all levels to ensure that qualified health staff handles waste and safe disposal practices, and guidelines are followed. Pharmaceutical industries should balance the manufacturing and consumption rates of medicine to avoid expiry. Modern technology should be applied to instability tests to prolong the pharmaceutical shelf life.

Take back options, collection events, and approved collection sites should be implemented and popularized through awareness campaigns. During production, safe disposal instructions should be included in the inserts or on the package to enhance public knowledge on safe disposal practices. The introduction of pharmaceutical waste management into the curriculum of the health sciences is necessary. Pharmacists are in a strong position to reduce the burden of unwanted pharmaceuticals by raising public awareness, training other health cadres, delivering patient care, and tracking disposal to ensure that this is achieved correctly.

Moreover, they can help to formulate and reforming policies for managing the use and release of high-risk pharmaceuticals into the environment. To avoid environmental pollution and health threats, wastewater and drinking water treatment plants should upgrade technology to eliminate traces of pharmaceuticals in water. Further research should be conducted across all nations to assess the magnitude of unsafe disposal practices.

Authors' contributions

DMN designed the study, carried out the research, and wrote the manuscript. AN and MNN advised on sources of research material, design, and editing manuscript. All authors have read and approved the manuscript.

Abbreviations

API	Active Pharmaceutical Ingredient
CCWTTs	Convectional contaminated water treatment technologies
DEA	Drug Enforcement Administration
E.A.s	Environment Assessment reports
EIC	Expected Introduction Concentration
EPA	Environmental Protection Agency
EPD	Environmental Protection Department
FDA	Food and Drug Administration
IV	Intravenous
KEMRI	Kenya Medical Research and Training Institute
KNH	Kenyatta National Hospital
MWWTPs	Municipal wastewater treatment plants
NEMA	National Environment Management Authority
NGOs	Non-Governmental Organisations

OECD	Organisation for Economic Co-operation and Development
PPB	Pharmacy and Poisons Board
PVC	Polyvinyl chloride
HELCOM	Helsinki Commission
U.K.	United Kingdom
U.N.	United Nations
UNICEF	United Nations Children Fund
USA	United States of America
WWTPs	Wastewater Treatment Plants
WHO	World Health Organisation

Sources of Funding

None

Acknowledgment

None

Conflicts of Interest

None declared

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

References

1. Rogowska J, Zimmermann A, Muszyńska A, Lydia W. Pharmaceutical Household Waste Practices: Preliminary Findings from a Case Study in Poland. Environmental Management. 2019;64:97–106. Available from: https://doi.org/10.1007/s00267-019-01174-7
2. Pharmacy and Poisons Board. Guidelines for the safe management of pharmaceutical waste. Pharmacy and Poisons Board, Nairobi. 2018;1(1):1-21. Available from: https://pharmacyboardkenya.org/files/?file=2018_3_13_Draft%20guideline_on_pharmaceutical%20waste.pdf
3. Jaseem M, Kumar P, John RM. An overview of waste management in pharmaceutical industry. The Pharma Innovation Journal. 2017 Feb;6(3):158-161.

4. Megan C. Consequences of Improperly Disposed Pharmaceuticals. Danielshealth [Internet]. 2019 [cited 2020 23 June]. Available From: https://www.danielshealth.com/knowledge-center/pharmaceutical-improper-disposal-consequences
5. World Health Organization. Guidelines for the Safe Disposal of Unwanted Pharmaceuticals in and after Emergencies: Interagency Guidelines. World Health Organization, Geneva. 1999:1-31. Available from: https://www.who.int/water_sanitation_health/medicalwaste/unwantpharm.pdf?ua=1
6. World Health Organization. Safe management of wastes from healthcare activities. WHO Press: World Health Organization, Geneva; 2014;2:1-329. https://apps.who.int/iris/bitstream/handle/10665/85349/9789241548564_eng.pdf;jsessionid=33B774CD1D3702CD16D02120503AC83E?sequence=1
7. World Health Organization. Healthcare Waste [Intenet]. 2020 [cited 2020 June 17]. Available from: https://www.who.int/news-room/fact-sheets/detail/health-care-waste.
8. Velagaleti R, Burns KP, Gill M, Prothro J. Impact of Current Good Manufacturing Practices and Emission Regulations and Guidances on the Discharge of Pharmaceutical Chemicals into the Environment from Manufacturing, Use, and Disposal. Environmental Health Perspectives. 2002 Mar;110(3):213-220.
9. Hristov S, Ristic G, Dordevic A. Development of model for household pharmaceutical waste management. Working and Living Environmental Protection. 2016 Dec;13(2): 121-128.
10. Offiong NO, Lema ES, Kang S, Inam E, Kang SY, Kim KW. Risk evaluation of pharmaceutical residues in wastewater from selected treatment plants in Gwangju, South Korea. J. Chem Soc. 2019 May;44(3):504-514.
11. Küster A, Adler N. Pharmaceuticals in the environment: scientific evidence of risks and its regulation. Philosophical Transactions: Biological Sciences. 2014 Sep; 369(1656):1-8. Available from: http://www.jstor.org.libproxy.csun.edu/stable/24501918
12. Zywno R. EPA's Approach to Pharmaceutical Waste. Natural Resources & Environment. 2014 Mar;28(3):58-59. Available from: http://www.jstor.org.libproxy.csun.edu/stable/24426147
13. Seleshie W, Abera K, Ayenew A. An assessment of pharmaceutical waste management by pharmaceutical industries and importers in and around Addis Ababa, Ethiopia. Ethiopian Journal of Environmental Studies & Management. 2018;11(4):425-440. Available from: https://ejesm.org/doi/v11i4.4

14. GAO Highlights. PRESCRIPTION OPIOIDS: Patient Options for Safe and Effective Disposal of Unused Opioids. United States Government Accountability Office. GAO-19-650. 2019 Sep:1-29
15. OECD. Pharmaceutical Residues in Freshwater: Hazards and Policy Responses, OECD Studies on Water. OECD Publishing, Paris. 2019 Nov:1-20. Available from: https://doi.org/10.1787/c936f42d en
16. Susmita R, Shah Y, Sajib A. PHARMACEUTICAL WASTE MANAGEMENT: A REVIEW. Ejbps. 2016 Nov;3(12):192-206.
17. Narvaez V, Jhon F, Jimenez C. Claudio. PHARMACEUTICAL PRODUCTS IN THE ENVIRONMENT: SOURCES, EFFECTS AND RISKS. Vitae [Internet]. 2012 Apr [cited 2020 June 20];19(1):93-108. Available from: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0121-40042012000100010&lng=en
18. Pines E, Smith C. Managing Pharmaceutical Waste: A 10-Step Blueprint for Healthcare Facilities In the United States. Healthcare Environmental Resource Center. 2008 Aug:1-93.
19. United Nations Educational, Scientific and Cultural Organization and Helsinki Commission. Pharmaceuticals in the aquatic environment of the Baltic Sea region – A status report. UNESCO Publishing, Paris. 2017;1:1-121.
20. Constantino VM, Fregonesi BM, Tonani KAA, Zagui GS, Toninato APC, Nonose ERS. Storage and disposal of pharmaceuticals at home: a systematic review. Ciência & Saúde Coletiva. 2020 Mar;25(2):585-594. Available from: 10.1590/1413-81232020252.10882018
21. Kadam A, Patil S, Patil S, Tumkur A. Pharmaceutical Waste Management, an Overview. Indian Journal of Pharmacy Practice. 2016 Jan;9(1):1-8. Available from: 10.5530/ijopp.9.1.2
22. Business Daily. Dangers of poor pharmaceutical waste disposal [Online]. 2017 [cited 2020 June 26]. Available from: https://www.businessdailyafrica.com/news/Danger-poor-pharmaceutical-waste-disposal/539546-4218120-yy1mtr/index.html.
23. Kermenidou M, Voudrias EA, Konstantoula AC. Composition and production rate of cytostatic pharmaceutical waste from a Greek Cancer Treatment Hospital. Global NEST Journal. 2019 Jan;21(2):131-140. Available from: https://doi.org/10.30955/gnj.002889

24. Environmental Protection Department. Guidance on Disposal of Unserviceable/ Expired Medicines for Licensed Pharmaceutical Traders. 2020:1-3. Available from: https://www.epd.gov.hk
25. Nipa NY, Ahmed S, Shahariar MD, Rahman M, Haider B, et al. Improper Management of Pharmaceutical Waste in South and South-East Asian Regions. J Environ Stud. 2017 Mar;3(1):1-7.
26. European Public Health Alliance. Drug resistance through the back door: how the pharmaceutical industry is fueling the rise of superbugs through pollution in its supply chains. Nordea Asset Management. 2016;1-11. Available from: https://www.medbox.org/document/drug-resistance-through-the-back-door-how-the-pharmaceutical-industry-is-fuelling-the-rise-of-superbugs-through-pollution-in-its-supply-chains
27. Laura K. Pharmaceutical Waste Management: Environmental Impacts [Internet]. 2012 [cited 2020 June 26]. Available from: https://www.michigan.gov/documents/deq/deq-oea-workshop-seagrant-presentation-LauraKamin_376219_7.pdf.
28. Ahsen S. Causes, Effects and Solutions to Pharmaceutical Waste. Nature love [Internet]. 2020. [cited 2020 June 27]. Available from: https://environmentbuddy.com/waste-management/%EF%BB%BFcauses-effects-and-solutions-to-pharmaceutical-waste/
29. Khaleej Times. Sex run by sheep after drinking Viagra water? Pfizer responds [Internet]. 2019 Dec [cited 2020 June 28]. Available from: https://www.khaleejtimes.com/offbeat/sex-run-by-sheep-after-drinking-viagra-water-pfizer-responds
30. Hallgren P, Wallberg P. Background report on pharmaceutical concentrations and effects in the Baltic Sea. Policy Area Hazards of the E.U. Strategy for the Baltic Sea Region. Swedish Environmental Protection Agency, Stockholm, Sweden [Internet]. 2015 Dec:1-88 [cited 2020 Jul 13]. Available from: www.swedishepa.se/hazards
31. Almeida MAR, Wilson AMMM, Peterlini MAS. Evaluating pharmaceutical waste disposal in pediatric units. Rev Esc Enferm USP. 2016 Oct;50(6):922-928. Available from: http:// dx.doi.org/10.1590/S0080-623420160000700007
32. Kalaji HM, Rastogi A. Pharmaceutical Compounds: An Emerging Pollutant (A Review on Plant-pharmaceuticals Interaction). Chiang Mai J. Sci. 2017 Mar;44(2):287-297.
33. Jones OA, Voulvoulis N, Lester JN. Potential Ecological and Human Health Risks Associated with the Presence of Pharmaceutically Active Compounds in the Aquatic

Environment. Critical Reviews in Toxicology. 2004;34(4):335–350. Available from: 10.1080/10408440490464697

34. Yasir A.A. Environmental Impact of Pharmaceuticals and Personal Care Products. Journal of Global Pharma Technology. 2017 May;9(9):58-64.
35. Alnahas F, Yeboah P, Fliedel L, Abdin AY, Alhareth K. Expired Medication: Societal, Regulatory and Ethical Aspects of a Wasted Opportunity. Int. J. Environ. Res. Public Health. 2020 Jan;17(787):1-17. Available from:10.3390/ijerph17030787
36. Towle EG, Bruno JA, Hemingway JJ, Eaton S. Pharmaceutical Waste Disposal: Current Practices in Tirana, Albania. Worcester Polytechnique Institute. 2016:1-65. Available from: https://digitalcommons.wpi.edu/iqp-all/742
37. Paudel E, Choi E, Shrestha N. Pharmaceutical Waste Management in Private Pharmacies of Kaski District, Nepal. International Journal of Innovative Science and Research Technology. 2019 Aug;4(8):543-565.
38. Peltoniemi T, Suomi R. Eliminating medicine waste in a Finnish university hospital — a qualitative study. Journal of Pharmaceutical Policy and Practice. 2019 Oct;12(27):1-7. Available from: https://doi.org/10.1186/s40545-019-0188-8
39. Richman C, Castensson S. Impact of waste pharmaceuticals: an environmental hazard or "Greenwash"? The Pharmaceutical Journal. 2008 Mar;280:335-342. Available from: https://www.pharmaceutical-journal.com/news-and-analysis/opinion/comment/impact-of-waste-pharmaceuticals-an-environmental-hazard-or-greenwash/10006281.article
40. Chakraborty S, Loutatidou S, Palmisano G, Kujawa J, Mavukkandy MO, Al-Gharabli S, Curcio E, Arafat HA. Photocatalytic hollow fiber membranes for the degradation of pharmaceutical compounds in wastewater. Journal of Environmental Chemical Engineering. 2017 Sep;5:5014–5024. Available from: http://dx.doi.org/10.1016/j.jece.2017.09.038.
41. Sarkar KK, Majee S, Pathak U, Mandal DD, Mandal T. Design and development of an integrated treatment system for pharmaceutical waste with toxicological study. Desalination and Water Treatment. 2019 Oct;5:75–85. Available from: 10.5004/dwt.2019.24341
42. Yusuf Y, Fitriani, Yuniarti F. Preliminary study on enzymatic degradation of model of pharmaceutical waste by laccase from trametes sp. Journal of Critical Reviews. 2020 Jan;7(1):205-208. Available from: http://dx.doi.org/10.31838/jcr.07.01.37

43. Shi X, Leong KY, Ng H.Y. Anaerobic treatment of pharmaceutical wastewater: A critical review. Bioresource Technology. 2017 Aug;245:1238–1244. Available from: http://dx.doi.org/10.1016/j.biortech.2017.08.150
44. Davarnejad R, Zangene K, Fazlali AR, Behfar R. Ibuprofen Removal from a Pharmaceutical Wastewater using Electro-Fenton Process: An Efficient Technique, International Journal of Engineering (IJE), TRANSACTIONS B: Applications. 2017 Nov;30(11):1639-1646. Available from: 10.5829/ije.2017.30.11b.03
45. Nyankson E, Kumar RV. Removal of water-soluble dyes and pharmaceutical wastes by combining the photocatalytic properties of Ag3PO4 with the adsorption properties of halloysite nanotubes. Materials Today Advances. 2019 Oct;4. Available from: https://doi.org/10.1016/j.mtadv.2019.100025
46. Thomas F. Pharmaceutical waste in the environment: a cultural perspective. Public Health Panorama. 2017 Mar;3(1):1-140.
47. World Health Organisation. Practical Pharmacy For Developing Countries. Hai Africa. 2010 March;21:1-10. [cited 2020 June 28]. Available from: http://origin.who.int/management/resources/drugs/practicalpharmacy21b.pdf
48. Gudeta T, Assefa D. Assessment of Pharmaceuticals Waste Practices Among Private Drug Retail Outlets in Ethiopia. Journal of Primary Care & Community Health. 2020 Feb;11:1–8. Available from: https://doi.org/10.1177/2150132720920496
49. Jovanovic V, Manojlovic J, Jovanovic D, Matic B, Donovic N. Management of pharmaceutical waste in hospitals in Serbia – challenges and the potential for improvement. Indian Journal of Pharmaceutical Education and Research. 2016 Oct-Dec;50(4):695-702.
50. The University of South Florida. Disposal of Hazardous Waste Pharmaceuticals. Environmental Health & Safety. 2019 Nov:1-13.
51. Tabash MI, Hussein RA, Mahmoud AH, El-Borgy MD, Abu-Hamad BA. Impact of an educational program on knowledge and practice of health care staff toward pharmaceutical waste management in Gaza, Palestine. Journal of the air & waste management association. 2016 Mar;66(4):429–438. Available from: http://dx.doi.org/10.1080/10962247.2016.1146638