

Review Article

IMPACT OF PHARMACEUTICAL INDUSTRIES ON ENVIRONMENT, HEALTH AND SAFETY

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ABSTRACT

Diverse classes of pharmaceutical compounds like analgesic, antidepressant, antihypertensive, contraceptive, antibiotic, steroids and hormones etc. have been detected in water samples from ng/l to µg/l range. Though the detected amounts are very tiny but highly toxic for human, animal and aquatic lives. Traditional wastewater treatment methods, such as activated sludge, are not sufficient for the complete removal of active pharmaceutical ingredients and other wastewater constituents from these waters. Environment and health are directly or indirectly affected by pharmaceutical effluents especially in the vicinity of pharma industrial zones. Pharmaceutical waste is a form of medical waste that includes unused medications, and occasionally frills such as used test strips, and other supplies. Pharmaceuticals are synthetic chemicals belonging to a wide group of different chemical families and may also react different in the environment. Pharmaceuticals are special kinds of chemicals. They are manufactured to be biologically active in living organisms, to be persistent to biodegradation and to have long half-lives. This makes them more risky in nature. Release is ongoing always and everywhere, diffuse and impossible to control. They cannot be forbidden. There is a need of regular monitoring of concentration of pharmaceutical compounds in pharmaceutical effluents entering into drinking water sources in order to save environment as well as living form of lives from health hazards. The present paper highlights such toxicity, health risk and assessment of environmental hazards due to pharmaceutical pollutants.

Keywords: Pharmaceutical waste, Industrial wastewater, Health Hazards, Drinking water sources, Biomedical waste.

INTRODUCTION

Trace amount of pharmaceuticals in drinking water for longer duration may cause substantial undesirable effects to human health and aquatic life, though concentrations of pharmaceuticals detected in drinking water are several orders of inferior magnitude than the minimum therapeutic dose [1]. There is currently no Bureau of Indian Standards limiting the levels of pharmaceuticals in wastewater or drinking water. It has been found that the pharmaceutical compounds reach the environment and can be considered as environmental pollutants. Several pharmaceutical production facilities were found to be sources of much higher environmental concentrations than those caused by the applications of drugs [2].

Pharmaceutical waste is perhaps generated through a wide mixture of deeds in a healthcare facility, including but not limited to I. V preparation, general compounding, breakages, the partially used ampoules, needles, and IVs, out-dated, unused preparations, fallow unit doses, personal medications and outdated pharmaceuticals. There are a number of different options available for the treatment and management of waste containing dodging, minimization, re-use, reutilizing, energy recovery and disposal [3]. Moreover, pharmaceutical compounds may enter the environment by diverse routes such as discharge of treated wastewater, seepage from landfills sites, sewer lines, runoff from animal wastes etc. Even though an assortment of physical and biological processes occurring in aquatic ecosystem may cause diminution of many pharmaceutical compounds, trace concentrations of human and veterinary pharmaceutical compounds as well as their metabolites have been detected in different water bodies like surface water, groundwater and drinking water sources [4, 5].

India's biomedical waste rules of 1998

Classification [6]

Definition of biomedical waste

The waste which is generated during the diagnosis, or immunization of human beings or animals, or in research deeds or in the manufacture or testing or analysis of biological,

Responsibility of operator

The operator regarding to any medical facilities, animal facilities ensure that BMWs are handled without any opposing effect to human health and the environment.

Recommended authority

State Pollution Control Boards (SPCBs) in states and Pollution Control Committees in territories are in charge for allowing and imposing the requirements of the Biomedical Waste Rules.

Segregation, packaging, transportation, and storage

According to the rules, BMWs not to be mixed with the other wastes. These should be segregated into labeled bags/containers. Transportation of BMWs is to be piloted in permitted vehicles. There should be no waste to be stored, unless special authorization is obtained from the regulatory experts.

Common disposal/incineration sites

Local public entities are required to give common disposal/incineration sites, and the operators of such sites are required to comply with the Biomedical Waste Rules.

Accident reporting

Each operator is critical to report any misfortune linked to the management of BMWs.

Annual reporting

The operators are crucial to submit an annual report to the approved authority to deliver information about amount of wastes produced, and ways of treatment.

Permitting

Each operator handling BMWs should provide facilities to 1,000 or more patients per month in order to obtain a license from the prescribed authority.

Recordkeeping

Each operator is essential to uphold records on the waste disposal of BMWs. And the records are to be inspected and verified by the approved authority at any time.

Sources of hazards in pharmaceutical industries

- Manufacturing and formulation installations.
- Handling and storage of hazardous chemicals including warehouses, god owns, tank forms in ports/fuel depots/docks.

- Transportation (road, rail, air, water, pipelines).
- Emission of pollutants—the air pollutants include carbon monoxide (CO), Nitrogen dioxide (NO₂), particulate matter of 10 microns or less (PM₁₀), Total suspended particulate matter (SPM), sulphur dioxide (SO₂), and Volatile organic compounds (VOCs). The most common VOCs include methanol, dichloromethane, toluene, ethylene glycol, N, N dimethyl formamide, and acetonitrile.
- Effluents, especially those that are not easily biodegradable and toxic in nature. The effluent releases could go directly to streams, rivers, lakes, oceans, or other bodies of water. The releases due to runoff, including storm water runoff, could also be a potential hazard.

Most common environmental hazard by pharmaceutical industries

The hazards from the pharmaceuticals could be categorized as:

- Ecotoxic-damage is caused to the environment.
- Carcinogenic-contribute to the causation of cancer.
- Persistent-remain dangerous for a long time.
- Bio-accumulative—accumulates as it makes its way up the food chain.
- Disastrous due to a catastrophe, mishap, calamity or grave occurrence in any area.

Classification of biomedical waste [7]

- ✓ Infectious waste
- ✓ Anatomical waste
- ✓ Medical waste
- ✓ Genotoxic waste
- ✓ Chemical waste
- ✓ Heavy metal waste
- ✓ Radioactive waste

Pharmaceutical waste management monitored by different regulatory authorities

- ❖ Local Publicly Owned Treatment Works (POTW)
- ❖ Department of Transportation (DOT)
- ❖ State Environmental Protection Agencies
- ❖ State Pharmacy Boards
- ❖ Drug Enforcement Administration (DEA)
- ❖ Environmental Protection Agency (EPA)
- ❖ Occupational Safety and Health Administration (OSHA)

Classification of pharmaceuticals compounds as environmental pollutants: [8]

- Anti Virals.
- Antiepileptic
- Hormones
- Antiseptics
- Analgesics
- Antibiotics
- Antihypertensive
- Beta-blockers
- Contraceptives
- Psychotherapeutics

Pharmaceutical waste classification

Chemo waste

Bulk chemotherapy waste

RMW incinerators have a reduced amount of restrictive emissions limits and permit requirements. Discarding “bulk” P-or U-listed chemotherapy agents as trace chemotherapy waste has been the grounds of substantial enforcement actions and fines and should be one of the first changes you implement in your pharmaceutical waste management program. Trace chemotherapy containers have long been used to discard listed chemotherapy drug waste that should be managed as hazardous waste. The trace chemotherapy waste is incinerated at an RMW incinerator, hazardous waste incinerator [9].

Trace chemotherapy waste

There is no acknowledged dissimilarity between bulk and trace chemotherapy contamination for P-and U-listed hazardous wastes since there isn't a lesser concentration limit under which these wastes can egress the regulatory system. Most state regulated medical waste regulations are either quiet or not specifically on the definition of trace chemotherapy waste. The unique orientation to set apart trace chemotherapy waste is found in an article written in 1984 by pharmacy personnel at the National Institutes of Health who pioneered applying the RCRA regulations to antineoplastic wastes. California's Medical Waste Management Act and Wisconsin's Medical Waste Rules identify trace chemotherapy waste and require incineration at a regulated medical waste facility or other approved treatment method.

Hazardous waste

A starting point for determining which pharmaceutical waste is hazardous, RCRA definitions must be considered. Drugs deemed hazardous by federal EPA regulations are categorized as “P list,” “U list,” or “chemical (D-list) characteristic.”

P-listed items are reflected acutely toxic (e. g., epinephrine, phentermine, physostigmine, nicotine,

Nitroglycerin, and warfarin>3%); U-listed items are considered toxic (e. g., phenol, lindane, choralhydrate, and selected anti-neoplastic waste) [10, 11].

Items on the chemical characteristic list are pharmaceuticals that cause wastes with any of the following characteristics

- ✓ Ignitability: D001 (40 CFR 261.21)
- ✓ Corrosivity: D002 (40 CFR Part 261.22)
- ✓ Reactivity: D003 (40 CFR Part 261.23)
- ✓ Toxicity: Multiple D Codes (40 CFR Part 261.24)

Non-hazardous waste

Some have well thought-out that once the manufacturer's packaging is opened, any unused or partially used product is nonhazardous pharmaceutical waste. Examples include unused or partially used vials, ampules, or bottles, unused or partially used i. v. bags and tubing containing drugs; discontinued medications that are not appropriate for reuse; and tablets and capsules that have been dropped or spit out by a patient. Outdated drugs being discarded may be also be included in this category. Discontinued medications that patients have brought from home and left are also considered pharmaceutical waste that should be disposed of in accordance with EPA, state, and Drug Enforcement Administration regulations. [12]

Properties of pharmaceutical effluents

Many pharmaceutical industries are accountable to produce toxic effluent as a outcome of their operation. The waste water generated from these industries possess solids, biodegradable and non degradable organic compounds etc. Pharmaceutical effluents propose basic information about the reliability of the aquatic habitat in rivers and streams, into which they are discharged. The

physicochemical analysis of the effluents should point toward that most of these industries obey the standard guidelines of Federal Environmental Protection Agency. An significant pollution index of industrial wastewaters is the oxygen content in chemical oxygen demand and biological oxygen demand, where the nutrients status are measured in terms of amount of nitrogen and phosphorus in waste water. Besides this, other significant water quality parameters include pH, temperature and total suspended solids [13, 14].

Regulations at national level

These points should be considered for regulations at national level.

- Factory act 1948 Compliance
- MoEF Environmental Clearance
- Environment Protection Act 1986
- Environmental Statements Submission to Pollution Boards-Form V
- Public Liability Act & Insurance 1991
- MSDS for Hazardous materials and compliance
- CCOE (PESO) License for classified solvent storage
- Indian Electricity Act 1936 & rules
- Disaster Management Act-2005
- Drugs & Cosmetic Act-1940
- Indian Boiler Act 1923
- Hazardous Waste Management Act & Rules
- The Petroleum Act-1934 & Rules-2002
- The Explosives Act-1884 & rules-1983
- Central Motor Vehicles Act for HW or Goods carrying-1989

Regulations at state level

These points should keep in mind for regulations at the state level.

- State Level Factory Rules-1963 and further amendments
- Pollution Control Board Consent To operate-a) WATER ACT 1974, b) AIR ACT-1984
- Stack Monitoring Reports for emissions to Air
- Work Environment monitoring-Ventilation, Illumination, Dust & fumes
- Noise Monitoring
- Formation of safety committee as per 73 L
- Hazardous Waste Disposal Records
- Petroleum products storage on site-type, storage, and License-class A solvents, Class B chemicals, HSD, LPG stock etc
- Fire Hydrant system & fire noc
- Trained first aiders
- EPR & ERT-Emergency Preparedness & Response, Emergency Response Team
- OHC-Occupational Health Centre, with Visiting Doctor & Male Nurse
- Approved Licensed Contractors
- ESI of Employees/Contractors/Sub Contractors
- Mock Drills-announced/un announced for Emergency Evacuation
- Safety Committee Meetings & MOM
- Safety & Environment Promotional Activities

Pharmaceuticals waste treatment [15]

Pharmaceutical waste is not one single waste stream, but many distinct waste streams that reflect the complexity and diversity of the chemicals that comprise pharmaceuticals. Pharmaceutical waste is potentially generated through a wide variety of activities in a healthcare facility, including but not limited to intravenous (IV) preparation, general compounding, spills/breakage, partially used vials, syringes, and IVs, discontinued, unused preparations, unused unit dose repacks, patients' personal medications and outdated pharmaceuticals.

Microwaving

Application of an electromagnetic field over the BMW provokes the liquid in the waste to oscillate and heat up, destroying the infectious components by conduction. This technology is effective if the ultraviolet radiation reaches the waste material. Before microwaving, BMWs require shredding to an acceptable size and humidification.

Incineration

Incineration is a disposal method in which solid organic wastes are subjected to ignition so as to alter them into residue and gaseous products. This method is constructive for disposal of residue of both solid waste management and solid residue from waste water management. This process reduces the volumes of solid waste to 20 to 30 percent of the original volume. Incineration and other high temperature waste treatment systems are sometimes described as "thermal treatment".

Deep burial

The Biomedical Waste Rules require that human anatomical and animal wastes in cities with the population less than 500,000 and in rural areas be disposed of by deep burial. Accordingly, the deep burial site should be pre-pared by digging a pit or trench of about 2 meters deep in an area that is not prone to flooding or erosion, and where the soil is relatively impermeable, there are no inhabitants or shallow wells in the vicinity, and the risk to surface water contamination is remote.

Autoclaving

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.

Chemical disinfection

Chemical disinfection is most suitable for treating liquid wastes such as blood, urine, stools, or health care facility sewage. Addition of strong oxidants like chlorine compounds, ammonium salts, aldehydes, or phenol compounds kills or inactivates pathogens in the BMW.

Waste management program

Health care facilities implement a waste management program that includes waste segregation to ensure that facilities meet *al.* applicable regulations and potentially minimize costs. For example, by separating the non hazardous pharmaceutical waste from hazardous pharmaceutical waste, facilities may minimize cost and still comply with applicable federal regulations. Another important part of the waste management program is to communicate with staff so all pharmaceuticals are disposed properly.

Waste segregation

The waste management plan should include a process to segregate pharmaceutical waste by how the facility plans to dispose of them. The process can identify the type of pharmaceutical (controlled or non-controlled, hazardous or nonhazardous, chemotherapy) either at the time of delivery or when the waste is collected. For example, some facilities find it useful after delivery and during stocking, to apply color-coded stickers on supplies that match the disposal bin color placed at their facility to collect and segregate various types of waste (e. g., black color indicates hazardous waste).

Training staff in proper disposal methods

After developing a waste management plan, the facility should train staff (pharmacy personnel, nurses on the patient floors, and others who will manage unused pharmaceuticals) to recognize the type of unused pharmaceutical and its proper disposal. The staff should recognize when unused pharmaceuticals should be returned to the pharmacy and when they should be disposed of and how. Training should be revisited to update and refresh staff on proper unused pharmaceutical management and waste handling. Staff can also provide feedback on how the program is working and ways to improve the process. Posters and signs should also be placed near disposal areas to remind staff of disposal policies. During periodic pharmaceutical stock inventory, consider auditing waste disposal practices to determine how well the facility staff is following the waste management plan. With the audit findings, the facility can identify where additional training is needed.

Health menace of pharmaceutical effluents

The long term experience of lower concentration of complex pharmaceutical mixtures on stream biota may result in acute and chronic damages, behavioral changes, and accumulation in tissues, reproductive damage and inhibition of cell proliferation. Several studies have demonstrated that fish exposed to wastewater effluents can exhibit reproductive abnormalities. Moreover, fish exposed to trace levels of birth control pharmaceuticals in the range of concentrations found in the environment show dramatic decreases in reproductive success, suggesting population level impacts are possible [16-20].

Advantage of pharmaceutical waste management [21]

- Nonhazardous drugs should be segregated into non-red and non-yellow containers that are labeled "Nonhazardous Pharmaceutical Waste-Incinerate only" and are disposed of at a regular medical waste or municipal incinerator that is permitted to accept nonhazardous pharmaceutical waste.

- Hazardous waste storage accumulation sites should be in the same locked area that houses mercury, xylene, formaldehyde, and other laboratory chemicals.

- The maximum storage time should be 90 or 180 d, as determined by the facility's waste generator status.

Reducing the pharmaceutical waste [22]

The following points should be considered to minimize the pharmaceutical waste

- Replacing Prepackaged Unit Dose Liquids with Patient-Specific Oral Syringes
- Controlled Substances
- Delivering Chemotherapy Drugs
- Monitoring Dating on Emergency Syringes
- Reviewing Inventory Controls to Minimize Outdates
- Considering the Management Options
- Developed to detail the organization's approach to identifying drugs that must be managed as
 - hazardous waste
 - Determining which non-regulated drugs will be managed as hazardous waste

Labeling drugs to facilitate segregation of hazardous waste

- Segregating waste streams
- Training staff (e. g., which staff, what information and how often)
- Setting up and managing satellite accumulation and storage accumulation areas

Effect on humans of different type of waste [23-26]

S. No.	Type of waste	Effect on humans
01.	Nuclear waste	<p>Hair The losing of hair quickly and in clumps occurs with radiation exposure at 200 rems or higher.</p> <p>Brain Since brain cells do not reproduce, they won't be damaged directly unless the exposure is 5,000 rems or greater. Like the heart, radiation kills nerve cells and small blood vessels, and can cause seizures and immediate death.</p> <p>Thyroid The certain body parts are more specifically affected by exposure to different types of radiation sources. The thyroid gland is susceptible to radioactive iodine. In sufficient amounts, radioactive iodine can destroy all or part of the thyroid. By taking potassium iodide, one can reduce the effects of exposure.</p> <p>Blood System When a person is exposed to around 100 rems, the blood's lymphocyte cell count will be reduced, leaving the victim more susceptible to infection. This is often referred to as mild radiation sickness. Early symptoms of radiation sickness mimic those of flu and may go unnoticed unless a blood count is done. According to data from Hiroshima and Nagasaki, show that symptoms may persist for up to 10 y and may also have an increased long-term risk for leukemia and lymphoma.</p> <p>Heart Intense exposure to radioactive material at 1,000 to 5,000 rems would do immediate damage to small blood vessels and probably cause heart failure and death directly.</p> <p>Gastrointestinal Tract Radiation damage to the intestinal tract lining will cause nausea, bloody vomiting and diarrhoea. This occurs when the victim's exposure is 200 rems or more. The radiation will begin to destroy the cells in the body that divide rapidly. These including blood, GI tract, reproductive and hair cells, and harms their DNA and RNA of surviving cells.</p> <p>Reproductive Tract Because reproductive tract cells divide rapidly, these areas of the body can be damaged at rem levels as low as 200. Long-term, some radiation sickness victims will become sterile.</p>
02.	Agrichemicals	Contact of humans to agrichemicals is common and results in acute and chronic health effects, including acute and chronic neurotoxicity (insecticides, fungicides, fumigants), lung damage (paraquat), chemical burns (anhydrous ammonia), and infant methemoglobinemia. A diversity of cancers also have been linked to exposure to various pesticides, particularly hematopoietic cancers. Immunologic abnormalities and adverse reproductive and developmental effects due to pesticides also have been reported.
03.	Environmental waste	Air pollution results are Cancer, neurobehavioral disorders, cardiovascular problems, reduced energy levels, premature death, asthma exacerbations, headaches and dizziness, irritation of eyes, nose, mouth and throat, reduced lung functioning, respiratory symptoms, respiratory disease, disruption of endocrine and reproductive and immune systems.

London Fog episode of 1952, where a sharp increase in particulate matter air pollution led to increased mortality among infants and older adults. Hazardous substances may irritate the skin or eyes, make it difficult to breathe, cause headaches and nausea, or result in other types of illness. Some hazardous substances can cause far more severe health effects, including: behavioural abnormalities, cancer, genetic mutations, physiological malfunctions (e. g., reproductive impairment, kidney failure, etc.), physical deformations, and birth defects. Soil pollution effects causes according to are cancer including leukaemia and it is danger for young children as it can cause developmental damage to the brain furthermore it illustrated that mercury in soil increases the risk of neuromuscular blockage, causes headaches, kidney failure, depression of the central nervous system,, eye irritation and skin rash, nausea and fatigue. Soil pollution closely associated to air and water pollution, so its numerous effects come out as similar as caused by water and air contamination.

Polluted drinking water or water polluted by chemicals produced waterborne diseases like, Giardiasis, Amoebiasis, Hookworm, Ascariasis, Typhoid, Liver and kidney damage, Alzheimer's disease, non-Hodgkin's Lymphoma, multiple Sclerosis, Hormonal problems that can disorder development and reproductive processes, Cancer, heart disease, damage to the nervous system, different type of damages on babies in womb, Parkinson's disease, Damage to the DNA and even death, meanwhile, polluted beach water contaminated people like stomach aches, encephalitis, Hepatitis, diarrhoea, vomiting, gastroenteritis, respiratory infections, ear ache, pink eye and rashes.

CONCLUSION

Water quality guidelines enforced in India needs to include analysis of most commonly used pharmaceutical compounds in drinking water sources. Moreover, the newest remedial measures need to be adopted at large in effluent treatment plants of pharmaceutical industrial units to check long term environmental and health hazards. The impacts of drugs are entering into and occurring on ecosystems, biota and humans. The side effects on human, aquatic and animal health need to be investigated through thorough safety and toxicological studies. Sincere efforts are required to diminish the problem along with some sufficient regulations to monitor or to control them. Pharmaceutical waste continues to be an innovative frontier in environmental management for health care facilities. The supervision of pharmaceutical wastes poses a great challenge to the policy planners, city administrators, medical personnel and workers in the recycling industry. It is interdisciplinary in nature, involving pharmacy, nursing, environment services, infection control, quality assurance, risk management, etc. The management of waste is an increasingly complex task with new waste classifications and disposal techniques being developed and released on a continual basis. It is interdisciplinary in nature, involving pharmacy, nursing, environment services, infection control, quality assurance, risk management, etc. Thus there is a need for adopting cost-effective system for providing improved medical treatment facilities and also require the execution of the new system to insure proper waste management and to diminish the amount of waste generation by awareness and education of all concerned. We should conduct an inventory of pharmaceuticals and unused pharmaceuticals to quantify the amount of medication the facility is disposing of and reduce unused pharmaceuticals by reviewing purchasing practices, using limited dose or unit dose dispensing, replacing pharmaceutical samples with vouchers, and performing ongoing inventory control and stock rotation. Properly manage unused pharmaceuticals by identifying types of pharmaceuticals and any federal and state requirements; when possible: reusing or donating unused pharmaceuticals, returning them to the pharmacy; sending them to a reverse distributor for credit and proper disposal. Segregate waste for disposal to ensure regulations are met and to reduce costs (e. g., nonhazardous pharmaceutical waste disposal in a solid waste landfill may be less expensive than disposal via hazardous waste hauler). Train staff in proper disposal methods.

CONFLICT OF INTERESTS

Declared None

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