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# A Review on Pharma Pollution

**Kumari Shalini*, Zaihra Anwer, Pramod Kumar Sharma,**

**Vipin Kumar Garg, Nitin Kumar**

**Department of Pharmaceutical Technology, Meerut Institute of Engineering & Technology, Baghpat Bypass Crossing, Delhi- Haridwar Highway, NH-58, Meerut-250005 (UP),India**

***Corres.author: shalu0581@yahoo.com, Mob. No. 91-9456470704***

**Abstract:** Recently, pharmaceuticals were thought to reach the environment primarily through usage or inappropriate disposal. Certain production facilities were found to be sources of much higher environmental concentrations than those caused by the usage of drugs. Widespread detection of waste pharmaceuticals in environmental samples and the risks associated with their introduction into wildlife habitats is becoming an important issue for both regulators and the pharmaceutical industry. Pharmaceutical companies should see that it is in their own interest to minimize drug use and pollution of the environment, since avoiding the spread of resistance will keep their medicines effective longer. Possible ways to stimulate action include changes in local and international regulations, including the implementation of appropriate environmental standards within existing industry guidelines as well as demands from prescribers and consumers of medicines. The lack of readily available information regarding the origin of drugs and the environmental impact of the production, however, prevents consumers from making informed decisions. We propose that increased transparency throughout the production chain would be one of several important steps for reducing pollution from the manufacturing of drugs.

**Key Words:** Pollution, Environmental, risk, Industry, Drugs.

## INTRODUCTION

It is recognized that pharmaceutical compounds reach the environment and can be considered as environmental pollution. Pharmaceuticals were thought to reach the environment primarily through usage or inappropriate disposal. Various Production facilities were found to be sources of much higher environmental concentrations than those caused by the usage of drugs [1].Pharmaceuticals plants generate a large amount of wastes during manufacturing, housekeeping and maintenance operations. While maintenance and housekeeping activities are similar from one plant to the next, the actual processes used in pharmaceutical manufacturing vary widely. Typical waste streams include spent fermentation broths, process liquors, solvents, and equipment wash waters, spilled materials, and used processing aids. Pharmaceuticals have been detected in wastewater treatment plant effluents, surface water, ground water, and drinking water. Different classes of drug have been documented as environmental pollutants such as analgesics, antibiotics, antiepileptic, antihypertensive, antiseptics, beta-blocker heart drugs, contraceptives, hormones, and psychotherapeutics [2]. Pharmaceutical products are used in human and veterinary medicine and are a class of emerging environmental contaminants. These are natural or synthetic chemicals designed to have a specific mode of action [3]. Worldwide detection of waste pharmaceuticals in the environment causes risks associated with their introduction into wildlife habitats and is becoming a serious issue for both regulators and the pharmaceutical industry [4]. Although different classes of pharmaceuticals are used in human and veterinary medicine, only a few are of environmental importance because of their consumption volumes, toxicity, and persistence in the environment. Pharmaceuticals in the aquatic environment have been reported in rivers,

sewage, streams, seawater, ground water, and drinking water. Measurable concentrations are usually low, may be in ng/l to µg/l in range [3]. yet may be high close to the point of input, particularly for veterinary medicines used in aquaculture where concentrations may reach the low to medium µg/l range in surface water [5].Wide range of drugs including antibiotics, analgesics, blood lipid-lowering agents, antiepileptic, and β-blockers have been found in the effluents and surface waters of several countries [2, 3, 6, 7, 8.] There is a growing need to assess the environmental risk. So monitoring of pharmaceuticals products in the surface water and/or ground water is essential. Pharmaceuticals undergo several biotransformation processes in the human body before the excretion and after that excreted material reaches surface water through sewage water and wastewater treatment plant (WWTP) effluents either as parent compounds or as metabolites. Relevant metabolites were included in the work and the various methodologies used for targeting and selection of metabolites. Metabolites are selected based on the basis of their excretion fraction, their pharmacological activity, and the consumption amount of the corresponding parent drug. Pharmaceuticals selected here belong to several therapeutical and pharmacological classes and include analgesics, nonsteroidal anti-inflammatories (NSAIDs), anxiolytics, several antidepressant classes including selective serotonin reuptake inhibitors (SSRIs), blood lipid lowering agents such as statins and fibrates, various anti-hypertensor classes (β blockers, sartans, calcium-channel blockers),antipsychotics, antibacterials, anticonvulsives and corticoids.

## PHARMACEUTICAL INDUSTRY

### INDUSTRY PROFILE

In the pharmaceutical industry various types of processes are involved in the manufacture of pharmaceutical products. Due to the diversity of these processes, it provides a general set of waste minimization guidelines that would apply to all drugs manufacturing process. Along with research and development, four methods used in the manufacturing of pharmaceuticals are considered:

1) Research and development
2) Chemical synthesis
3) Natural product extraction
4) Formulation.

### RESEARCH AND DEVELOPMENT

Research and development (R&D) department in the pharmaceutical industry include chemical research, Microbiological research and pharmacological research. In this a wide range of chemical and biological laboratory wastes are produced. The most common chemical wastes produced from research and development department includes halogenated and non-halogenated solvents, photographic chemicals, radionuclide, bases, and oxidizers [9].

### CHEMICAL SYNTHESIS

In drug manufacturing plants, reaction vessels and ancillary equipment are often arranged into separate, process units, process functions (i.e., flow rate, pH, and temperature) according to good manufacturing practice protocols. At the end of whole process equipment is thoroughly cleaned. Chemicals used in chemical synthesis operations range include organic and inorganic reactants and catalysts. Manufacturers use a large group of solvents listed as priority pollutants[10], and these are used for product recovery, purification, and as reaction media.

### NATURAL PRODUCT EXTRACTION

Natural product extraction is the production of pharmaceuticals from natural material sources such as roots, leaves, barks and animal glands. Such pharmaceuticals, which typically exhibit unique pharmacological properties, include allergy relief medicines, insulin, morphine, alkaloids, and papaverine etc. During each process step, the volumes of materials are reduced and final purification may occur on volumes very less than the initial volume. Wastes from natural product extraction include spent raw materials such as leaves and roots, water-soluble solvents, solvent vapors and waste waters. Extraction waste waters typically have low biological oxygen demand (BOD), chemical oxygen demand (COD) and a pH in the range of 6 to 8 [10].

### FORMULATION

Pharmaceutical formulation is the preparation of various dosage forms such as tablets, capsules, liquids, parenterals, and creams and ointments etc. Tablets account for over 90 percent of total medications taken orally [9], and types are: plain compressed, coated, and molded. Capsules, in hard or soft form, are the second most widely used oral dosage form for solid drugs. The third type of pharmaceutical formulation is the liquid dosage form prepared for injection or oral use, which includes solutions, syrups, elixirs, suspensions, and tinctures, all of which are usually prepared by mixing the solutes with a selected solvent. Ointments are usually prepared by melting a base, which is typically the petroleum derivative petrolatum. This base is then blended with the drug and the cooled mixture is passed through a colloid or roller mill. Creams are oil-in-water or water-in-oil emulsions.

There are three main human activities which play major role for changes in ecosystems: chemical pollution, habitat fragmentation, alteration of community [11]. These chemicals are referred as

persistent bioaccumulative toxicants (PBTs) or persistent organic pollutants (POPs) such as lead, mercury, and dioxin, and they have highly detrimental effects over long periods of time. Bioaccumulation means tendency to increase concentration when a toxin is consumed in a succession food chain. Such as mercury, this is found in larger concentrations in fish than in shellfish, and is more concentrated in bigger fish. By the identification and regulation, the EPA (environmental protection act) and state and local municipal governments have curbed the most egregious of these chemicals to varying degrees.

**TOXICOLOGY CAUSED BY SOME PHARMACEUTICAL PRODUCTS**

**ANTIBIOTICS:**

Antibiotics are widely used, but studies show that up to 95% of antibiotic compounds can be released unaltered into the sewage system. This phenomenon may be due to accelerated resistance of bacterial pathogens against various antibiotics. High concentrations of antibiotics can lead to change in microbial community structure and affect food chains. Stream surveys documents microorganisms that are resistant to a wide array of antibiotics, including vancomycin [12]. Certain bacteria which are isolated from wild geese near Chicago, Illinois were reported to be resistant to ampicillin, tetracycline, penicillin, and erythromycin [13]. Contamination of microbial communities in septic tanks, sewers, soil, receiving waters and other environmental compartments create a widespread pool of antibiotic-resistant microbes and risk by the widespread use of antibiotics as growth promoters in livestock is being debated[14, 15]. Antibiotic and other drug resistance is already a major issue in medicine, with significant health and economic impacts, shown in tuberculosis and malaria, and multiple resistances is easily developed[16].If new forms of resistance start to come not only from human treatments and hospital settings, but by inter-species transfers from the environment and a revival of major epidemics is a distinct possibility.

**ANALGESICS AND NONSTEROIDAL ANTI-INFLAMMATORY DRUGS:**

Non-steroidal anti-inflammatory drugs (NSAID), such as ibuprofen, naproxen and diclofenac, are widely used medication and consequently are often detected in sewage, surface water and may be in ground water. Diclofenac, ibuprofen, acetylsalicyclic acid, ketoprofen, naproxen, indomethacin and phenazone have all been found in surface water. Diclofenac, ibuprofen, and propyphenazone are the most commonly found drugs in the water systems after clofibric acid. Diclofenac has been proven to be acutely toxic for vultures and cattle's [17]. Ibuprofen is one of the most commonly used drugs in the world and causes high levels of environmental pollution. The most sold drugs worldwide [18], NSAIDs have an estimated annual production of several kilotons [19]. NSAIDs such as ibuprofen, naproxen and aspirin are most common drugs which is usually found in significant quantities in municipal effluents[20,21].

**ANTINEOPLASTICS:**

Cancer therapy compounds are administered to control cancerous cell and interact with cell proliferation. Antineoplastics generally have long lived physiological effects such as ifosfamide in concentrations of up to 1.91 µg/L in the influent and effluent of treatment plants serving chemotherapy hospitals (Bay Area Pollution Prevention groups). This drug totally resistant to alteration during a two month bench scale simulation of sewage treatment, emerging essentially unchanged and also found that up to 30% of palatinates including carboplatin and cisplatin reside in the body for years and are slowly excreted into residential sewage systems [7].

**ENVIRONMENTAL RISK ASSESSMENTS**

There are laws in the United States and Europe that require prospective Environmental Risk Assessments (ERA) as part of the drug registration process. However, meaningful effort on this front is simply not possible with the currently limited state of knowledge on environmental transport, fate, and effects of pharmaceuticals. It does not take into account possible cumulative effects of different drugs affecting the same receptors[11]. Risk assessment is the procedure in which the risks caused by inherent hazards involved in processes or situations are estimated either quantitatively or qualitatively. In the life cycle of chemicals, risks can arise during manufacture, distribution, in use, or the disposal process. Risk assessment of the chemical involves the identification of the inherent hazards at every stage and an estimation of the risks by these hazards. Risk is estimated by incorporating as a measure the hazardous problem actually causing harm and severity of harm in terms of the consequences to people or the environment.

**DISPOSAL OF UNWANTED WASTE PHARMACEUTICALS PRODUCTS:**

In this we consider two parameter i.e. disposal of unwanted chemicals and metabolic excretion.

**DISPOSAL OF UNWANTED CHEMICALS:**

The unused, unwanted, or expired medications may be a challenge for human beings. Pharmacies may send unused or expired medications back to the original manufacturer. They may employ a reverse distribution

company to take care of manufacturer returns and incinerate those products that are non returnable. Little is available in the way of formal guidelines on drug disposal especially at the level of the final end user i.e.patient[22]. It is reported that approx one third of the total volume of pharmaceuticals sold in Germany and 25% of that sold in Australia was disposed with household waste or in the drain [23]. In the pharmacies surveyed, 97% policies is placed regarding disposal of expired undispensed medication, in which most cases was to return the medication to the manufacturer. In most of cases 25% of the pharmacies indicated that the issue of drug disposal was addressed only at the customer's request. In the patients surveyed, 1.5% returned medications to a pharmacy, 54% disposed medications in the trash, 35.4% flushed drugs down the toilet and sink, 7.1% did not dispose medications, and 2% stated they used all medication prior to expiration. In another survey performed in Canada in 1995 [24] and it shows that 63% of the patients surveyed had disposed medications in the past. The methods used to dispose these medications were: 46%, toilet; 32%, trash; 17%, pharmacy; 2%, physician; 5%, other. It was also determined in this survey the categories of medications that constitute the largest percentage of the overall costs of unwanted pharmaceuticals are: Cardiovascular therapies (high blood pressure, heart and circulation): 25.7%; Analgesic and Anti-Inflammatory: 19.3%; Endocrinological and Neurological: 15.3%; Gastro-Intestinal: 12.9%.

**METABOLIC EXCRETION:**

Pharmaceuticals products are biotransformed in the body and biodegradation modifies the chemical structure of the active molecules, which change their physicochemical and pharmaceutical properties. Metabolism may lower activity or enhance water solubility. In some cases metabolism is frequently incomplete and excretion rates range from 0 to 100% [23]. That means in many cases, a large portion of the drugs is not assimilated by the patient's body and it is excreted as feces, urine, vomit, etc.

**POLLUTION PREVENTION CONTROL**

The environmental impact and effect of pharmaceuticals in the environment is not clear at this moment but it creates big problems that the issue would not be resolved in the near future due to the fact that science and technology required to fully assess this risk is still in earliest stages of development. Humans are an integral part of the environment and it has been proven that there are inseparable connections between human health and the quality of the environment, high quality health care and environmental protection are intimately linked. Pollution prevention establishes a hierarchy in the type of measures environmental risk. In the case of hazardous waste this hierarchy is as follows:

- Minimization/reduction
- Reuse/Recycling

**MINIMIZATION AND REDUCTION:**

•**PUBLIC AWARENESS**: This play very important role in prevention of pollution. Increase public's sense against environmental responsibility by showing how their actions as individuals collectively contribute the impact of pharmaceuticals in the environment.

•**PATIENT COMPLIANCE AND EDUCATION**: Patient's awareness which is related about the importance of completing their treatments and following physician's directions carefully and also awareness about expired medicines.

•**HEALTHY LIFE STYLE**: Preventive health measures like: exercise, stress management, nutrition, and medications are to maintain our bodies and souls in good health.

• **PRACTITIONER'S EDUCATION:** Health care practitioners are properly educated and fully understand the importance of selecting the right medication and therapy for each patient and also the implications of improper use and disposal of pharmaceuticals.

**REUSE & RECYCLING:**

The legal framework and the resources required to allow patients and health care facilities to return unwanted medications that could still be used by other patients. Some drugs that may be recycled (for example, controlled substances like Valium and Tylenol with Codeine must be destroyed instead of returned, and the returned drugs cannot have less than 120 days before expiry date), there are many drugs that have potential to be rescued and returned for resale and reuse [25].

**REGULATORY FRAME WORK**

Pharmaceutical household waste is regulated by US Environmental protection act some current regulation that have to be taken into account when designing a pharmaceutical take back program in the US.

**RESOURCE CONSERVATION AND RECOVERY ACT (RCRA):**

The Federal Resource Conservation and Recovery Act (RCRA) cover all hazardous products such as pharmaceuticals waste. It only regulates pharmaceutical waste, which can be reprocessed, reused or an unsorted group of unwanted pharmaceuticals, some of which may have future use. This is the basis for the reverse distribution industry. U.S. EPA has authorized reverse distribution of pharmaceuticals waste. The U.S. EPA authorization

specifically returns industry not to be used as a waste management system and waste-like (like a broken container or contaminated prescription) cannot be shipped as products to a reverse distributor [26].

**US DRUG ENFORCEMENT ADMINISTRATION (DEA):**

Certain Pharmaceuticals are regulated by the U.S. Drug Enforcement Administration (DEA) and are known as "controlled substances". These are important for specific drugs that have a potential for abuse, such as narcotics or tranquilizers such as codeine, Valium, anabolic steroids, Ritalin, and Lomotil. The DEA lists controlled substances in five schedules. Schedule I drugs have no medicinal value and Schedules II to V drugs given to patients according to prescription.

**HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA):**

The Health Insurance Portability and Accountability Act (HIPAA) administered by the U.S. Department of Health and Human Services (DHHS) sets a standard to protect the privacy of personal health information. These standards require measures to ensure security of personal medical information, like that on prescription labels. HIPAA technically covers only medical care providers such as pharmacies and also covers business associates. Business associate is entitled to collect waste from pharmacies. Waste management contractor is defined as a business associate, and then HIPAA requires the pharmacy to enter into a written agreement with waste management contractor to protect private patient information [26].

**CONCLUSION**

Pharmaceuticals are biologically active compounds used daily by the public. Concentrations of waste pharmaceuticals have been found to be at their highest in wastewater and sludge associated with sewage treatment works. It is clear that pharmaceuticals have a major impact on the nature, particularly capable of affecting host immunology and physiology leading to changes in susceptibility and associated pathological symptoms. Due to the high number of pharmaceutical drugs used in human medicine throughout the world, it is necessary to select the pharmaceuticals to search for, prior to implementing any environmental measurements and any extensive environmental risk assessment (ERA).The pharmaceutical industry currently uses reverse distributors for the collection of unwanted pharmaceuticals from Pharmacies and Health Care Centers. This system could be used as a foundation for an integrated pharmaceutical product take back program that would cover general public as well. This initiative could also be seen as an extension of the product stewardship programs already fostered by the pharmaceutical industry.

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