Toxics Link
for a toxics-free world

Insights into the Pharmaceutical Effluent Treatment Plant

A Key to Check Antibiotic Pollution

NOVEMBER 2021

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About Toxics Link

Set up in 1996, Toxics Link is an Indian environmental research and advocacy organization engaged in disseminating information to help strengthen the campaign against toxics pollution, provide cleaner alternatives and bring together groups and people affected by the problem. Toxics Link's Mission Statement is: "Working together for environmental justice and freedom from toxics."

We have taken upon ourselves to collect and share both information about the sources and the dangers of toxins in our environment and bodies, and information about clean and sustainable alternatives for India and the rest of the world. The unique expertise of organization lies in the areas of hazardous, medical and municipal waste, international waste trade, and the emerging issues of pesticides, Persistent Organic Pollutants (POPs), hazardous heavy metal contamination etc. from the environment and public health point of view. We have successfully implemented various best practices and have brought in policy changes in the aforementioned areas apart from creating awareness among several stakeholder groups.

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01 Introduction

Water is an essential component of multiple processes in different manufacturing industries. Water is used as a coolant, solvent or in many industrial chemical or biological reactions. After the manufacturing process is completed, wastewater is produced as a byproduct. This wastewater contains various toxic materials, depending on the type of wastewater.

Further depending upon the type of industry and the manufacturing process, the toxicity of wastewater varies accordingly. Therefore, it cannot be directly disposed to the environment and has to be treated to remove the harmful materials from it. The adoption of the stringent Water (Prevention and Control of Pollution) Act, 1974 by the Govt of India has put a mandate on the industries to install Effluent Treatment Plant (ETP).

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1.1 About Effluent Treatment Plant (ETP)

ETP is defined as a process design for treating the industrial wastewater for its reuse or safe disposal to the environment. The untreated wastewater entering the ETP or wastewater treatment plant is known as influent and the treated wastewater is known as effluent. Different industries have varying wastewater composition and require different ETP designs to treat their effluents. Apart from the industries, there are growing requirements of ETPs in non-industrial processes including hotels, housing society and hospitals, etc.

1.2 Need for Effluent Treatment Plant (ETP)

01 Treatment (or cleaning) of industrial effluent and recycling it for further use

02 Reduction in the usage of fresh or potable water in industries

03 Reduction in expenditure on water procurement

04 Complying with the standards for discharge of environmental pollutants from various industries set by the government

05 Safeguarding environment against pollution and contributing to sustainable development

1.3 Design of ETP

The design and size of any ETP depends on the quantity and quality of discharge effluents from the industries. It also depends on the land and fund availability for construction, design and maintenance.

Generally, small-scale industrial facilities face problems in setting up individual ETPs due to lack of space, resources, capital cost, and specialized manpower for operation and maintenance. In such cases, Common Effluent Treatment Plant (CETP) is preferred over ETP. CETP are treatment systems specifically designed for collective treatment of effluent generated from small-scale industrial facilities in an industrial cluster.[1] CETP helps small scale units in terms of land conservation, better treatment,

The Ministry of Environment, Forest and Climate Change (MoEF & CC), Government of India has launched the centrally sponsored scheme, namely, Common Effluent Treatment Plant (CETP) in order to make a cooperative movement of pollution control especially, to treat the effluent, emanating from the clusters of compatible small-scale industries.

1. Padalkar A V., Kumar R. Common effluent treatment plant (CETP): Reliability analysis and performance evaluation. Water Sci Eng. 2018;11(3):205-213. doi:10.1016/J.WSE.2018.10.002

easy operation and maintenance, and shared expenses. The Ministry of Environment, Forest and Climate Change (MoEF & CC), Government of India has launched the centrally sponsored scheme, namely, Common Effluent Treatment Plant (CETP) in order to make a cooperative movement of pollution control especially, to treat the effluent, emanating from the clusters of compatible small-scale industries.[2]

1.4 Difference between Effluent Treatment Plant (ETP) and Sewage Treatment Plant (STP)

There is an inherent confusion between Effluent Treatment Plant (ETP) and Sewage Treatment Plant (STP). Therefore, it is important to understand that there are two broad categories of wastewater treatment processes based on their usages in different settings. Sewage is wastewater generated from residential areas like community whereas industrial effluent is waste water generated from various industries. The process treating industrial effluents is known as ETP, while that employed for sewage treatment is known as STP.

The major differences between ETP and STP are highlighted below

Effluent Treatment Plant (ETP)	Sewage Treatment Plant (STP)
ETP is the process of removal of toxic and non-toxic chemicals from industrial wastewater	STP is the process of removal of contaminants from wastewater and household sewage, both runoff (effluents) and domestic
It uses primary, secondary and tertiary treatment technologies such as oil and grease chamber, flocculation and biological methodologies	It includes physical, chemical, and biological processes to remove physical, chemical and biological contaminants
Requires specialized staff for operations and maintenance	Easy to operate
ETP is also a preferred technology for pharmaceuticals, chemicals, textiles and even hospitals because of the hazardous nature of wastewater	STP is generally preferred in case of household wastewater discharge and utilized in societies and apartments

2. Mondal P. Types of Wastewater Treatment Process: ETP, STP and CETP. Accessed October 29, 2021. https://www.yourarticlelibrary.com/water/types-of-wastewater-treatment-process-etp-stp-and-cetp/27418

02 Treatment levels & Mechanisms of ETP

Treatment levels

An ETP is designed to treat physical, chemical and biological substances present in the wastewater. The flowchart of a typical ETP is shown in Figure 1. Depending on the level of treatment required, an ETP is divided into four different levels, each designed to remove a certain type of material in the effluent as briefly discussed below:

- **Preliminary treatment**

  Removal of physical waste (gross solids and materials that can be easily collected) from the wastewater

  Involves physical separation techniques (e.g., sedimentation, filtration, etc.)

- **Primary treatment**

  Removal of floating and settable materials, such as oil and grease and organic matter

  Involves both physical (same as preliminary level) and chemical processes (e.g., chemical coagulation, flocculation, etc.)

- **Secondary treatment**

  Removal of biodegradable organic materials and suspended matter

  Involves both chemical (same as primary level) and biological processes (e.g. suspended-growth and the attached-growth/fixed film processes)

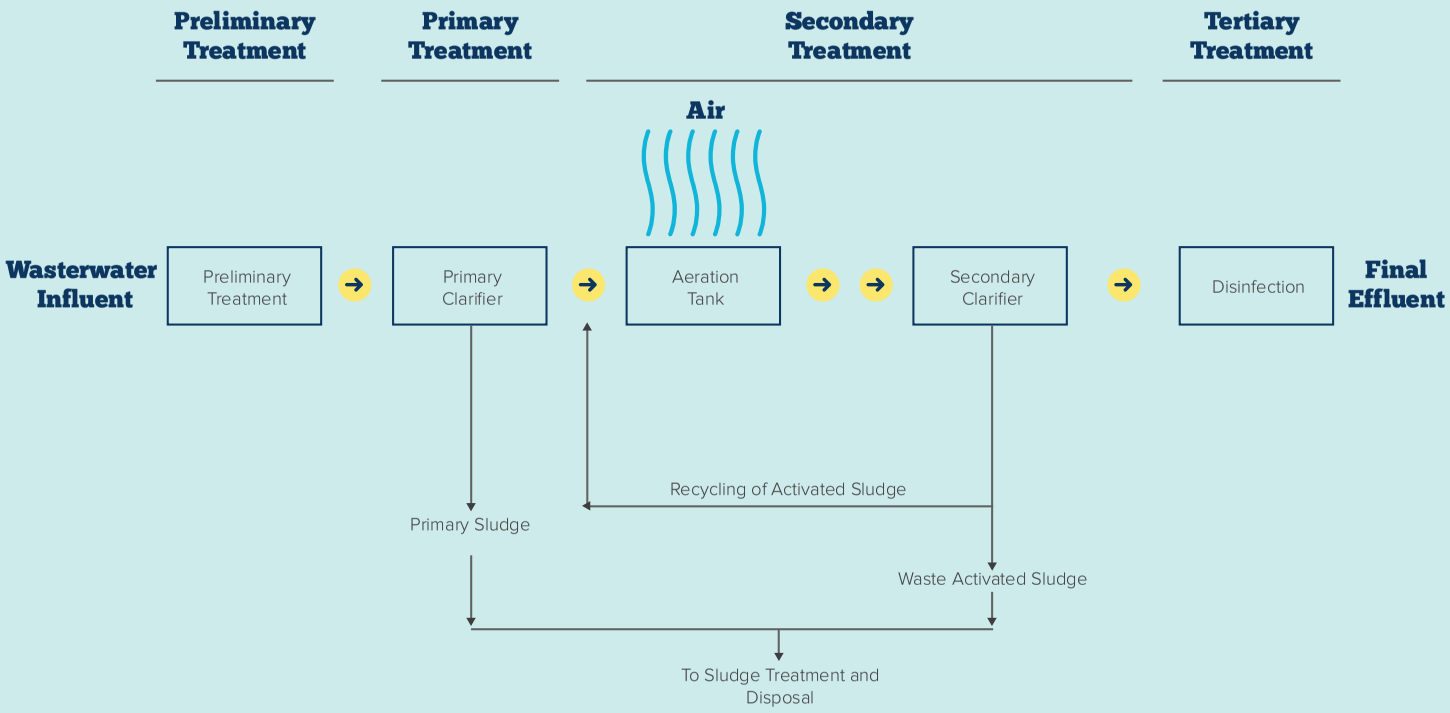
- **Tertiary treatment/Advance treatment**

  Final treatment (or polishing) to improve the wastewater quality before it is reused, recycled or disposed to the environment

  Removal of remaining organic and inorganic compounds using the physical, chemical and biological processes (as summarized in the previous levels) utilized together

  Adds additional cost to the treatment process but produces high quality effluent which can be reuse further for commercial and industrial purposes

Figure 1. **Flow chart of a typical ETP**



03 Pharmaceutical industry and effluents

The pharmaceutical industry manufactures thousands of drugs or active pharmaceutical ingredients (APIs) for a range of treatment applications including cancer therapy, antidepressants, steroids, antibiotics, etc. Increase in global demand for drugs has made pharmaceutical industry one of the major 26 polluters of solid wastes and effluent into the environment.[3] While the extent of the impact of pharmaceutical pollution on humans, animals, and the environment is the topic of ongoing research, antibiotic APIs have been linked to the growing problem of antimicrobial resistance (AMR) and the rise of antibiotic-resistant superbugs.

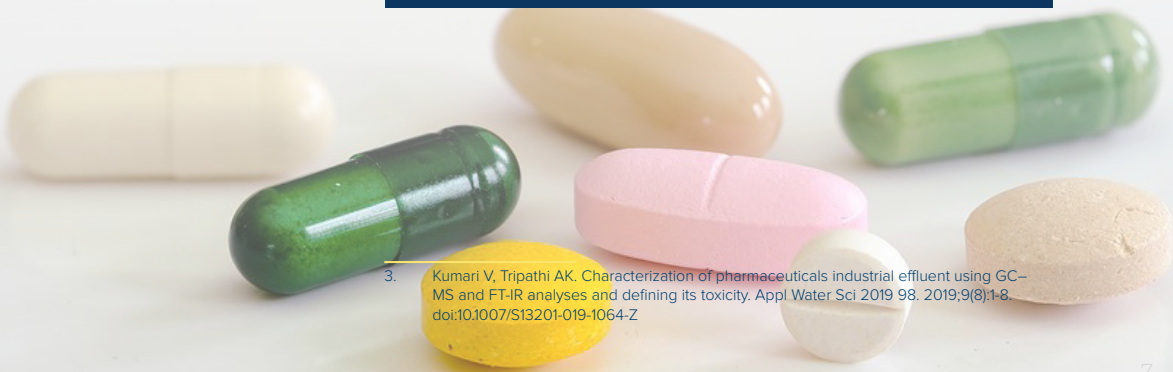
Pharmaceutical industry can be divided into two stages as per their manufacturing activity:

- **Active Pharmaceutical Ingredients (bulk active drugs)**

  A typical bulk drug manufacturing unit involves a series of reactions, separation and purification steps to make the desired end product. The bulk drug or active pharmaceutical ingredient (API) then goes for formulation.

- **Finished Dosage Forms (Formulation)**

  Formulation means a medicine in the forms of tablets, capsules, liquids, ointments processed out of or containing one or more bulk drugs.



3. Kumari V, Tripathi AK. Characterization of pharmaceuticals industrial effluent using GC–MS and FT-IR analyses and defining its toxicity. Appl Water Sci 2019 98. 2019;9(8):1-8. doi:10.1007/S13201-019-1064-Z

Pharmaceutical wastewater contains a high level of pollutants because of the presence of non-biodegradable organic matter such as antibiotics, other prescription drugs, non-prescription drugs, animal and plant steroids, reproductive hormones, betalactamides, anti-inflammatories, analgesics, lipid regulators, anti-depressants, cytostatic agents, personal care products, detergent metabolites, flame retardants, product of oil use and combustion, and other broadly used chemicals, i.e., spent solvents, reaction residues, used filter media, heavy metals (such as lead, mercury, cadmium, nickel, and chromium), and other pollutants.[4,5]

4. Babaahmadi F, Dobaradaran S, Pazira A, Sajjad Eghbali S, Khorsand M, Keshtkar M. Data on metal levels in the inlet and outlet waste-water treatment plant of hospitals in Bushehr province, Iran. Data Br. 2017;10:1-5. doi:10.1016/j.dib.2016.11.054
5. Singh A, Ramola B. Heavy Metal Concentrations in Pharmaceutical Effluents of Industrial Area of Dehradun (Uttarakhand), India. India J Env Anal Toxicol. 2013;3(3):173. doi:10.4172/2161-0525.1000173

Pharmaceutical sector falls within the category of high polluting industries. This sector generates strong wastewater having high chemical oxygen demand (COD) which require proper disposal. Moreover, it also produces hazardous waste which require effective treatment. As purity of the final product is very important, pharmaceutical industry requires very high-grade purity water apart from other raw materials for its manufacturing process. The rejects (both unreacted and converted portion of raw materials) contribute to major pollution load to pharmaceutical ETP.

A typical pharmaceutical industry involves several batch reactors to get the required product and each reaction yields different kinds of pollutants depending on particular reactants and processes. There are number of streams with different characteristics from different sections of the plant which may require segregation and corresponding treatment instead of conventional end of pipe treatment system for combined effluent **(Annexure)**

ACT

According to The Environmental (Protection) Rules, 1986, the general standards for discharge of effluents from industries are focused only on COD, Biochemical oxygen demand (BOD), suspended solids, heavy metals, etc. Most of the pharmaceutical industries comply with these standards. However, there are no standards for APIs in pharmaceutical effluents and therefore, the industries do not monitor or reveal these compounds. Recently, MoEF&CC proposed standards for antibiotic residues in the treated effluents, but the draft is still to be notified.

3.1 Challenges associated with treatment of pharmaceutical effluents

- Highly diverse nature of pharmaceutical wastewater as the composition of raw materials varies widely for one class of products to another
- Many pharmaceutical companies do not reveal the quantity and nature of toxic substances under a false impression of confidentiality of composition to escape from stringent pollution control norms. Thus, without completely revealing the magnitude of toxic substances, they continue to release pharmaceutical wastes into the environment
- Often, illogical mixing of industrial effluents and domestic sewage in industries results in very complex wastewater which makes treatment difficult

3.2 Why conventional ETPs are not successful at treating drug residues?

APIs are challenging to treat with conventional wastewater technologies because they are chemically stable, often recalcitrant and non-biodegradable. In many cases, conventional on-site pharmaceutical ETPs are either ineffective at treating APIs or unable to treat APIs to the levels required to minimize environmental impacts. There is a significant concentration of antibiotics and other drugs which can kill microorganisms involved in the biological treatment; therefore, biological treatment is not effective in the removal of APIs from pharmaceutical wastewater. Following are some important points to be taken into account in context of conventional ETPs.

- In line with current regulations, the existing ETPs are designed to meet the requirements for BOD, COD and TDS but there is no specific consideration with regards to API content or antibiotic residues. Therefore, it is difficult to determine the removal efficiency of APIs in the existing treatment technologies as there are no standards yet and these compounds are not regularly monitored

- In some cases, it has also been observed that traces of pharmaceutical products reappear in the treated water samples from WWTP. This points to the failure of existing facilities in complete removal of APIs.[6]

- The existing treatment strategies are not only ineffective to treat APIs completely but can also introduce other problems such as formation of unknown pharmaceutical metabolites and resistant bacteria

A few studies conducted till now have pointed out that the existing technologies are not capable of treating API residues. A Toxics Link study found Ciprofloxacin at 296 µg/L in the sample collected from secret outlet discharging effluent to the river in the Baddi-Nalagarh industrial zone, Himachal Pradesh.[7] In the recent case of "Veterans Forum for Transparency in Public Life v/s State of Himachal Pradesh & Ors", the inspection and compliance report submitted to the Hon'ble National Green Tribunal clearly highlighted the inefficiency of CETP at Baddi in the removal of APIs.[8]

The pharmaceutical industries in India have adopted various treatment options i.e., Anaerobic Digesters, Activated Sludge Process (ASP), Electro-coagulation followed by ASP, and tertiary treatment i.e., Multiple-effect Evaporator (MEE) and Reverse osmosis (RO).[9]

ETPs are mandated in every Health Care Facility to treat the wastewater generated from the hospital in order to comply with the effluent standards prescribed under the Biomedical Waste

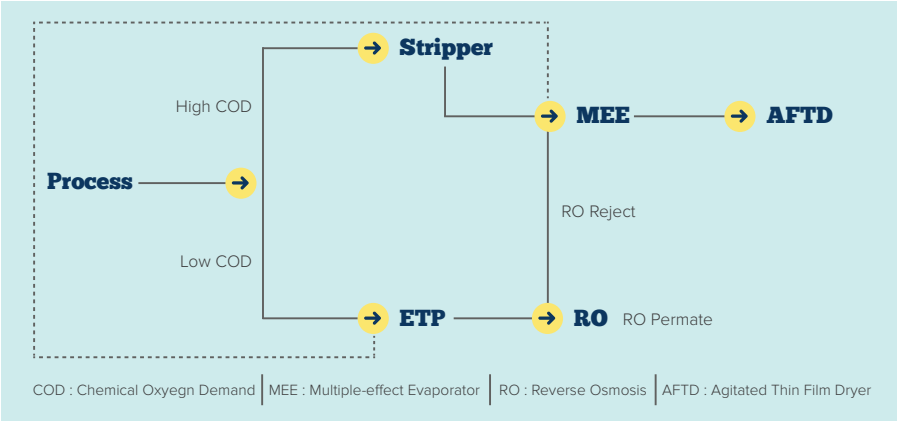
6. Hedgespeth M, Sapozhnikova Y, Pennington P, Clum A, Fairey A, Wirth E. Pharmaceuticals and personal care products (PPCPs) in treated wastewater discharges into Charleston Harbor, South Carolina. Sci Total Environ. 2012;437:1-9. doi:10.1016/J.SCITOTENV.2012.07.076
7. Toxics Link. Pharmaceutical Pollution in India: An Emerging Concern.; 2020. Accessed October 29, 2021. http://toxicslink.org/docs/Pharmaceutical pollution in India An emerging concern.pdf
8. https://greentribunal.gov.in/sites/default/files/news_updates/Report%20of%20the%20Joint%20Committee%20in%20OA%20No.%20136%20of%202020%20(Veteran%20Forum%20for%20Transparency%20in%20Public%20Life%20Vs%20State%20of%20HP%20&%20Ors.).pdf
9. https://cpcb.nic.in/openpdffile.php?id=UmVwb3J0RmlsZXMvMzAxXzE0NzEzNDM5ODJ-fUGhhcm1hY2V1dGljYWxzIENlbnRyYWwgWm9uZS5wZGY=

Management (BMW) Rules, 2016. Sources of wastewater in the hospital are wards, laboratories, disinfectants, floor washing, washing of patient area, hand washing, laundry, discharge of accidental spillage, firefighting, bathroom/toilet, etc.[10] The hospital effluents may also contain drug residues; however, the BMW Rules do not focus on complete neutralization of drug residues from hospital wastewater before discharging.

3.3 Zero Liquid Discharge in Pharmaceutical Industries

Many pharmaceutical companies, especially in India, are considering ways to minimize their liquid discharge. Therefore, some have adopted a zero-liquid-discharge (ZLD) program for their facilities. ZLD is a closed-loop cycle that minimizes or eliminates discharge of any liquid effluent by recycling and treating all wastewater. With a ZLD system not initially designed to fully deactivate antibiotic residues in the waste streams, as well as lack of regular monitoring data, the effectiveness of the deployed treatment technologies to eliminate APIs is not fully established.

Figure 2. A typical Effluent Treatment Plant with Zero Liquid Discharge



10. Implementation Guidelines for Management of Healthcare Waste in Health Care Facilities, MOEFCC

It should be noted that the requirement of high-quality standards in most of the pharmaceutical industries are limiting the sector to do only partial ZLD.[11] Moreover, despite widespread awareness and National Green Tribunal guidelines for adoption of ZLD, its use has been limited to units of major multi-national companies.[12]

Although, a typical ETP with ZLD (as depicted in Figure 2), implies no liquids are discharged from the manufacturing units, that does not mean the pharmaceutical residues do not enter the environment. While one could justify it by saying that since the manufacturing units are not discharging any liquid waste, there is no possibility of any discharge of antibiotics into the environment. However, there is no evidence to substantiate this conclusion. Apart from the direct discharge of treated wastewater with active ingredients into the environment, there are other possible sources contributing to the problem, such as:

- Discharge of API-rich wastewater during plant shutdowns
- Discharge of APIs into the environment through storm water drainage
- Improper disposal of solid wastes into the environment
- Re-use of treated wastewater within the premises of the manufacturing facilities for horticulture
- Accidental spills of concentrated waste streams within the manufacturing facilities

11. http://sustainabilityoutlook.in/content/market/zero-liquid-discharge-outlook-indian-industry-755079
12. https://www.downtoearth.org.in/blog/waste/zeroing-in-on-discharge-76089

04 Emerging technologies for treatment of pharmaceutical wastewater

4.1 Membrane separation processes

- Promising technology for treatment of wastewater containing APIs since it is able to produce a high quality permeate without increasing its toxicity
- Can be scalable, and applied to a broad range of contaminants
- Nanofiltration is the most recently developed pressure driven membrane separation process, and has been widely used in aqueous systems such as the concentration of antibiotic aqueous solutions
- Other examples of relatively new and robust membrane separation processes are forward osmosis, membrane distillation

4.2 Advanced oxidation processes

Advanced oxidation processes (AOPs), on the other hand, are found to be most effective treatment technology for completely mineralizing the pollutants to inorganic compounds, CO_2 and water.[13] AOPs are low cost, easy to operate and effective options for treatment of pharmaceutical wastewater and can also be coupled with biological or conventional physico-chemical processes for designing cost effective solutions. These processes are based on the generation of highly reactive hydroxyl radicals which can rapidly oxidize the target pollutants non-selectively.[14]

13. Poyatos JM, Muñio MM, Almecija MC, Torres JC, Hontoria E, Osorio F. Advanced Oxidation Processes for Wastewater Treatment: State of the Art. Water, Air, Soil Pollut 2009 2051. 2009;205(1):187-204. doi:10.1007/S11270-009-0065-1
14. Chelliapan S, Sallis P. Removal of organic compound from pharmaceutical wastewater using advanced oxidation processes. J Sci Ind Res. Published online 2013. Accessed October 29, 2021. https://www.semanticscholar.org/paper/Removal-of-organic-compound-from-pharmaceutical-Chelliapan-Sallis/271af2d1d0beeec344d23a81bfb-658b401a8f0b6

It has also been reported that the combinations of AOPs are more efficient in removal of organic compounds than individual techniques.[15]

Some of the advanced oxidation processes that have the potential to degrade APIs are:

- Photocatalysis
- UV or solar irradiation
- Electrooxidation
- Fenton and photo-Fenton processes
- Wet air oxidation
- Ultrasound irradiation and
- Microwave treatment

4.3 Hybrid Technologies

Hybrid technologies involve combinations of one or more conventional/advanced treatment technologies for the complete eradication of pharmaceutical contaminants.[16] As none of the single treatment technologies can remove all the target compounds, the use of hybrid technologies can help overcome this problem. The technology basically uses the conventional filtration step to remove any solid matrix and the sludge is removed for incineration. The clear wastewater is then treated by the different combination of processes.

Some examples of hybrid technologies

- Two-phase anaerobic digestion (TPAD) system and a subsequential MBR
- Ozonation (pretreatment) coupled with biological activated sludge treatment

Most widely accepted way of determining the presence of pharmaceuticals, including antibiotics, is based on laboratory testing methods that involve physical separation and mass chromatography techniques. USEPA Method 1694 determines pharmaceuticals in environmental samples by high performance liquid chromatography combined with mass spectrometry (HPLC/MS/MS)

15. Chelliapan S, Sallis P. Removal of organic compound from pharmaceutical wastewater using advanced oxidation processes. J Sci Ind Res. Published online 2013. Accessed October 29, 2021. https://www.semanticscholar.org/paper/Removal-of-organic-compound-from-pharmaceutical-Chelliapan-Sallis/271af2d1d0beeec344d23a81bfb658b401a8f0b6
16. Patel S, Mondal S, Majumder SK, Das P, Ghosh P. Treatment of a Pharmaceutical Industrial Effluent by a Hybrid Process of Advanced Oxidation and Adsorption. ACS Omega. 2020;5(50):32305-32317. doi:10.1021/ACSOMEGA.0C04139

05 Pharmaceutical wastewater treatment for removal of APIs: International case-studies

Haupt Pharma (Germany)

Haupt Pharma in Germany is the biggest site for formulation of high potential sexual hormones in Europe. In 8 formulation lines all types of sexual hormones like 17α-ethynylestradiol (EE2) are formulated and packed for final application. The wastewater from this industry is treated by Advanced Oxidation Process developed by Belmar technologies, UK (https://www.belmartechnologies.co.uk) to remove all hormones in a proper way to release clear and clean water into the municipal sewer. The treatment system was able to remove sexual hormones like EE2 from inlet concentration of 10 to 100 mg/L to less than 0.01 mg/L in the outlet.

GSK (Singapore)

Amoxicillin manufacturing site of GSK in Singapore (https://www.gsk.com/en-gb/contact-us/worldwide/singapore/) is one of the biggest sites for production of antibiotics worldwide. It is a well-known fact that biological treatment plants are not very capable of treating the strong wastewater from antibiotic manufacturing lines which resulted in incineration of the waste by GSK. The manufacturing site was in search for a more suitable process to be applied for removal of target compounds from the contaminated wastewater. A photo-oxidation pre-treatment system has been installed based on the UV process at GSK for elimination of residual amoxicillin and non-bio-available organics from the strong process wastewater. Due to pre-treatment by photo-oxidation, the existing biological system at GSK is also able to handle this wastewater.

Merck (Switzerland)

The pharmaceutical manufacturing site of Merck & Cie in Altdorf Switzerland (https://www.merckgroup.com/ch-en) is producing an antihypertensive containing a phenolic structure. The wastewater generated in the facility was initially collected and sent to incineration for significant costs. Later a process was successfully developed for treating this wastewater by elimination of all aromatic structures, all solvents and increasing bioavailability of the remaining organics. A recuperation system was integrated into the UV-plant for achieving oxidation with highest efficiency. Toxicity was found to be completely removed. Moreover, installation of this unit was significant improvement for Merck combined with huge cost saving.

Pharma Action (Germany)

The GMP compliant heparin processing plant of Pharma Action (Toennies Group) (https://www.cphi-online.com/pharma-action-gmbh-comp245280.html) has achieved a supply chain, in which the entire process: starting from animal slaughter, extraction of prime raw material to the final refinement into API occurs within a single company. The process wastewater is treated with UV oxidation to break down the organic substances. With this method, the treated water can be recovered and reused in the same process.

Some other case studies

- Axine's (https://axinewater.com/industries/) electrochemical advanced oxidation process (EAOP) technology is commercially proven and capable of treating a diverse range of complex APIs and/or organic pollutants to achieve the most stringent Predicted No-Effect Concentration (PNEC) levels through multiple oxidation mechanisms. This technology has been installed at many US pharmaceutical manufacturing plants
- Arvia's Nyex™ Treatment Systems (https://arviatechnology.com/pharmaceutical-residues/) have already successfully treated challenging wastewaters containing pharmaceutical residues in the UK, Europe and China from different sources

Recommendations for pharmaceutical effluent treatment and reducing pharma pollution

- Use of hybrid technologies has been shown to successfully remove APIs. Therefore, a comprehensive policy is necessary for upgradation of ETPs and CETPs to evaluate and adopt these technologies. Some of the sustainable and effective technologies in operation in developed countries can be adopted. In addition, various Indian research institutions can also be funded to develop indigenous treatment systems
- A regulatory framework should be developed to frequently monitor effluents from pharmaceutical industries and discharge bodies for API concentrations
- The proposed standards for antibiotic residues in the treated effluents of the pharmaceutical industries under the Environment (Protection) Amendment Rules, 2019 should be notified; following which, India will become the first country in the world to have legally enforceable discharge limits for antibiotics in waste from the pharmaceutical industry
- Environment (Protection) Amendment Rules should also include discharge standards for other API residues in addition to limits for antibiotic residues. Apart from antibiotic residues, the regulatory body should also come up with discharge standards for other API residues. The discharge standards can be formulated based on the PNEC values for these compounds

Suggested Resources

1. Gadipelly C, Pérez-González A, Yadav GD, et al. Pharmaceutical Industry Wastewater: Review of the Technologies for Water Treatment and Reuse. Ind Eng Chem Res. 2014;53(29):11571-11592. doi:10.1021/IE501210J
2. United States Environment Protection Agency (US EPA). Economic Analysis of Final Effluent Guidelines and Standards for Pharmaceutical Manufacturing Category - 1998.; 1998. Accessed October 29, 2021. https://19january2017snapshot.epa.gov/sites/production/files/2015-11/documents/pharmaceutical-manufacturing_economic-analysis_1998.pdf
3. Organisation for Economic Co-operation and Development (OECD). Pharmaceutical Residues in Freshwater: Hazards and Policy Responses. OECD; 2019. doi:10.1787/C936F42D-EN
4. Caldwell DJ, Mertens B, Kappler K, et al. A risk-based approach to managing active pharmaceutical ingredients in manufacturing effluent. Environ Toxicol Chem. 2016;35(4):813-822. doi:10.1002/ETC.3163
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6. Pal P. Treatment and Disposal of Pharmaceutical Wastewater: Toward the Sustainable Strategy. 2017;47(3):179-198. doi:10.1080/15422119.2017.1354888
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8. Martínez F, Molina R, Rodríguez I, Pariente MI, Segura Y, Melero JA. Techno-economical assessment of

coupling Fenton/biological processes for the treatment of a pharmaceutical wastewater. J Environ Chem Eng. 2018;6(1):485-494. doi:10.1016/J.JECE.2017.12.008

9. Angeles LF, Mullen RA, Huang IJ, et al. Assessing pharmaceutical removal and reduction in toxicity provided by advanced wastewater treatment systems. Environ Sci Water Res Technol. 2019;6(1):62-77. doi:10.1039/C9EW00559E

Annexure: Different processes and wastewater generated in each process of the pharmaceutical industry

Process	Inputs in the processes	Wastewater
Reaction	Solvents, catalysts, reactants, (e.g. benzene, chloroform, dichloromethane, toluene, methanol, ethylene glycol, xylenes and hydrochloric acid)	Process wastewaters (high BOD, COD and TSS) with spent solvents, catalyst, reactants
Separation	Separation and extraction solvents (e.g. methanol, toluene, acetone and hexanes)	Spills, leaks, spent solvents
Purification	Purification of solvents (e.g. methanol, toluene, acetone and hexanes)	Spills, leaks, spent solvents
Drying	Finished active drug and intermediates	Spills, leaks, spent solvents
Natural product extraction	Plant roots, animal tissues, extraction solvents (e.g. ammonia, chloroform and phenol)	Equipment cleaning, spills, leaks, spent solvents (low BOD, COD and TSS)
Fermentation	Inoculum, sugar, starches, nutrient, phosphates, fermentation solvents (e.g. ethanol, amyl alcohol, methanol, acetone, etc.)	Spent fermentation broth, wastewater containing sugar, nutrients, etc. High BOD, COD and pH 4–8
Formulations	Active drug, binders, sugar syrups, etc.	Equipment cleaning, spills, leaks, spent solvents (low BOD, COD and TSS)

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