Challenges of Pharmaceutical Pollution in India:
Study on Baddi, Himachal Pradesh
1. An Overview of Pharmaceutical Industry:

1.1. Introduction

Active Pharmaceutical Ingredients (APIs) are biologically active substances which are now being frequently discharged into the environment and are being extensively found in varied environmental matrices. APIs are generally non-biodegradable compounds present in the environment, they do not readily go under metabolization in human or animal bodies and are excreted as such. They are designed in a way to have a longer lifetime inside the human or the animal body to have maximum effect on the target organisms. Owing to this property, these compounds have high persistence once in the environment. However, some of the compounds are found to be excreted in their parent form with very little degradation or transformation, e.g., amoxicillin (80-90% excretion in parent form) and some are degraded almost entirely and are excreted in their metabolic forms. This raises an immediate need to trace the degradation rates, half-lives, persistence and mobility of pharmaceutical pollutants in the environment.

Across the globe, including India, APIs are being observed in the environment due to poor treatment of the effluents by drug manufacturing facilities. Furthermore high consumption rate, over prescription and the tendency to self-medicate coupled with poor disposal facilities are contributing significantly to the APIs in the environment.

1.2. Global Pharmaceutical Industry

The pharmaceutical industry is one of the largest industries in the world and has expanded globally. Incidentally in USA itself this industry was found to be continually growing when there was no growth seen in other top industries of the country. It is reported that the global pharmaceutical market is expected to be worth 1.57 trillion by 2023.

1.3. Pharmaceutical Industry in India

The Indian pharmaceutical sector is currently the third largest in terms of volume and tenth largest in terms of value and contributes 1.72% to the GDP (As per the Annual report 2019-2020 of the Department of Pharmaceuticals). The country is the largest provider of generic drugs globally, it accounts for 20% of the global exports. It is the source of 60,000 generic brands across 60 therapeutic categories and manufactures more than 500 different Active

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1 Dosed without prescription: Preventing pharmaceutical Contamination of our nation’s drinking water; NRDC White Paper, 2009
3 Pharmaceutical report, 2019, IBEF
Pharmaceutical Ingredients (APIs). Pharma Vision 2020 launched by the Government of India in 2016 aimed to make India a major hub for end-to-end drug discovery.

The Indian Pharmaceutical sector was valued at USD 33 billion in 2017. The India Equity Brand Foundation (IBEF), a body set up by the country's Ministry of Commerce and Industry has predicted that the pharmaceutical industry is expected to grow at a CAGR of 22.4% in the future.

India is also amongst the top 20 pharmaceutical markets exporting to more than 200 countries with its major destinations being USA, Russia, Germany, Austria, UK, West Europe, Japan and Australia. It ranked 11th in the top exporting countries in the year 2019.

2. Pharmaceutical Pollution: A Global Challenge

In the last few decades, pharmaceutical pollutants are being increasingly detected in all the environmental matrices including surface water, ground water, drinking water, soil, biota etc across the globe. And this may cause adverse impacts on human health and the environment. Though pharmaceutical pollution is a global concern, manufacturing hubs like China and India have emerged as the hotspots of pharmaceutical pollution in recent years.

**Cocktail Effect**

It refers to the cumulative impact of pharmaceutical compounds when they react with one another or they react with other chemicals already present in the environment; such as pesticides. It is a major contributor to the development of antimicrobial resistance. The presence of this mix of pharmaceuticals affects the microbial colony of the concerned environmental matrix leading to the development of resistant strains of microbes.

The persistent and diffused exposure to low doses of pharmaceutical synthetic chemicals, for long periods of time, is not well known or studied. These compounds have a potential to bioaccumulate and biomagnify in the organisms and can thus reach high trophic levels finally causing serious health hazards to humans.

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4 Pharma 2020 vision by Government of India
The scientific bodies, regulatory agencies, research institutions and many NGOs are conducting global studies to find out the extent of pharmaceutical pollution. This kind of pollution is not just a local problem as the contaminants travel through multiple sources and can thus reach a completely different location than its point of production, use or disposal; the issue is being discussed at the national and the global platforms.

The impacts of the presence of drugs in the environment are being observed since a few years now. Pharmaceutical compounds like Diclofenac, Ciprofloxacin, Ethinyl estradiol, Ibuprofen and many other metabolites are detected in various countries including India.

3. Regulations in India to address Pharmaceutical pollution

The Government of India, in January 2020, notified an amendment to the Environment (Protection) Rules specific to the effluent standards of Pharmaceutical industries. Although, it is still in the draft stage, the finalized regulations may be notified soon.

This amendment is specific to the Bulk and Formulation viz. Pharmaceutical industry. Other than general effluent parameters, the standard for APIs- Active Pharmaceutical Ingredients has been added as 0.05 mg/l. The most important addition to the rules is the concentration values of antibiotic residues in the treated effluent of any Bulk drug and formulation as well for CETP (Common Effluent Treatment Plant). It has listed out a total of 121 antibiotics against their concentration values. For example:

- Itraconazole- 0.004 µg/l
- Amoxicillin- 0.10 µg/l
- Azithromycin- 0.01 µg/l
- Ciprofloxacin- 0.02 µg/l
- Sulfadiazine- 288 µg/l

4. Pharmaceutical pollution: A major Concern for India

India has emerged as a hub for bulk and generic drug production with increasing number of manufacturing units in the country. Further, a major policy thrust also played a key factor in making it one of the topmost destinations of pharmaceutical production. At the same time due to lack of infrastructure and little efforts to regulate the pollution from these industries, the pharmaceutical sector has evolved as one of the major contributors to the environmental crisis in the country. The Indian Pharmaceutical Industry has been ranked as one among the 17 highly
polluting industries of India as per the report of CPCB and MOEF&CC\textsuperscript{5}. There are research studies which have confirmed that Indian rivers are found to be contaminated by these drugs 150 times more than the US Rivers\textsuperscript{6}.

4.1 Patancheru Incident: A wake up call!!

The gravity of pharmaceutical pollution in India was highlighted in 2007, by a scientist named DG Joakim Larsson. Dr. Larsson conducted a study\textsuperscript{7} in Hyderabad, on the effluents of Patancheru enviro tech limited (PETL), an effluent treatment plant near Hyderabad, India. It is located in the Patancheru–Bollaram industrial zone located approximately 32 km outside Hyderabad. This industrial zone and its nearby villages are home to more than 100 industries supplying to the leading pharmaceutical firms throughout the world\textsuperscript{8}. The cluster is the source of severe water pollution, and has on two separate occasions (in 2010 and 2013) been subject to a ban on further expansion by the Indian Ministry of Environment and Forests (MoEF) owing to its status as a ‘critically polluted' area\textsuperscript{9}.

4.2 Sikkim: An Emerging Pharma Hub of India

Sikkim known for its landscapes, glaciers and ecology, emerged as a new pharmaceutical manufacturing hub for India. The state in 2007, was included in the Centre’s North East Industrial and Investment Promotion Policy, under which all new units as well as existing units which go in for substantial expansion in Sikkim will be eligible for incentives for a period of ten years from the date of commencement of commercial production\textsuperscript{10}. By 2009, the state has already become home to 14 major pharma companies and has attracted pharma investment up to Rs 2500 crores.

However in spite of being a new hub, pollution from pharmaceutical industries also emerged as a major challenge in Sikkim. In 2019, the State Pollution Control Board issued a closure notice to pharmaceutical companies in Sikkim- Alembic Pharmaceuticals and Ideal Cures

\textsuperscript{5}The Emerging Environmental Burden from Pharmaceuticals; Geetha Mathew, M K Unnikrishnan, 2012
\textsuperscript{6}https://purewaterfreedom.com/pharmaceutical-contamination
\textsuperscript{7}Effluent from drug manufactures contains extremely high levels of pharmaceuticals, Larsson et al., 2007
\textsuperscript{8}Environmental pollution with antimicrobial agents from bulk drug manufacturing industries in Hyderabad, South India, is associated with dissemination of extended-spectrum beta-lactamase and carbapenemase-producing pathogens, 2017
\textsuperscript{9}Impacts of pharmaceutical pollution on communities and environment in India- Nordea Asset Management, 2016
The SPCB reportedly found the two industries discharging industrial waste beyond the permissible limits into Teesta River. Alembic Pharmaceutical was allegedly discharging 100 KLD effluents into Teesta River. It was also found that for the last two years highly toxic effluents from the plant’s collection tank is being siphoned off and dumped in the river.  

5. Pharmaceutical Hub: Baddi-Barotiwala- Nalagarh (BBN)

Baddi is an industrial town and a Nagar panchayat in the Southwestern Solan district of Himachal Pradesh, a hill state of northern India. The town lies on the border of Himachal Pradesh and Haryana states in the Shivalik Hills, around 35 kilometres west of Solan. It has recently emerged as the capital of pharmaceutical industries. 

More than half of India’s pharmaceutical production, mainly formulations, would originate from Himachal Pradesh in few years as 200 odd medium and large-scale units are coming up in and around Baddi.

It all began in 2002, when the state government provided tax and central excise concessions to attract companies to establish manufacturing units. The excise concessions ranged from 30-100 percent along with up to 15% of capital investment subsidy for commercial drug production.

The Baddi-Barotiwala-Nalagarh industrial belt is now considered to be the second largest pharma cluster of India. The state supplies 35 percent of pharma formulations in Asia through approximately 700 manufacturing units, around 650 of which are in Baddi. The total turnover of the pharma industry in this belt is around Rs 40,000 crore, contributing a significant share in the Rs 1.10 lakh crore domestic pharma market.

As per the data from National Pharmaceutical Pricing Authority of India, 2007, the country has 10563 manufacturing units with approximately 350 units in Baddi, Himachal Pradesh.

13 https://thepharmaupdate.com/2019/12/16/list-of-pharmaceutical-companies-in-baddi/
14 https://thepharmaupdate.com/2019/12/16/list-of-pharmaceutical-companies-in-baddi/
15 https://thepharmaupdate.com/2019/12/16/list-of-pharmaceutical-companies-in-baddi/
16 https://baddi.expresspharmaonline.com/whybaddi.html
17 Directory of Pharmaceutical manufacturing units in India, 2007; National Pharmaceutical Pricing Authority, Government of India
However, this data is dated and needs to be revised to get an update on the number of pharmaceutical units in the area. The entire list of the number of pharmaceutical industries in Baddi can be found here (https://www.yumpu.com/it/document/view/5997543/the-directory-of-pharmaceutical-manufacturing-units-in-india-nppa and http://www.pharmatips.in/Articles/Pharma-Companies/List-Of-Pharmaceutical-Companies-In-Baddi.aspx)

5.1 Environmental Challenges in Baddi –Barotiwala-Nalagarh cluster

During the last few years, a number of environmental pollution cases have come into notice in this industrial area. Baddi-Barotiwala-Nalagarh (BBN) Industrial Area, which is now one of the largest manufacturing hubs in India has been the root cause of the contamination of Sirsa River. The river has been categorised in the severely polluting category viz Red category\(^\text{18}\). As per a recently published report by Himachal Pradesh State Pollution Control Board\(^\text{19}\), the main source of pollution in Sirsa river includes commercial and industrial waste from the Baddi-Nalagarh area.

Locals have also complained\(^\text{20}\) that most of the industries do not comply with the regulations and that they discharge the liquid waste through pipes and other outlets that open behind the plant or run underground and open into bushy areas. This released waste water accumulates in or flows through nallahs, canals and rivulets into the Sirsa river. It has also been noticed that the effluents are also injected into the ground at night by digging borewells or released during rains.


\(^{19}\) Comprehensive report on Prevention and Control of Pollution in River Sirsa: Action Plan, Haryana State Pollution Control Board

In 2017, locals reported large scale fish mortality in the Sirsa River at Sitalpur, in Baddi, Solan district. Another incident in July, 2019 reported thousands of dead fish in a river below the Jagatkhana bridge in Nalagarh Industrial area. Over the years, the incidences of dead fish have been reported quite a number of times, it is not really surprising for the locals anymore to find dead fish on the river beds, as many of the locals have reported about the illegal discharge of the untreated effluent directly into the river specially during monsoon, leading to poor water quality, increased BOD, that subsequently causes death of the aquatic species particularly fishes. The first incident was reported as early as in 2000, when dead fishes were found floating in Sirsa river.

Recently, in March 2020, a tanker was caught dumping untreated industrial effluent from a pharmaceutical unit into Malpur Khud viz rivulet. This rivulet further meets Sirsa river. The entire rivulet turns dark blue as soon as the effluent was dumped into it. SPCB officials caught the tanker while dumping the waste and thus started further investigation. They found that the waste belonged to a pharma company.

6. Toxics Link’s Assessment in Baddi Nalagarh Industrial Area

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6.1 Indicative Research Study

Toxics Link has initiated an indicative study to assess possible impacts of the effluents being released from the pharmaceutical units in the Baddi-Nalagarh industrial zone. Though most of the pharmaceutical units in this industrial zone are formulation units and are categorised as an “Orange Category” industry, there are some literature studies that have indicated instances of APIs releasing from these industries to the nearby streams. Therefore, these industries should take utmost precaution to prevent the release of these pollutants into the environment. In this context, Toxics Link did the physical assessment of the zone and also collected water samples from some of the locations to get an indication of the presence of pharmaceutical compounds in the water.

6.2 Observations

During the study it was observed that the industrial zone is very poorly planned to manage the effluents released from the different industries. During the visit and after discussion with the villagers in the surrounding areas, it came into light that apart from pharma industries there are also a number of textile industries located in this industrial zone. Baddi is the old industrial zone and now the new pharma industries are coming up in the Barotiwala-Nalagarh zone. Moreover, though some of the industries in Baddi are connected to ETP, lack of any treatment facilities in Nalagarh is posing a serious challenge to the environment in the surrounding location. Even the villagers have reported that pollution has evolved as a serious concern in the surrounding Nalagrah area day by day. Shockingly the villagers have shown the secret outlet which is used by the industries to release the effluents from their units which clearly shows that the mindset of the industries is “Solution to Pollution is dilution” without realising the larger impact of API on the ecosystem. Also, it was quite evident that the effluents were being discharged during the night to avoid scrutiny.

6.3 Sampling locations
To get an indication on the nature of pharmaceutical pollution in BBN area, a primary assessment of water samples was conducted through a lab-based study. The water samples were collected from these secret effluent outlets which are connected directly to the small nallah. Two samples of water were collected from the above-mentioned sampling points. As the effluents are being released in the night, the water samples were collected from the left-over water in the outlets. All the samples were collected in plastic bottles.
6.4 Results and Discussion

The test results found Ciprofloxacin in a concentration of **296.1 µg/l**. Though the concentration of Di-chloro methane could not be assessed, it was detected in one of the sampling locations.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Concentration (µg/l)</th>
<th>Sampling point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>296.1</td>
<td>One</td>
</tr>
<tr>
<td>Di-chloro methane</td>
<td>Detected</td>
<td>Two</td>
</tr>
</tbody>
</table>

Since this is an indicative study the results don’t clearly point towards the presence of pharmaceutical pollution in the water bodies in BBN area. However, the presence of these two pharmaceutical ingredients have raised the larger issue of the magnitude of pharmaceutical pollution particularly in this area. It is to be noted that Ciprofloxacin was also detected in Patancheru in very high concentration raising concerns about its implications. Incidentally, this is the first kind of study where these compounds are detected in the BBN area. Most importantly the concentration is also quite high as the new draft regulation of the country has limited the concentration of this antibiotic at 0.02 µg/l. The detected concentration of 296 is actually **14800 times** higher the required concentration.

**COVID and AMR**

The world today is facing one of the biggest pandemics- COVID-19, AMR can probably make the pandemic even more deadly. In a recent report in Wuhan¹, China it was found that 50% of the patients who died from coronavirus were also tested positive for secondary infections. Since, antibiotics act as our first line of defence and the number of cases of antimicrobial resistance are already on the rise, it is important to conduct more studies to understand the implications of AMR on such pandemics. The current COVID-19 pandemic threatens to further weaken the already crumbling antibiotic management infrastructure. There are perhaps more interlinkages between AMR and COVID that need to be studied and most importantly countries like India which have AMR on the rise, need to establish a connect between the two and study the potential impacts of antimicrobial resistance on COVID-19 patients.
7. Conclusion and Recommendations

7.1 Conclusion

It has been established that there is a correlation with increasing amount of drug production and use, the number of pharmaceuticals and its metabolites are detected in various environmental matrices. The ill impact of pharma pollution has been well documented globally and in India therefore there is an emerging need to reduce this pollution load from the environment. Globally a number of countries have initiated regulatory and technological interventions to minimise the impact of pharmaceutical pollution. As India has emerged as a major producer of generic drug manufacturers and with the increased use of drugs in the country, there is a need to develop appropriate regulatory actions with an adequate monitoring system in place so that the impact of the pharmaceutical pollution can be reduced in the country. In this context some of the recommendations are as proposed below.

7.2 Recommendations

1. The proposed draft regulation should be enforced immediately with an adequate monitoring and surveillance system in place.

2. The regulation must also consider inclusion of other pharmaceutical pollutants apart from 121 antibiotics that it has listed at present.

3. The state pollution control (SPCB) and Central Pollution Board (CPCB) should be capacitated and trained to do more testing and also need to sensitize the magnitude of problems associated with AMR.

4. Stringent legal and punitive actions must be taken against the industries which are illegally discharging their untreated waste water into nearby water bodies.

5. The ETP and STP infrastructure as well as TSDF facilities should be equipped with the latest technology to minimize the risks and remove the API from the waste water.

6. The government should support small-scale manufacturers to install and implement environmentally sound waste treatment plants. Manufacturers with high-end WWTPs should also be strictly monitored.

7. The approval of pharma industries needs to be strictly scrutinized considering the level of threat associated with these industries.

8. The industries need to accept their responsibilities for their products and should place an adequate management system from the cradle to the grave. Further the industries should adopt an utmost precautionary approach and pollution control devices should be installed to prevent discharge of pharma waste along with waste water.
9. There should be provisions of conducting an ERA (Environment Risk Assessment) before releasing any new drugs in the market to minimize the impact of pharma pollution from the end use.
ANNEX 1

Test Methodology

The collected water samples were sent to Shriram Institute of Industrial Research and Spectro laboratory in New Delhi for analysis.

Spectro Laboratory tested the water sample for **Dichloro methane** using GC-MS. This method involves purging the sample with an inert gas and passing the gas through a trap containing 2,6-diphenylene oxide polymer, silica gel, and coconut charcoal to adsorb the purged chloromethane and other halocarbons (called the “purge and trap” method). After the purging is complete, the trap is heated to desorb the chloromethane. The desorbed chloromethane is analyzed by GC MSD directly by injecting.

**Ciprofloxacin** was analysed by The Shriram Institute using LC-MS. Method of Analysis was as follows:

i) Prior to sample preparation, Oasis HLB cartridge was preconditioned by adding 4mL MeOH and 6mL distil water (DW).

ii) Took 50 ml of sample and adjust its pH to 6. This was filtered using 0.45 µm Millipore filter to remove any impurities present.

iii) The water sample was passed through the pre-conditioned cartridge at flow rate of 5-B mL/min using a vacuum extraction manifold.

iv) Next, 10 mL of ultra-pure water was used to wash the cartridge, which was subsequently air-dried for 5min.

v) Acidified methanol (10m1 of MeOH, 3mL of 0.5 N HCL) was used to elute the analyte into a glass test tube.

vi) The extracts were completely dried under a gentle flow of nitrogen, and the volume was reconstituted to 1 mL using a mix of water/methanol (9:1).

vii) The extracts were filtered through 0.45 pm filters, transferred to auto sampler vials, and were analyzed using LCMS/MS.