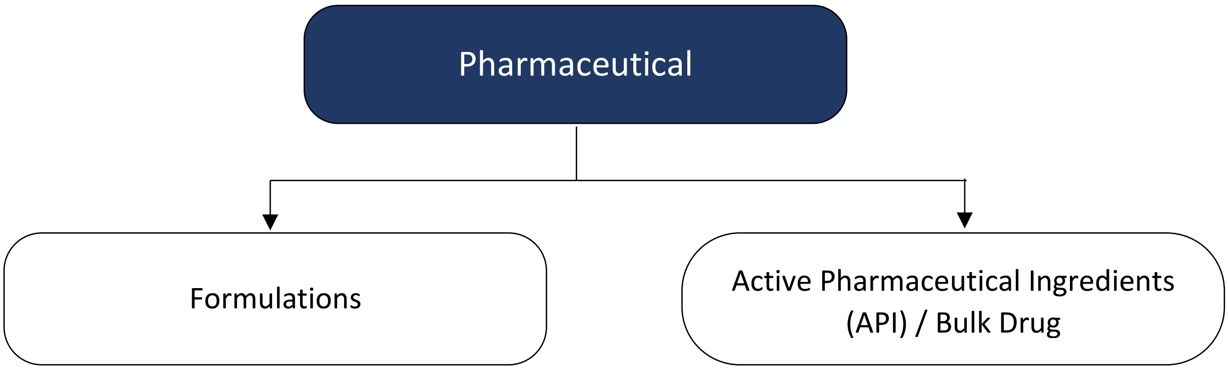
CASE STUDY

Issues & Solutions – Indian Pharma API Effluent

Structure of Pharma Sector in India



API Stands for Active Pharmaceutical Ingredient. The products are the raw material used for making drugs or medicines. Major challenge today in Pharma API is their effluent & treatment thus achieving Environment Sustainability. The reasons affecting the same are -

- **Recalcitrant /Non-biodegradable COD** due to usage of Solvents in API
- **Ammoniacal Nitrogen**

Recalcitrant / Non-biodegradable COD

The recalcitrant COD in Pharma effluent is due to solvents present in the process. The majority solvents used are

Methanol	TBME (Tert-Butyl Methyl Ether)	Heptane
MDC (Dichloromethane)	Ethyl Acetate	THF (Tetrahydrofuran)
IPA (Isopropyl Alcohol)	DMSO (Dimethyl Sulfoxide)	DMF (Dimethyl Formamide)
Hexane	EDC (Dichloroethane)	

Majority API manufacturers are under contract Manufacturing. Based on the market demand, the products are manufactured. At a time, there can be 20-25 products under manufacturing. Thus, it makes almost impossible to quantify the effluent parameters & solvents in the same. Hence, the exact effluent parameters can’t be calculated.

Ammoniacal Nitrogen

Along with various solvents, there are few API products which are amine based, which results in Ammoniacal Nitrogen (NH_3-N) in effluent. This stream is generally segregated as High COD but as ammonia is not free and cannot be condensed, hence not get removed in the solvent strippers & will be carried to MEE condensate creating issues in ETP again.

Sources of Effluent generation in API Industry.

Layer Separation - This is the last stage of API manufacturing. Here, Product layer is separated from Aqueous layer due to difference in the density. This Aqueous Layer is effluent and will be collected either in drums or pumped to the High COD stream collection Tank.

Generally, Layer Separation is controlled using manual operations. Hence, the extent of product being taken to Aqueous layer depend on the personal expertise & interpretation of the operator. Any mistake in the same can lead to more solvents in effluent. The operators always try to achieve more product yield and hence, there is always a possibility to find solvents go in the effluent.

Centrifuge Separation - This is also type of product separation and the centrate thus separated will be taken to High COD Stream Collection Tank.

Reactor 1st wash - Generally Reactor first wash by water/solvent is taken to High COD Stream Collection Tank.

Reactor 2nd wash - Some Industries take this to High COD stream, but major industries take it to ETP i.e. Low COD stream to reduce load on the High COD Stream.

Utility Waste - Utility waste comprises Cooling Tower blowdown, Boiler blowdown, WTP RO Reject, DM regeneration waste. This stream will have Low COD but will be having High TDS.

Floor wash - Floor wash from the factory is generally considered as Low COD stream unless somebody drains oil / solvents during floor washing.

It is well known fact that if the effluent is segregated by High COD, High TDS, Low COD-Low TDS, the designed system delivers best efficiency. However, despite of this fact, many industries don't follow this and ETP issues remains unresolved.

Ultimately, effluent is generated from washings. So, the COD & BOD completely depend on the part of raw material, products and byproducts.

Now, if we segregate the Effluent streams, it will look like something like this -

Streams	High COD-High TDS	Low COD - Moderate TDS	Low COD – Low TDS
Layer Separation	✓		
Centrifuge Waste	✓		
1st Reactor Wash	✓		
2nd Reactor Wash	✓		
3rd Wash onwards			✓
Utility Waste		✓	
Floor Wash			✓

** 2nd wash always been issue for ETP. So, segregation of this stream varies as per product.*

Design Basis Formulation

Consideration

1. There are various products at a time being manufactured. So, major challenge in API is - effluent varies in quality & quantity almost every day.
2. High COD streams like Layer Separation, Centrifuge Waste & 1st Reactor wash waste have COD due to solvents present in it.
3. High COD streams are generated batch wise whereas Low COD streams are generated continuous basis. This point is very important for Tank sizing and appropriate selection of Pretreatment unit operations.
4. 2nd Reactor wash stream is generally sent to Low COD stream. Here, Biological system is very critical as the same have aerobic bacteria. Bacteria are absolutely like human beings which requires oxygen, digestible food, and healthy environment. If you disturb them by giving solvents, system gets disturbed. Many occasions, if the system gets disturbed to major extent, it requires external aid for recommissioning.
5. Floor washing effluent is again an issue as the drains are diverted to ETP. Any toxic waste / Oily waste drained can come to ETP. Discipline in the operating staff can only keep the parameters in control.
6. Few Pharma Industries use Silica columns for specific products, from where there can be leaching of silica possible. Silica can create issues in Reverse osmosis & Multi Effect Evaporators and can increase the CIP frequency. Generally, this effluent volume is not high.
7. Utility streams are moderate in TDS & have lesser concentration of COD & BOD. This stream (After Neutralisation) directly can be added after biological systems before tertiary system. This can reduce Hydraulic load on Biological system.
8. TDS of any effluent need to be monitored as Organic & inorganic. Organic TDS can be reduced by striping & biological systems. For Inorganic TDS removal, RO & Evaporators are required.

Low COD - Low TDS Stream

Major effluents in this category are - Reactor 3rd Washings onwards, Floor washings and Utility waste.

Utility waste contains - WTP RO Reject, DM regeneration waste, Cooling Tower blowdown, Boiler blowdown etc.

General parameters found in the Low COD stream are –

pH	6.5 - 8.5
COD	3,000 - 5,000 mg/lit
BOD	1,000 - 2,000 mg/lit
TDS	3,000 - 6,000 mg/lit
Ammoniacal Nitrogen	0 - 50 mg/lit
Solvents	Traces
O&G	10 - 20 mg/lit

** After taking so much care & followed discipline, there should not be any solvents coming to ETP. However, some traces of solvents like Methanol may come to ETP. Methanol with few other solvents is biodegradable if in ppm.*

High COD Stream

This stream creates major issues in treatment. This comprises Aqueous Layer, Centrifuge waste, 1st & 2nd Reactor washing.

Aqueous Layer may or may not be high TDS stream but the same is at extreme pH @1 or pH@14. It requires to be neutralised and due to this, TDS increases marginally.

While generating requirement for ETP & ZLD, Major pharma Industries share the High COD effluent parameters as COD, TDS & pH only. For the ETP suppliers, it is very much required to get many details to design the system accordingly.

- For solvent removal, Solvent stripper is used. Only providing COD values will not solve the purpose. Industries to list out the solvents they use in their process.

- If there are amine-based products, Ammoniacal nitrogen for the waste stream need to be monitored regularly. If possible, it is always better to segregate the stream and treat separately even for the neutralisation. Ammonia is not in free form, hence can't be completely removed even in the solvent stripper. A separate small system can be provided for this stream treatment.

General High COD Stream Parameters

pH	6.5 – 8.5*
COD	50,000 – 1,00,000 mg/lit
BOD	Can't be generalised
TDS	50,000 – 60,000* mg/lit
Ammoniacal Nitrogen	NIL – 2000 # mg/lit
Solvents	2% - 10%

Indian Pharma API Effluent Treatment face various challenges due to its varying products, Usage of solvents, indiscipline in Effluent discharge & operational issues.

"Foremost challenge of all is the Unawareness about our own effluent & mindset we have – It **happens like this only"**

Solvent percentage in effluent varies & it completely depends on the production practices and the Disposal of the effluent. The fight between Product Yield & effluent generation is age old and is continued. However, there have been improvements in the process such as recovering precious solvents and save them from getting ***dirty*** as part of effluent. After primary modifications at process side, reduction in the effluent is quite possible.

For Pharma API units, design Basis formulation needs following steps

- Know your own effluent & its sources first
- Reduce the effluent at source by either recovering solvents or modifying the process.
- Rather than segregating it as per conventional methods, segregate as per their parameters
- Designed Parameters should not be Very High or Very Low, it should be optimum or in range, which helps designer to design best suitable system for you
- Water balance diagram is very important in pharma API as only RO permeate goes out of the loop. Other all effluents are treated in loop.

1. Read between Effluents

When you list our all-effluent sources & its parameters, you should use the experience to segregate it as per their parameters. Generally, the segregation is High TDS-High COD and Low TDS-Low COD etc.

But for API, the effluent segregation should be based on Toxicants, Reducing agents, Solvents, Low TDS & Low COD effluent.

Concentration of low volatile solvents & its azeotropes carries an important role in High COD streams.

2. Biological ETP issues

Operating ETP is a major challenge in Pharma API due to following facts –

- Solvent usage & by mistake disposal
- MEE condensate having Low volatile solvents mixed with Raw Low COD ETP stream disturbs ETP

Indicative solution to first issue is disciplined disposal of the effluent & proper monitoring of every effluent drain. Second issue is discussed further in MEE point later in this article.

3. Reverse Osmosis (RO) Design & Operations

- Actual TDS of the RO reject is very less and thus gives higher hydraulic load on MEE
- If the max. recovery is not possible practically, higher hydraulic load is again on MEE.

Indicative Solution

- RO systems are generally designed for higher recoveries in today's time ~80% in API industry.
- RO designs are done based on higher TDS levels, resulting in very high TDS in reject in projections. In reality the rejects TDS is low, and it gives higher load on MEE
- RO projections to be done on TDS range and not on max. TDS.
- Optimum recovery projections to be considered while designing MEE system.

4. Zero Liquid Discharge (ZLD) Doesn't work

Generally, ZLD systems comprises Stripper for solvent-based effluent (from layer separation & Centrifuge from process), Multi-effect Evaporator for mixed stream of Stripper bottom & ETP RO Reject mixed effluent, followed by ATFD for treatment of MEE bottom product.

Stripper Design

- TDS of the effluent fed to Stripper is 4-5% and COD is almost 5-10%. In today's scenario, when stripper is designed for Effluent, it is generally designed on hydraulic load rather than its solvents by majority suppliers.
- Generally Effluent strippers are designed with packed bed design with fixed height of packed bed. Unfortunately, for majority cases, proper solvent stripping calculations are not done while designing the system or even steam requirement is not calculated properly.
- Everybody talks about % of solvents / water in top product, which is kept as 70%/30% majority times. Stripper is not evaporator & hence the top product should contain very less water & majority solvents.
- No suppliers talk about what is % solvents carried to MEE system through stripper bottom. This is obvious as even End user doesn't know what they will be feeding to stripper (everyday, the composition changes).
- Ammoniacal nitrogen presence can be a major failure of ZLD system as it interferes almost in everything. If significant concentration of NH_3-N is in the effluent in, it can't be treated like other solvents. NH_3-N presence interferes in evaporation as well andit also shows its presence in MEE condensate which need to be treated again.

Indicative Solutions

*The concept & attitude of "**ETP can eat anything"** need to be changed.*

- End user should recognize the effluent generation pattern & solvent concentrations in the effluent.
- Theoretical requirement & Actual solvent usage to be monitored
- Surprisingly strippers are designed based on Flow & COD. Stripper is required to be designed based on the solvents (can be) present & not COD levels.

- Designer & End user to choose the solvents from list based on their experience & design stripper not only on hydraulic basis but based on the solvents present in the feed. Here, projections to be done for each concentration range of the solvents for stripping.
- Ammoniacal Nitrogen stream to be segregated & to be treated separately if NH3-N is significant in concentration.
- There is a possibility that Actual feed stream to stripper varies a lot from designed values due to Azeotrope formation, carryovers & solubility issues. But the stripper operations will not be drastically out of design.
- Customers/End users should understand that their own effluents require higher Steam consumption in stripper to get separated & should not hype on the opex in that case. Generally, when customers doubt on higher opex on papers, end up with even more opex in actual plant. This is true for API industries.
- Ultimately, stripper needs to be designed properly & not just hydraulically fabricated.

MEE Issues

- MEE feed is a mixed stream from Stripper bottom (TDS 4-5%) & ETP RO Reject (TDS 0.5-1.5%). High COD stream is generated batch wise and RO reject is on continuous basis hence, TDS varies from 0.5% - 3.5% based on hydraulic ratio of both the streams. System needs to take care of it.
- Stripper doesn't work efficiently & present gifts of volatile solvents & NH3-N to MEE, which interferes in MEE operation. Here, stripper plays very important role in MEE operations.
- MEE achieves Evaporation duty on raw water but not on effluent - API effluent vary in quality & can have scaling potential salts present in it. Tubes tend to chock more often and the same results in inefficient Evaporation operation. Also, presence of solvents plays important role in inefficient operations.
- Selection of Evaporation type is equally important – Selection of Falling film evaporators results in scaling of tubes more often.

Indicative Solutions

- MEE need to be designed for TDS range than Min. Or Max TDS
- Majority Industries opt for Forced circulation evaporators whereas few goes for falling film, which results in continuous chocking of MEE Tubes.
- Steam temperature plays an important role in MEE designing. If the same is kept high at >100 Deg C, first effect tends to get chocked more - Many customers fail to understand why it is done by supplier! First effect high temperature results in low HTA and thus helps in reduce the cost & Opex.
- Many suppliers come with an idea of using Adiabatic Evaporator, which is nothing but cooling tower which runs on the feed stream to MEE effluent. They showcase some evaporation in the Adiabatic evaporator thus achieving lesser steam consumption. The idea is good & workable mainly in summertime & tends to fail esp. in the rainy seasons. For Pharma API, it's not a wiser decision as the MEE feed also contain solvents.

- Tube diameter also carries an important role. If the tube diameter is less, automatically costs are lowered & thus the recirculation flowrate also will be less. These low diameter tubes are difficult to clean when get chocked by hardness / silica.
- Effluent Velocity inside tubes, if kept low, it tends to scale more and lowers the efficiency.
- One more very important point while designing the MEE system is Boiling Point elevation (BPE). Majority of times, the same is not considered, but plays vital role in MEE HT calculations. e.g. NaCl is having BPE of 7-8 deg c at 40% Concentration whereas 18-22 deg C for CaCl2 at 50-55% Concentration. Hence, it is always advisable to consider the salts which may be present in the effluent. Salts can be calculated based on complete water balance diagram across factory.

ATFD Issues

ATFD product is not powder but only lumps - ATFD product quality depends on the organics present in the ATFD feed (MEE Product). If there are more organics present, the ATFD product will have more lumps.

Indicative Solution - High boilers will be carried to ATFD from Stripper & MEE and hence, there won’t be any control on it, but the major control end user can have - Efficient stripper & MEE installation and operations.

MEE Condensate can’t be recycled or even can’t be treated with existing system

- MEE Condensate contains low volatile solvents & sometimes, Ammoniacal nitrogen which have COD ranging from 3000-5000 mg/lit. This is an extra generated effluent & is approx. 20-25% of the effluent fed to ETP.
- ETP is designed using conventional biological process. This condensate sometimes, can become shock load to ETP resulting in killing the bacterial culture & washout the MLSS.
- Majority of API today facing this issue.

Indicative Solution

- MEE condensate can be treated using advanced oxidation process (AOP) before it is fed to biological system. AOP converts the complex compounds into simple chain & the resultant can be fed to biological process. Thus, the bacterial culture can be saved from toxicants.
- AOP comprises use of combination of Oxidants & UV together, combination of which generate Hydroxyl radicals. These have the highest oxidation potential amongst available oxidants. It breaks the complex molecule into simple chain. The resultant simple molecules can be easily broken using existing biological process.

Major issue

- While generating the enquiry, End Users should think about how they will ask the suppliers to demonstrate the plant with full capacity. Generally, when suppliers install the plant, the effluent generation is hardly 40-50%. It impacts suppliers & End users both.
- When End user reaches to plants 100% capacity after 2-3 years from installations, they again need to go for ETP & ZLD expansion/modification. This happens due to parameter change because of additional products, changed mandates, relocation or under-designed plant etc. Hence, any plant average life today in 6-7 years.
- Performance can be supported by various ways, e.g. opting for bigger raw effluent tanks etc.

It is always advisable to hire expert people from Industry so that better enquiry document can be prepared & the same way suppliers can be selected.

Abbreviations

- AOP - Advanced Oxidation Process
- ATFD - Agitataed Thin Film Dryer
- BPE - Boiling Point Elevation
- COD - Chemical Oxygen Demand
- ETP - Effluent Treatment Plant
- HT - Heat Transfer
- MEE - Multieffect Evaporator
- NH3-N - Ammoniacal Nitrogen
- Opex - Operating Cost
- RO - Reverse Osmosis system
- UV - Ultravoilet
- ZLD - Zero Liquid Discharge

** After Neutralisation*

 # To be segregated

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