Course Name: Industrial Wastewater Treatment

Prof. Alok Sinha

Department of Civil Engineering, IIT(ISM), Dhanbad

Week – 11

Lecture 3: Treatment of wastewater produced from pharmaceutical industry

Welcome back. So, we are in module 11, lecture 3 and we are discussing about the treatment of the wastewater produced from the pharmaceutical industries. So, in this lecture, we will be covering about the production of the synthetic drugs. We will talk about that how we can produce, how we can manufacture the synthetic drugs as we have already discussed about the antibiotics, about the manufacture of the antibiotic drugs in our previous lecture. So, in this lecture, we will be discussing that how the synthetic drugs are produced and what are the processes that results in the wastewater generations and similarly, we will also discuss what are the wastewater characteristics which are generated from the synthetic drugs manufacturing process. So, the pharmaceutical industry, it can utilize a very vast array of the complex batch type processes and technologies during the manufacture of the pharmaceutical products.

So, we can have a number of processes which are mostly of the batch reactor types and these batch reactors, the medicines are produced in the batch reactors and then basically we convert it into the various usable form. For example, these batch processes may be resulting in various manufacturing processes. For example, we can have the chemical synthesis initially and then we can later on go for the purification and extraction of those drugs from the various chemical processes that we use during the manufacture of the pharmaceuticals. So, there is a diversity in the processes.

For example, we are using a number of drugs are being manufactured which may require different type of chemicals, which may also require different type of processes and so it will be very impractical to provide a general set of waste minimization guidelines as the waste generated from the different processes will be of different nature. Similarly, there can be a number of chemicals that we are using during the synthesis of these pharmaceuticals. So that's why we cannot make a generalized guidelines for all the drugs. So here we can have different methods which are generally used for the manufacture of the synthetic drugs. For example, we can have the research and development first of all.

So, research and development are needed so that we can arrive at a certain formula and then we can also test those drugs on the various organisms so that we can know that what is the impact of these drugs, what are the side effects of these drugs, what can be the toxic effects of these drugs that can happen to the people who are taking it. So lot of clinical trial as well as lot of research and development during the manufacturing process, during the

formulation of the drug, during the fixing of the chemical composition of the drugs so that has to be followed and later on we have to also check that whether these drugs will be safe for the use or not and what are its effects that whether it is able to treat the patient or not. So once this is done, so then later on we go for the chemical synthesis of the drugs. For example, there can be number of processes by which we can produce the drugs. We can have the chemical synthesis, we can have the natural product extraction, we can have the fermentation process and lastly, we can go for the process of the formulation where we convert the drugs into the end use so that we can take it either orally or we can inject the drug, or we can take it from by any other route.

So, the major groups that includes for during the manufacture of the pharmaceuticals includes the antibiotics for such as penicillin and streptomycin so this we have already discussed in the previous lecture and similarly we can have tetracycline, we can have chloramphenicol, and we can have the antifungals etc. So, there can be a number of drugs which basically may be used for counteracting the effects of the microbes in our body. Similarly, we can have other synthetic drugs for example we can have the drugs like sulfur drugs, we can have anti tuberculosis drugs, we can have anti-leprotic drugs, we can have analgesics, anesthetics and anti-malarial drugs. So, there can be number of synthetic drugs which are not manufactured from the microorganism or from basically the fermentation process so these drugs may be produced by using certain chemical processes. Similarly, we can have the production of the vitamins which can be used from the natural extracts.

Similarly, we can produce the synthetic hormones which may be required by the body if the body is not able to produce the hormones in a sufficient amount and then we can have the glandular products also which are made from the tissues of the animals. Similarly, these glandular products are generally made so that they can target a specific organ in our body and similarly we can have the drugs which are of vegetable origin like for example we can have quinine, we can have strychnine, we can have brucine, emetine and digitalis glycosides. So, we can also have a number of vaccines that can be produced and these vaccines as we have seen during the COVID-19 period for example the Covaxin or Covishield were produced in large amounts in India so that the people can be safeguarded against the COVID-19 virus. Then we can have other pharmaceutical chemicals which may include but are not restricted calcium gluconate, we can have ferrous salts, we can have nikethamide, we can have glycerophosphates, we can have chloral hydrates, saccharine, antihistamines which includes meclizine and buclizine. Similarly, we can have number of tranquilizers for example we can have meprobamate and chlorpromazine.

Similarly, we can have number of anti-filarial, we can have diethyl carboxylic acid citrate, and we can have oral antibiotics drugs which includes Tolbutamide and chlorpropamide. So, we can have a number of manufacturing process which involves the preparation of the process intermediates for example it is necessary that we are having the raw material but that raw material needs to be converted to the final product or to the final pharmaceutical

so there can be a number of chemicals that will be required in the intermediate process. So, the preparation of the process intermediates may also be one of the manufacturing processes. Similarly, we have to introduce a number of functional groups during the chemical synthesis process so which may lead to the formation of the synthetic drugs. Similarly, we can have number of reactions like coupling and esterification and later on we may go for the process of separation by washing, stripping etc. and finally we go for the purification of the final products. So, these are some of the steps that may be used for manufacturing of the synthetic drugs and similarly there can be number of processes which are involved for making the drugs into the usable form. For example we can go for the granulation of the purified product, we can go for the drying, we can go for the tablet pressing so that we can make tablet out of it, we can go for the printing and coating of these drugs that are produced, we can go for the filling of these drugs which are produced in the powder form in form of capsules and lastly we may go for the packaging and supplying it as an end product. So, during these processes a number of air emissions, liquid effluents as well as solid waste are generated, and we are concerned with the liquid effluents so we will be considering that what are the wastewater that is generated from the various processes and what are their characteristics. So, the research and development are a very important part of any pharmaceutical industry, and it may encompass a number of research for example we can have the research in the chemical area, we can have the research done in the microbiological area similarly, we have to do research in the pharmacological area also.

These research for example when we go for the synthesis of any drug so we have to have a certain compound that we need to prepare and that may require a number of chemical reactions. So that's why it is very important that this chemical research has to be done so that we can optimize the conditions so that we can enhance the product as well as we also have to see that there is no toxicity being induced in the drugs. Similarly the microbiological research is also needed if we are producing the drugs from a certain microbes for example as we have seen in case of antibiotics so a number of microbes basically have been utilized so that we can produce these drugs out of the fermentation process and similarly the pharmacological research is also needed so that the effects of these drugs on the various end users so it can be ascertained. So that's why it is very important that the cooperative efforts of a number of people which are specialized in different branches so they may provide their input for the manufacture of these drugs. For example, we can have the persons from the medicines, we can have the persons from the organic and analytical chemistry, microbiologist, the biochemist, the physiologist, pharmacologist, toxicologist, chemical engineers as well as the pathologist.

So, we can see that the microbiologist or the basically the medicine people they can tell us about what can be the dose that we need to give and what can be the effects of these drugs on the person who are taking it. Similarly, the chemistry people as well as the microbiological people so they may be used for the manufacture of the chemical compound

as well as the extraction of the drugs from various type of microbes. Similarly, the biochemist is needed for the different type of activities for the production of the biological drugs. So, then we can have lot of physiologist and pharmacologist, and toxicologist can assess the impact of these drugs on various living things. Similarly, the chemical engineers are also needed so that the process which is utilized so we can have a number of equipment, we can have a number of processes so these processes need to be optimized and for that we need a chemical engineer so which can basically enhance production quantity as well as the quality.

And similarly, the pathologist is needed so that we can conduct a number of tests on various type of organisms so that we can find out that what is the impact of these drugs on certain living things. So, once the formula for the drugs has been established so based on the study which is done in the research and development lab so then basically the Central Drug Standard Control Organization so they provide their approval so that that drug can be taken for the large-scale production. So, in the research and development a wide range of chemical as well as biological laboratory waste may be produced as we are using a number of chemicals as well as we are also using a number of biological processes also. So, the common chemical waste that can be generated from the R&D process may include halogenated and non-halogenated solvents, it may include number of photographic chemicals, it may also include radionuclide, similarly it can include the bases as well as acids and the oxidizers. So, these are some of the generalized chemicals that may be found in the wastewater because this chemical waste basically they may be induced in the water during the washing process, during the equipment washing process, during the floor washing process or during the spills also these things may come out into as the waste.

Similarly, the biopharmaceutical research may lead to the lot of waste material which may include the biological as well as the medical wastes. So, after the research and development is done and once the medicine has been formulated so we may go to the synthesis of the drugs and there can be different routes by which these drugs can be synthesized. For example, one of the examples is the chemical synthesis and most of the drugs today they are produced by using the chemical synthesis process. So here we use a number of batch reactor vessels which may be utilized in a number of steps for example the reaction process, the separation, the purification process etc. so that we can get the desired end product.

And several chemical reactions, recovery process and chemicals so they are employed so that we can produce a wide variety of drugs which may confirm to the right specification. So that's why for each and every drug we can have different type of chemical reactions, different recovery processes and different chemicals which may be needed for the manufacture of the certain specific type of drugs, and they should also meet the desired specifications. So, this means that within a manufacturing plant there can be a number of reaction vessels and the ancillary equipment which are helping these reactions to happen and so they may be arranged in a separate dedicated units so that we can manufacture a

specific pharmaceutical so that we can conduct the specific operations in the specific units. So, some of the pharmaceutical products they are also manufactured in a single product campaign so basically it may be possible that certain drugs may be required for a few weeks or few months only. For example, when the season changes so in that case it is possible that certain drugs may be required for limited period so in that case a single product campaign may also be done by the pharmaceutical companies and here during the campaign the reagents as well as the functions for example the flow rate, pH and temperatures are constantly monitored and so that we can ascertain that whatever process is being utilized so it confirms to the good manufacturing practice protocols.

And similarly, when the campaign may end so then all the equipment which have been used for manufacture of that specific drug so they are thoroughly cleaned, and the cleaning process may again lead to the generation of the wastewater. So, the chemicals which are used in the chemical synthesis operation process so it may vary widely so it may include number of chemicals like organic chemicals as well as the inorganic chemicals as well as certain catalysts which can basically enhance the process of the manufacturing. And then a large variety of solvents are also used which can be used for the recovery, purification and the reaction media. So, these solvents may be listed in the priority pollutants by US EPA so that's why it is very important that whatever the solvents you are using so they can be recovered after their use. So, all the steps which are used in the organic synthesis so they generate a mother liquor which contain number of unconverted reactants, it may contain the reaction byproducts, it may also contain the residual products which is there in the organic solvent base.

And similarly, during this chemical synthesis a number of acids, bases and cyanides and metals may also be generated. So, volatile solvents can also result in the air emission so we are using these volatile solvents so the air emissions can be reduced by employing the scrubbers or by condensers so that we can recover the solvent vapors, we can condense the solvents, we can also reuse these solvents for the different processes. So, the aqueous waste stream which results from the chemical synthesis so it may result from the mixable solvents, it may result from the filtrates, it may result from the concentrates, the equipment cleaning, the wet scrubbers, the spills so they all impart to the wastewater stream which is generated from the chemical synthesis plant. So, the wastewater stream may also contain high concentration of certain toxic elements so that's why it is very important that we the pretreatment of such type of wastewater may be required so that we can discharge it in the sewer lines. So, the waste water which is generated from the chemical synthesis it typically contains very high BOD values, the COD is also high, the total suspended solids are also high and the pH may range from 1 to 11.

So, after the chemical synthesis another process that can be used for the synthesizing the synthetic drugs so that can be from the natural product extraction for example there can be number of natural materials like roots, leaves, animal glands etc. So, these natural materials

like roots, leaves and animal glands so they may find their way in the wastewater generated from such natural extraction products. So certain pharmaceuticals like allergy relief medicines, insulin, morphine, alkaloids, papaverine, so they all are produced by using the natural product extraction method. So after the product is extracted so recovery and purification process of the extracted drugs so it may include number of processes like precipitation where we use the metals like lead and zinc as a precipitation agent and similarly there can be a number of solvent extraction that may be done where basically we may use ketones or alcohol so that we can recover the product and we can purify the product or we can extract the product from the solvents. So, solvents are also used in the product recovery so they can dissolve fats and oils so which can contaminate the product so that's why it is very important that the solvent may be used so that we can have the dissolution of the unwanted material or basically the toxic material also which may otherwise contaminate the final product.

So, we can also use ammonia or basically hydroxides for pH control processes and similarly the waste which is generated from the natural product extraction so it may include number of spent raw materials for example we can have leaves and roots or herbs basically that we use for the manufacture of these type of drugs and similarly we can have number of water soluble solvents that we use for the product recovery, we can have the solvent vapors also and then the waste water that is being generated from the various processes like equipment washing or floor cleaning or the spills. So, the natural product extraction wastewater typically has the low BOD values, low COD values and low TSS values and the pH is in the range of 6 to 8. Then we have the fermentation process also used for the manufacture of the drugs and fermentation process we have already discussed so we will just brush it up for example a number of vitamins, steroids and antibiotics can be produced by using the fermentation process where we use the batch reactors for the seed preparation. So, after the seed preparation we may go for the fermentation process, fermentation process may lead to the recovery of the product so after the recovery we go for the purification steps. So, the fermented broth that is generated so it is generally filtered so that we can remove the solids which may be generated because of the molds that is we are using for production of the antibiotics or other medicines.

So, this filtrate is then basically processed by using solvent extraction we can use the method like precipitation we can go for ion exchange method or we can also go for the adsorption chromatography and later on we can basically purify the drugs by using this method extract the drugs and later on we can go for extraction as well as the purification of these drugs. So the wastewater that is generated from here so it may contain lot of aqueous fermentation medium for example we can have steep corn, fish meal or molasses that we use in the fermentation liquid so similarly it may also contain lot of solid debris like for example the mycelium or the moats basically that may be found in the wastewater similarly we can have the filter cakes the diatomaceous earth which may also come during

the filtration process. So, the wastewater generated from the fermentation has high BOD, COD, TSS and pH may vary between 4 to 8. The wastewater generated from the fermentation process we have already discussed in detail in the previous section. After the process of the drug synthesis is over so then we go for the formulation process.

So, formulation process means that is we prepare the drugs so that it can be taken up in a certain dose. For example, we can prepare the tablets out of the drugs that is formed, the capsules can be formed, the liquids basically can be formed like syrups, we can have the parenteral formed that is in the form of the syringes or injections. We can also prepare these drugs in the form of creams and ointments so that they can be applied on the surface of the skin. So, then the tablets which are formed so they nearly account for the 90% of the medication that is taken orally so we can have different type of tablets that are formed. For example, they can be plane compressed, they can be coated or molded.

Similarly, capsules may be prepared which is the second largest form that is used as the pharmaceuticals so they can be prepared in either hard form or they can be in the soft form. For example, when we talk of the soft form so they can be in the form of gel. Similarly, we can have another type of the pharmaceutical formulation that is highly used that is basically the liquid dosage so this may include in form of the solution, syrups, elixirs, suspensions, tinctures they can either be taken orally or they can also be injected in the body. So, the parenteral forms which are injected in the body they can be done by using intramuscular or intravenous or subcutaneous process. So, the parenteral that are prepared so they may be prepared either as a solution or they may be prepared as dry solids which can be basically dissolved immediately before the injection, or they can also be prepared as a suspension as dry insoluble solids which can be suspended just before the injection, or they can be prepared as emulsions also.

And then after the parenteral we can also have another type of formulation of the pharmaceuticals in form of ointments and creams. So here this may be used for the local use, or this basically can be used on the surface of the skin. So the ointments can be prepared by using a certain melting base and this melting base may be a petroleum jelly and this base is blended with the drugs and then basically this mixture which is blended with the petroleum jelly as well as the drugs so they can be cooled and later on it can be passed through a colloid or roller mill so that we can form a smooth paste out of it which can be applied to the body. So, the pharmaceutical dosage forms can be of different type for example if we talk of the liquids so then we can have the syrups which may contain the sweetener, the solvents, medicinal agents etc. and similarly we can have the tinctures which may contain natural drugs extracted with appropriate solvents.

Similarly, we can have spirits or essences which may contain lot of alcohol, water, volatile substances and then we can have the nasal, ear drops for example we can contain lot of aqueous solution it may contain the isotonic that is having the same salt concentration as

found in the cells of the body. Similarly, the pH is also close to the nasal fluid, sprays or drops can be used here. The ophthalmic drugs basically are sterile so basically the sterilization is only done for the ophthalmic drugs otherwise we can use certain preservatives for preserving the liquid drugs. So basically, the pH also should be maintained so that the pH is nearly close to the pH of the tears and then basically it can have certain viscosity builders. Similarly, the Otic that is applied to the ears so it may be glycerol based.

Similarly, we can have number of insufflations which are actually medicated powder which can be put into the body for example the ophthalmic patients so they may be using a number of such insufflations so that they can put those insufflations inside the body so that the length capacity can be enhanced. Similarly we can have a number of drugs which are made in the solid form for example we can have the bulk powder which basically may be dissolved or mixed in water or it can be taken as externally or internally and similarly we can have number of effervescent powders which may release carbon dioxide from it and these may be taken orally for example a number of antacids or other drugs basically they can put directly into the water and then basically they can be taken directly. Similarly, we can have number of gels, jellies and magmas which may have viscous colloidal dispersions. Similarly, we can have masks or molded solid pills where basically we provide a certain adhesive or binding agent so that the molding of the pills can be done. Similarly, we can have number of troches, lozenges as well as the pastilles which are compounded with glycerol-gelatin and basically dissolved slowly in the mouth as we take it and similarly, we can have number of coated tablets which leads to the extended release of a certain compounds so this is protected by a certain coating so that the medicine may last for long.

Similarly, we can have number of granular dosages also which is having a particle size larger than the powders. So, after the formulation process is over so then we must also talk about the wastewater generation. So, the wastewater generation from the formulation process may result from a number of steps for example we can have the cleaning and sterilizing of the equipment, we can have the chemical spills during this process, we can have the rejected products that can come into the wastewater and similarly the processes that we are using for the formulation so that can also result in the generation of the wastewater. So, the wastewater that is generated from the equipment wash water so this is generally it contains large amount of inorganic salts, it may contain sugars, it may contain syrups etc. and similarly the typical characteristics of this wastewater may be low BOD, COD, TSS and near neutral pH. So, a number of processes so they may result in the wastewater generation for example when we talk of the process liquors this may arise from the organic synthesis, and this may contain a number of contaminated solvents.

Similarly, the spent fermentation broth so which arises from the fermentation processes it may contain lot of contaminated water. Similarly, the spent natural product raw materials which arise from the natural product extraction process so it may contain lot of leaves,

tissues etc. and lot of organics which are coming out from this process. Similarly, the spent aqua solutions so it may arise from the solvent extraction process so it may be containing contaminated water which may be contaminated by the solvents, it may also be contaminated by certain extracted toxic constituents. Similarly, the scrubber water from the pollution control equipment so it may arise from the dust or hazardous vapor generating processes and it may also lead to the contaminated water. The spills which are arising from the manufacturing lab and operations so this may also result in a number of chemicals into the wastewater and the wastewater, which is generated from the equipment cleanings, extraction residue so it may contain lot of chemicals which are used during the process it may also contain lot of toxic elements into it, it may also contain lot of solvents also into it.

So, this may be contaminating the water and similarly the spent solvent arise from the solvent extraction or the wash processes so it may also contain lot of wastewaters which is contaminated by solvents. So, as we have discussed so this wastewater may be generated from the equipment cleaning after the batch operation so it may contain lot of toxic organic residues. Similarly, the composition it may vary depending upon the product that we are manufacturing similarly the materials which are used during the process and similarly it will also depend upon the process that we are using for making that drug. The cooling waters are normally re-circulated so they do not come into the wastewater, and it has been reported that some wastewater may also contain mercury in the range of 0.1 to 4 milligrams per liter, cadmium in range of 10 to 600 milligrams per liter and then we can also have isomers of hexachlorocyclohexane, 1,2-dichloroethane and other solvents that can be found in the wastewater.

So, we can see a synthetic drug plant which is located at Hyderabad so they have reported that two different type of wastewater one is coming out from the acidic waste section and other wastewater is coming out from the rest of the sections so this may be having a flow of 307 cubic meter per day. So, the acidic wastewater is having a flow rate of 307 cubic meters per day whereas the composite wastewater is having a flow rate of 202 cubic meters per day. So, the pH of the acidic waste may be as low as 0.6 whereas the composite waste is having an alkaline pH, and it is nearly 9.3. So, acidity is very high in case of the acidic waste is nearly 57564 milligrams per liter as calcium carbonate whereas the alkalinity in case of the composite waste may be nearly 10574 milligrams per liter. So, the BOD here in this case is 9400 milligrams per liter in case of the acidic waste drug and the COD is 13745 so this means that in this case the BOD by COD ratio may not be very low. Whereas in the composite waste we can see that that the BOD values are nearly 15250 milligrams per liter whereas the COD values are 28540 milligrams per liter so in this case also we find that the BOD by COD ratio may be nearly 0.5. So, the wastewater coming out from such plants may be treated biologically also as the BOD by COD ratio is not very low.

So, it depends upon the type of the drugs that we manufacture from that plant and what is the biodegradability of that wastewater so depending upon that we can employ different type of treatment processes that we will be discussing in our coming lectures. Similarly, we find that the chloride levels are also very high for example in the case of the acidic waste it is 20500 milligrams per liter whereas in case of the rest of the section it is 17000 milligrams per liter. So, the sulphate which is coming out from these sections for example if we consider the acidic waste so the sulphate may be very high because we are using acids here so it may be nearly 37800 milligrams per liter whereas in the composite section this may be diluted to nearly 14800 milligrams per liter. The total nitrogen may have a value of 6202 milligram per liter similarly in the composite waste it is nearly 566 milligrams per liter. So, this nitrogen may be enhanced because of the ammonium salt that we are using during the process.

Similarly, the total solids percentage is nearly 8.27 and in the composite waste it is nearly 1.73 and the volatile solids is basically having a higher concentration, so it is basically nearly 6.66 percent whereas in the composite waste it is nearly 1.7 percent only. And we see that there can be wide variations of the wastewater characteristics that can be generated from different type of plants, so this means that we have to employ the wastewater treatment according to the wastewater characteristics that are being generated from a specific pharmaceutical industry and we are going to discuss about the wastewater treatment in our coming lectures. So, these are the references that we have used for the preparation of this lecture.

So, thank you.