Organic Chemical Technology

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Lecture - 12
Fermentation Industry

Welcome to the MOOCs course organic chemical technology. The title of today's lecture is fermentation industry part 1. In this lecture and then coming couple of lectures, we will be discussing about the fermentation industry and then different types of products produced in the chemical plants by using the fermentation process. The production of ethanol, citric acids, etc. by fermentation in chemical plants would be discussed in the next class. Today's class primarily will be concentrating on fermentation and then generalized concepts of the fermentation process and then engineering problems of the fermentation process in general because some of the major engineering problems are common to majority of the fermentation processes.

So, that is the reason those such kind of major engineering problems also we are going to discuss in general to fermentation industry, but not specific to any of the fermentation industry, okay? So, because as we have been discussing these major engineering problems are associated with the individual plant, right? But so many things are very common in fermentation industry even from one plant to the other plant that is the reason some of the important issues like scaling up of the plant and then sterilization of the media, etc. those kind of things are very common in almost all fermentation industries. So, such kind of common engineering problems also we are discussing in today's lecture on fermentation.

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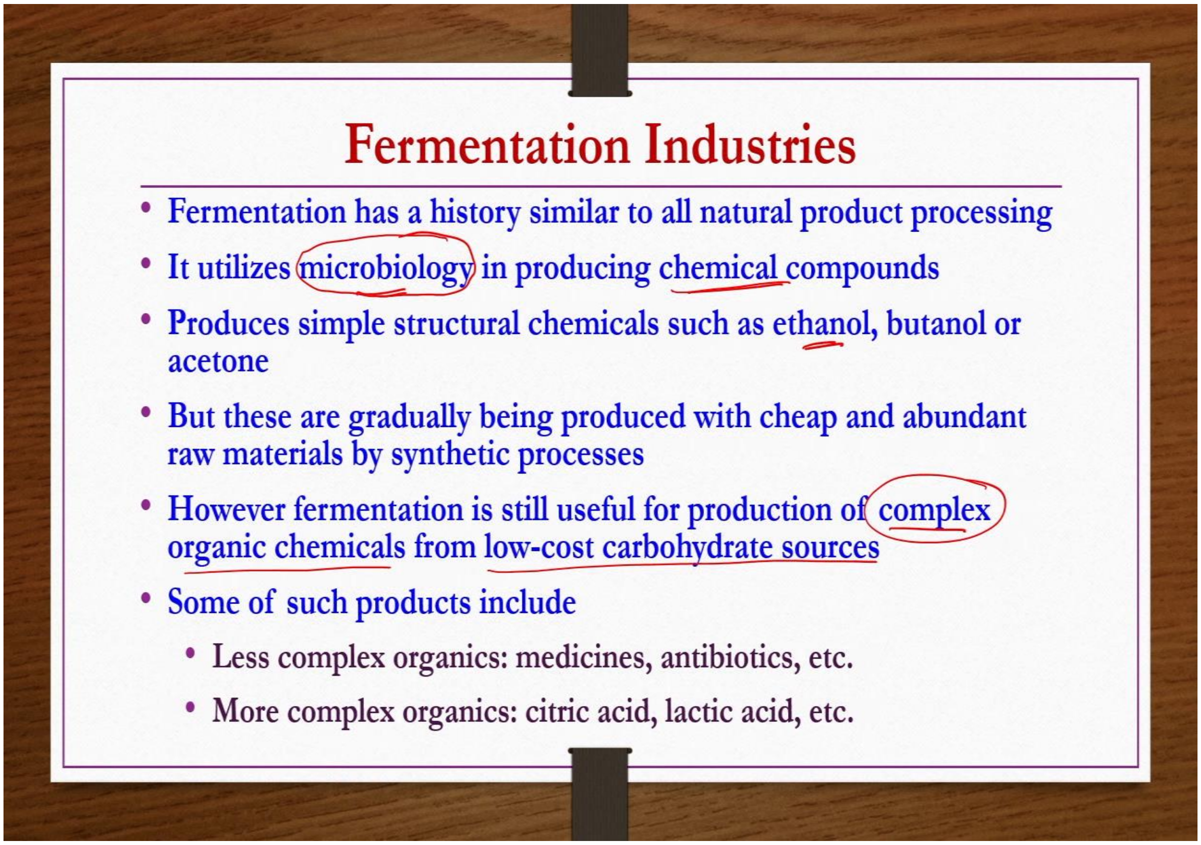

Fermentation industries, in last couple of weeks we have been discussing different types of natural product industries, something like you know oils and fats industries, soap manufacturing process and then sugar and starch industries, etc. So, all of them are natural product processing industries only and this fermentation is also having similar history. For example, the curd that you make from the milk using a bacteria that also part of the fermentation, it is occurring because of the fermentation only, right? So, production of different types of alcohol known for the centuries and then that is also by the fermentation only, right? And then different types of mixture to make idli, dosa, etc. made by the fermentation process and of course, after the fermentation you do the post processing to get the desired product that is a different issue. But basically in all these kinds of natural processes, fermentation is occurring and then that is the reason fermentation is also having history same like a natural product processing. Even pencil in antibiotic whatever is there that is also because of the fermentation process only.

In fact, that is one of the most important investigation of the fermentation process because of that one only fermentation industry has taken a boom and then is being competable with the different types of synthetic industries, okay? Fermentation what it does? It utilizes microbiology in producing chemical compounds. So, without going into details of microbiology because fermentation itself is a very separate subject if you take it as a specialization or elective course, so then we cannot go into the all details of the fermentation because we are having this as a chapter only in the course. So, we cannot go into the details of microbiology, but basically in the fermentation, what is the fermentation or what fermentation does? It utilizes the microbiology concepts in producing chemical compounds. When you feed this bacteria, yeast, etc. with high energy content, food along with some kind of nutrients if required, so then what these microorganisms they do? They not only grow their numbers, their size, but also they produce new chemicals, right? So producing chemical compound that is what it does.

Produces simple structural chemicals such as ethanol, butanol or acetone. So, alcohol production by fermentation is known for the centuries. Similarly, butanol, acetone, etc. were also being produced long back from the molasses and then blackstrap of the sugar industry by doing some kind of fermentation processing, right? But after 1930s, 1940s, what happened? This petrochemical industry has taken a boom and then it started producing huge number of chemicals, benzene, toluene, xylene and then not only the common gasoline, diesel, kerosene, etc., different types of chemicals and hexane, etc.

are also being produced and then ethanol, butanol, acetone, these kind of things are also being produced. Very economically using a very cheap raw materials or abundantly available raw materials, okay? So, because of that one production of such kind of simple structural chemicals like ethanol and butanol and acetone has become uneconomical, but these are gradually being produced with cheap and abundant raw materials by synthetic processes especially in petrochemical industries.

However, fermentation is still useful for production of complex organic chemicals from low cost carbohydrates sources. So, simple ones you can produce using the synthetic process very economically, but complex organic production by synthetic processes are not that much economical for many of them, right? Something like citric acids, etc., that production of citric acid and production of vitamin B2 or vitamin B12, etc., are better to produce by the fermentation process or also majority of the antibiotics whatever available in pharmaceutical industry they are also produced by the pharmaceutical industries and all of them are complex in nature, complex in chemical structure, but it may be low complex or high complex, but some they are not simple as ethanol and butanol, okay? Some of these products include less complex organic something like medicines, antibiotics, etc., and then more complex organics like citric acid, lactic acid, gluconic acid, etc. We are going to see list of products also by different methods and all those things that we are going to see in the subsequent course of today's lecture.

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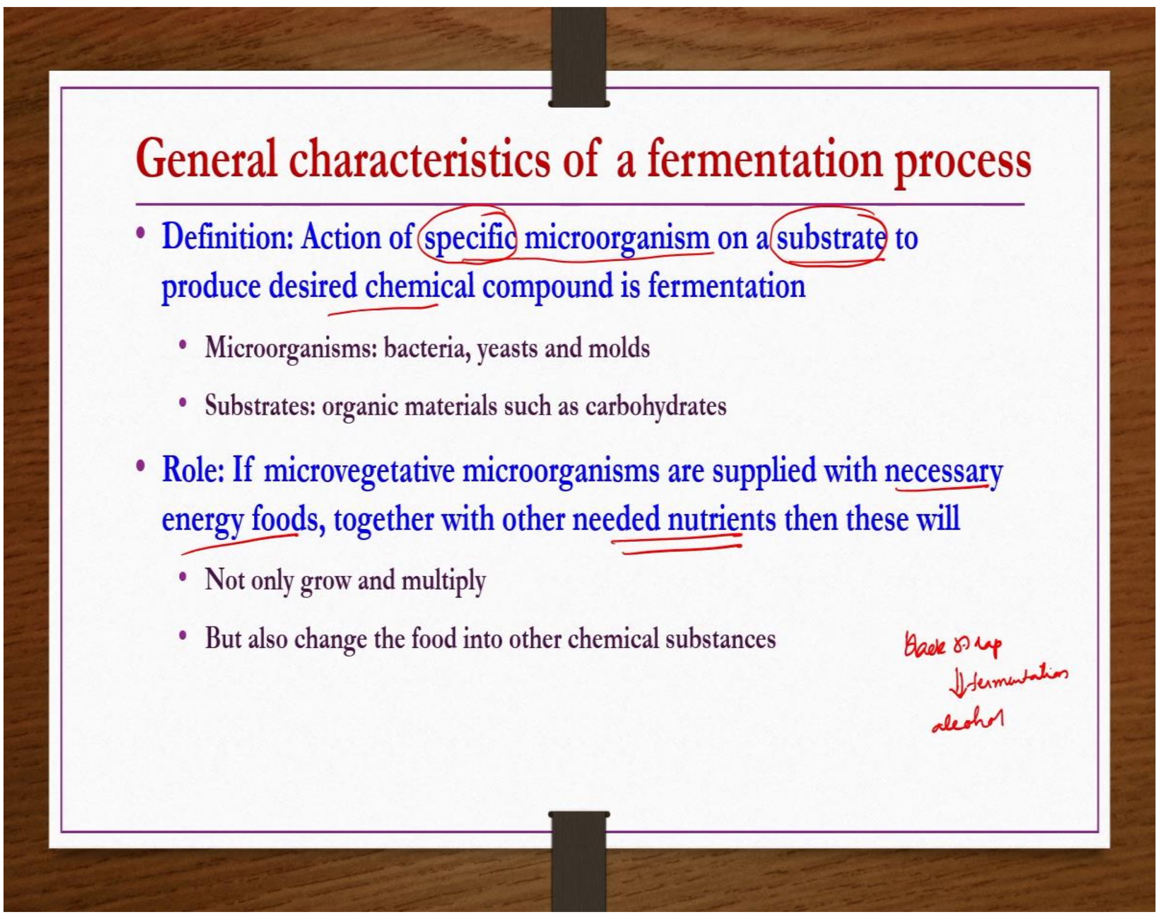

Now, general characteristics of fermentation process if you see what happens? Definition of the fermentation actually it is action of a specific type of microorganism on a substrate to produce desired chemical compound, right? So, the microorganism whatever is there, they are also specific to the product that you are going to produce and then substrate also you have to produce raw material, etc. They are all depending on the product your raw material will change and then accordingly your microorganism whatever required that will also be changed, okay? So, in general if you want to define fermentation action of a specific microorganism on a substrate to produce desired chemical compound is known as the fermentation.

So, what does it mean or what is the role of fermentation process that we are going to see? So, what kind of microorganisms are in general used in fermentation industries are some kind of bacteria, yeast and molds. We will see some of them. Substrates, what are the common substrates? Organic materials such as carbohydrates, sugars, corn, etc. These kinds of things are used as substrates. Role that is what these microorganisms they do.

If micro vegetative microorganisms are supplied with the necessary energy foods together with other needed nutrients if required may not be required for all the process, but some process definitely they may be required. Then what these micro vegetative microorganisms will do? They not only grow and multiply their concentration but also change the food into other chemical substances. Let us say black strap of sugar industry whatever is there that would be used by the microorganism and then fermentation will take place and then you get alcohols like ethyl alcohol etc. you may get.

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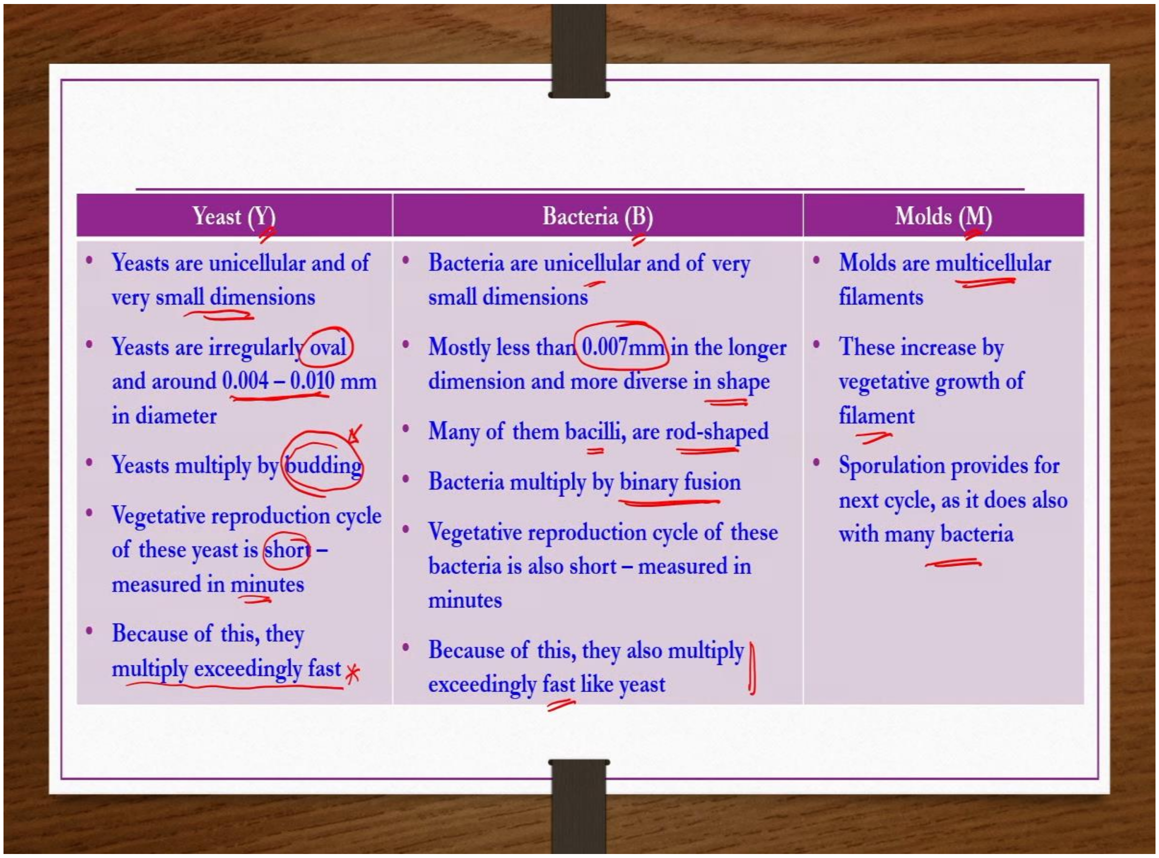

So, we see a few details about microorganisms as I mentioned. So, yeast, bacteria and then molds these are represented by this capital Y, capital V and capital M respectively. Yeast are unicellular and of very small dimensions in general. They are irregularly oval in shape and then around 0.004 to 0.010 mm in diameter approximately 400 to 1000 microns they may be in diameter. Yeast multiply by budding because their size has to be increased actually the number has to increase. So, that number increasing how it takes place by budding and then vegetative reproduction cycle of these yeast is short so within short period they may be reproduced. So, in general that is measured in minutes only not much and then because of this a short reproduction cycle time they multiply exceedingly fast which is good. Actually fermentation processes are very slow processes they takes hours sometimes days also. So, if the things are able to done in minutes that means such kind of fermentation processes are very fast that is what you can understand.

Bacteria are also unicellular and of very small dimensions. Usually they are less than 700 microns or 0.007 millimeters in the longer dimension and more diverse in shape not necessarily oval shape in general they would be more diverse. Many of them are bacilli or rod shaped bacteria. They multiply by binary fusion and then for them also vegetative reproduction cycle is short measured in minutes and because of this again here also they multiply exceedingly fast like yeast.Whereas the molds are multicellular filaments these increase number by vegetative growth of filament. Sporulation provides for next cycle as it does also with many bacteria. So, a few important difference between yeast bacteria and molds are presented here.

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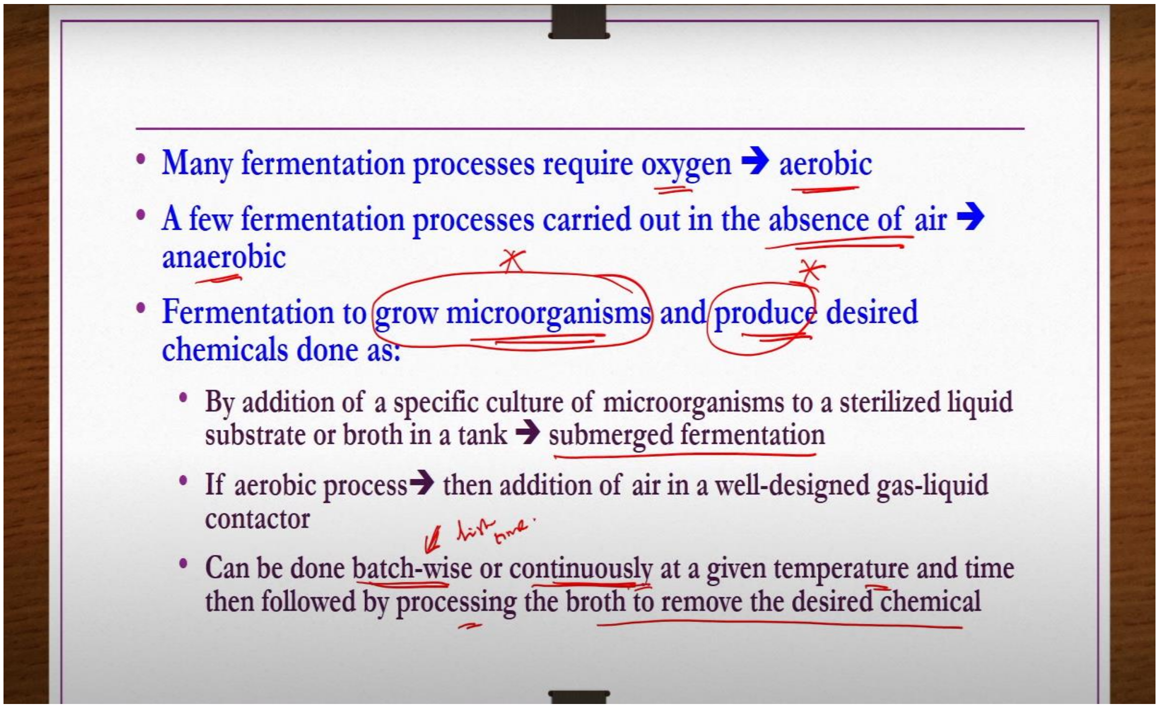

Now the fermentation process whatever is there sometime it is occurring in presence of oxygen sometimes it is occurring in the absence of oxygen. So, fermentation processes which require oxygen are known as the aerobic processes and many of the fermentation processes are aerobic, but however a few occur in the absence of the air as well they are known as the anaerobic fermentation processes. Now if this fermentation to occur there should be some kind of reactor or contacting medium or equipment is required.

Fermentation to grow microorganisms, so microorganism growth and produce desired chemicals done as in submerged fermentation where addition of a specific culture of microorganisms to a sterilized liquid substrate or growth in a tank is done. If aerobic process then addition of air in a well designed gas liquid contactor are provided. So they can be done batch wise or continuously at a given temperature and time then followed by processing the broth to remove the desired chemical. So, now what you understand until now fermentation they have to grow the number has to be grown microorganisms or micro vegetative microorganisms whatever are there which are used or which are fed with some kind of substrate to produce some chemicals.

So, two important things are there not only just producing the desired chemical but also the number has to grow then only it can be process can be feasible or for the next cycle you have the microorganism ready so that you can continue the next cycle. So, the growth is also very much essential. So, in the fermentation primarily two important things are taking place. One is the growth of microorganism and then other one is the production of desired chemicals and then that can be done either of these ways. In general any process may be carried out either batch wise or continuously. So, batch wise processes are preferred in general where high process time is there or residence time is very high. So, then even if you are getting uniformity of the product and then better yield etc by continuous process it is preferred to go for the batch wise process if your residence time or process time is very high. And then in fermentation industry almost all fermentation processes are batch process because of the same reason of high residence time or high process conversion time.

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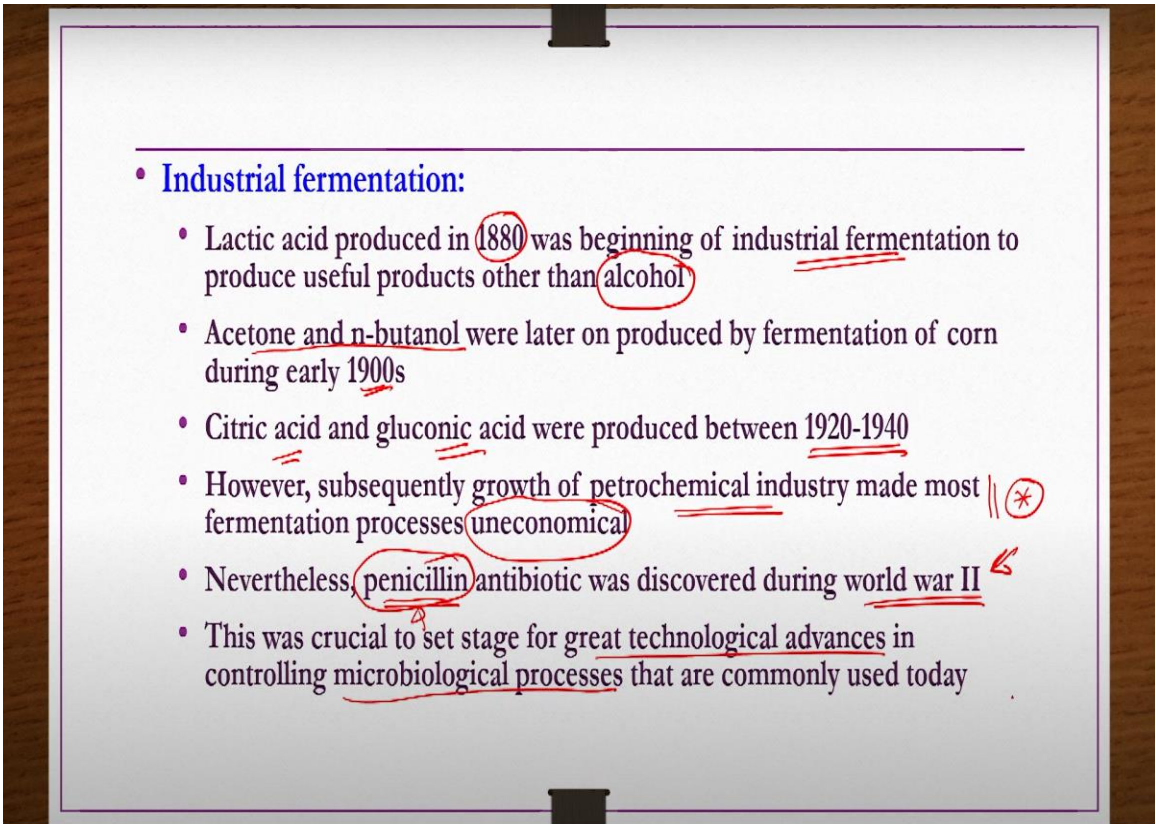

Now, we see importance of fermentation at the industry or industrial fermentation. Lactic acid was produced in 1880 before that only alcohols were being produced by fermentation process. So, around 1880 lactic acid was produced that was the beginning of industrial fermentation. Then later on acetone and then n-butanol were also produced around early 1900s whereas around 1920 and 1940 citric acid and gluconic acids were produced by the industrial fermentation process. However, subsequently growth of petrochemical industry made most fermentation processes uneconomical. Anyway, anything that you do if that is not economical, so you cannot implement in the chemical plant because you do in large size and then you invest lot of capital funds as well as the operational maintenance and so many other costs are involved. So, then if the process is uneconomical you cannot move forward.

So, same was the truth for the fermentation industry also once the petrochemical industry has taken boom around 1940 or after that then fermentation industry has slowed down literally. But there comes the king of fermentation industry product that is penicillin antibiotic that was discovered during the World War II. It was very useful those days because of the World War many people were getting injured and then this bacteria or antibiotic produced by the penicillin whatever is there that was curing the wounds very quickly. So, after this penicillin antibiotic development fermentation industry was never set back and then it was moving forward and then competing with the other synthetic chemical industries as well. Because most of the antibiotics that are available in today's pharmaceutical industries are because of the fermentation process only. This was crucial to set stage for greater technological advances in controlling microbiological processes that are commonly used today.

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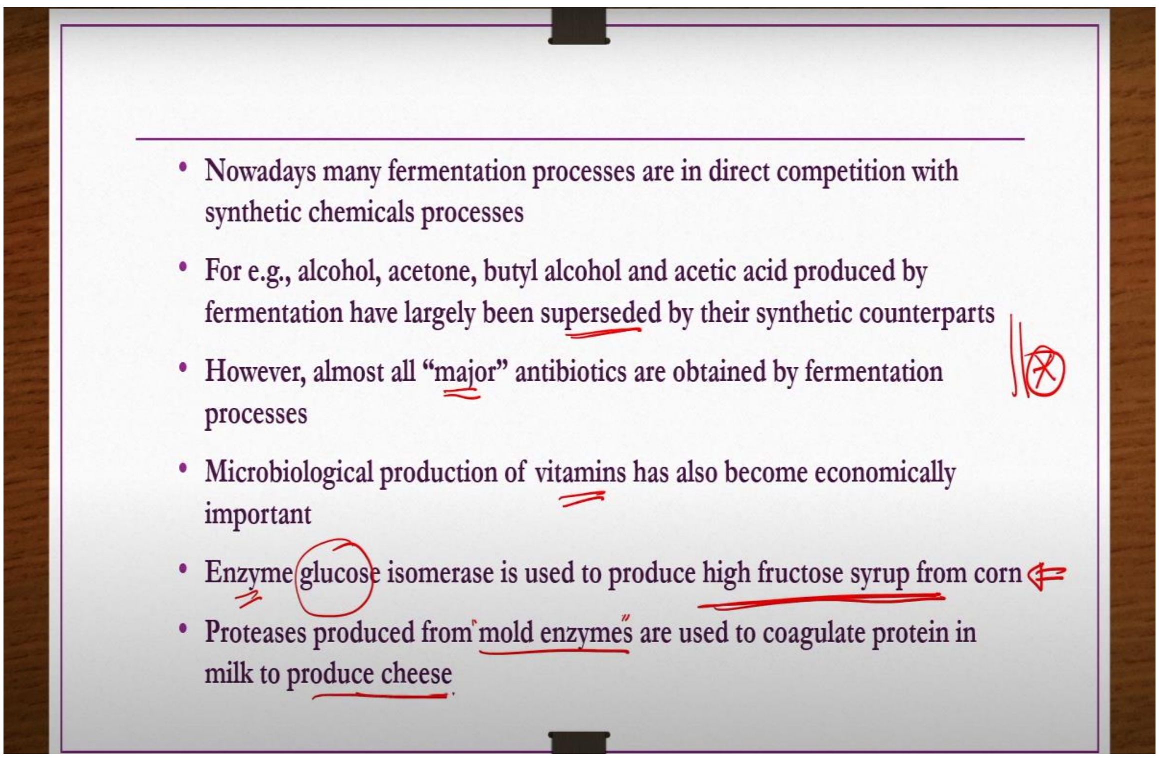

Nowadays many fermentation processes are in direct competition with synthetic chemicals process because of the boom that fermentation industry has gone after discovery of this penicillin antibiotic. For example, alcohol, acetone, butyl alcohol and acetic acid produced by fermentation have largely been superseded by their synthetic counterparts, but not the other complex chemicals like medicines, citric acid, lactic acid, etc. They are produced economically by fermentation process only not by the synthetic processes. However, almost all major antibiotics are obtained by fermentation process.

So, there the role of fermentation industry is there. Microbiological production of vitamins like vitamin A, vitamin B2, vitamin B12, etc. has also become economically important because of such kind of fermentation processes. In the previous week, we have seen that glucose has been converted to high fructose containing sugar syrups. So, in that process we have used glucose isomerase enzyme. So, that is also by fermentation process. There also in that process also fermentation was taking place and also proteases produced from mold enzymes are used to coagulate protein in the milk and to produce cheese.

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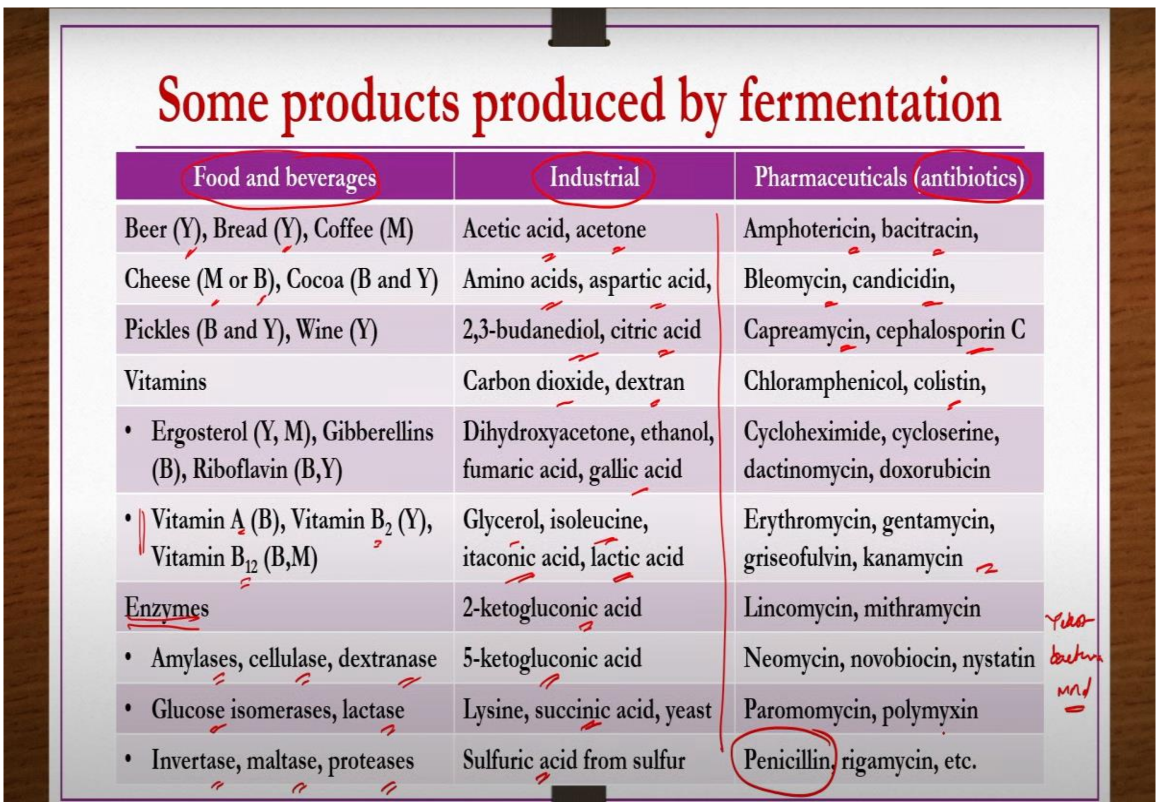

Some products produced by fermentation

Food and beverages	Industrial	Pharmaceuticals (antibiotics)
Beer (Y), Bread (Y), Coffee (M)	Acetic acid, acetone	Amphotericin, bacitracin,
Cheese (M or B), Cocoa (B and Y)	Amino acids, aspartic acid,	Bleomycin, candicidin,
Pickles (B and Y), Wine (Y)	2,3-budanediol, citric acid	Capreamycin, cephalosporin C
Vitamins	Carbon dioxide, dextran	Chloramphenicol, colistin,
• Ergosterol (Y, M), Gibberellins (B), Riboflavin (B,Y)	Dihydroxyacetone, ethanol, fumaric acid, gallic acid	Cycloheximide, cycloserine, dactinomycin, doxorubicin
• Vitamin A (B), Vitamin B_2 (Y), Vitamin B_{12} (B,M)	Glycerol, isoleucine, itaconic acid, lactic acid	Erythromycin, gentamycin, griseofulvin, kanamycin
Enzymes	2-ketogluconic acid	Lincomycin, mithramycin
• Amylases, cellulase, dextranase	5-ketogluconic acid	Neomycin, novobiocin, nystatin
• Glucose isomerases, lactase	Lysine, succinic acid, yeast	Paromomycin, polymyxin
• Invertase, maltase, proteases	Sulfuric acid from sulfur	Penicillin, rigamycin, etc.

Now, we see a few common products produced by fermentation. They are presented in a tabular column. This tabular column should be read column wise. First column is the food and beverages produced by fermentation whereas the second column is the different types of chemicals produced by the industrial fermentation and then third column different types of medicines antibiotics produced by the fermentation in pharmaceutical industry. Here within the parenthesis y, b, m, etc. are given. So, as I already told y for the yeast, b for the bacteria and then m for the molds that have been used to produce such kind of products. So, let us say under food and beverages you can see beer, bread, coffee, cheese, cocoa, pickles, wine, many are there.

Even some vitamins also there like ergosterol, gibberellins, riboflavin, vitamin A, vitamin B2, vitamin B12, all of them are produced by the industrial fermentation process. Likewise, several enzymes are also produced by the fermentation process. These enzymes are useful in producing several types of chemicals that shown in the second column. What are some of the enzymes? They are nothing but amylases, cellulase, dextranase, glucose isomerases, lactase, invertase, maltase and proteases. Now, coming to the different types of chemicals produced by industrial fermentation and the chemical plants are acetic acid, acetone, amino acids, aspartic acid, 2, 3-butanediol, citric acid, carbon dioxide, dextran, dihydroxyacetone, ethanol, fumaric acid, gallic acid, glycerol, isoleucine, itaconic acid, lactic acid, 2-ketogluconic acid, 5-ketogluconic acid, lysine, succinic acid, yeast, sulfuric acid from sulfur, etc.

Coming to the some of the antibiotics or medicines that are produced by fermentation in pharmaceutical industries are amphotericin, bacitracin, bleomycin, candicidin, capreamycin, cephalosporin C like that so many are there here. So, even the penicillin, so like that n number of pharmaceutical medicines or antibiotics are also produced by the fermentation process. Now, we see chemical conversions in fermentation process. Actually, when the fermentation occurring or when a micro vegetative microorganism utilizes the substrate, when they grow their number and then produce some kind of new chemicals, then what happens? Different types of chemical reactions takes place something like oxidation, reduction, hydrolysis, esterification, etc. These kinds of reactions take place. But however, later on it has been found that the overall reaction mechanism of any given fermentation process if not all process but many of the fermentation processes, the reaction mechanism is very complex, then the people started taking the concept of fermentation itself as a chemical conversion, right?

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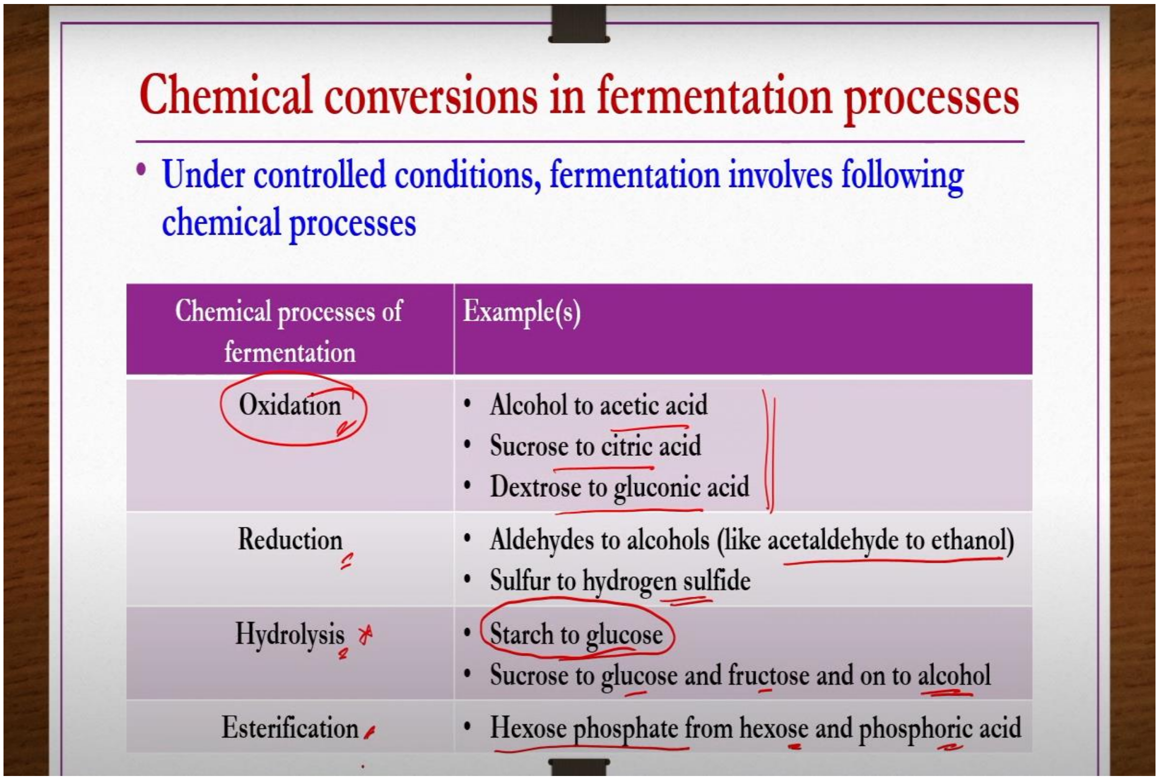

However, we see a few examples where the chemical conversion process is very simple and straightforward as any common reaction, okay? We see some of them now. Under control condition, fermentation involves following chemical processes, let us say some of these simple chemical processes which occur in fermentation or like oxidation. Example, production of acetic acid from the alcohol or sucrose to citric acid production or dextrose to gluconic acid production. In these fermentation processes, oxidation is the primary reaction that takes place. Likewise, reduction is also possible like aldehydes to alcohol production, acetaldehyde to ethanol if you are producing, their reduction takes place, sulphur to hydrogen sulphide production also reduction takes place.

Likewise, hydrolysis like starch to glucose that we have seen in the previous chapter on sugar and starch industries, hydrolysis is one of the important reactions. So, there such kind of hydrolysis also occur in the fermentation processes. Then sucrose to glucose and fructose and then on to several alcohols also under such conditions also hydrolysis is one of the important reaction in the fermentation. Then esterification is also sometimes occurs in the fermentation process. Let us say from hexose and phosphoric acid if you are producing hexose phosphate, so that is nothing but esterification reaction. Like this n number of reactions are possible and many of the fermentation processes are very complex.

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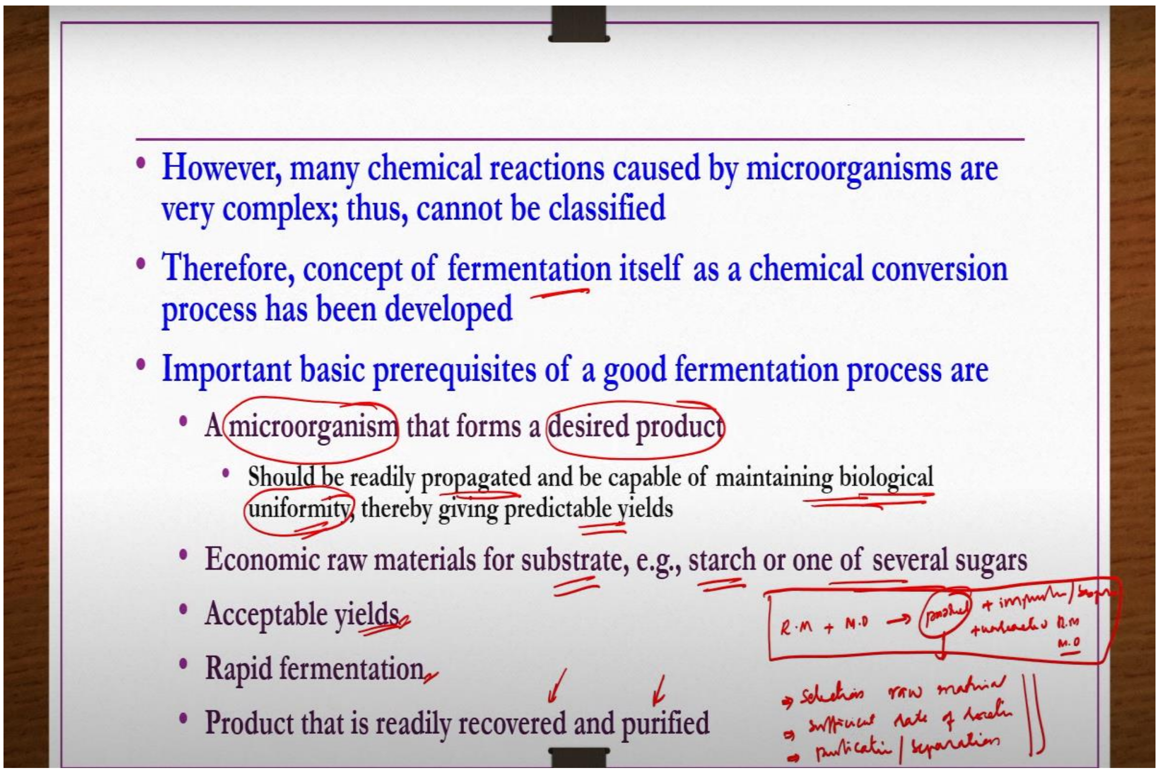

So, many chemical reactions caused by microorganisms are very complex. They are not simple as shown in the previous slide as with example. So, because of majority of the chemical reactions caused by microorganisms are very complex, they cannot be classified and then because of that one concept of fermentation itself as a chemical conversion process has been developed. Important basic requirements of a good fermentation process are listed below. These are all in general to any fermentation process. A microorganism that forms a desired chemical, you take a substrate and then you take a microorganism. So, that microorganism has to be specific to consume the substrate and then produce the desired chemical not the undesired one or some other impurities. So, these microorganisms should be readily propagated, their number has to be increased readily. They should not take days and weeks, they should increase their number in minutes or maybe in few hours and should be capable of maintaining biological uniformity also.

It is not like that you know one particular microorganism of one size, other one is the bigger size or different size something like that, that should not be the case. Biologically they should be uniform, thereby giving predictable yields. The process if the microorganisms which are grown or propagated because of the fermentation if they are uniform biologically then obviously the yields whatever you expect they would be predictable as per your selection. Then also economic raw materials for substrate, for example several sugars that are available that you can use because these are the substrate that will be consumed by the microorganisms and then you get desired chemical. If the substrate itself is not economic then process cost may be increased.

Acceptable yields, actually fermentation process, they are slow process as already mentioned. So, if the process is slow, so from the product quantity point of view considerable quantity of the product you get after long time, long time in the sense several hours or maybe a couple of days that is a very long time if you take it from the industry point of view. And then the time is higher and then quantity is also small then the process may not be very much feasible. So, that is the reason the yields has to be acceptable, they should not be very low because the process most of the fermentation processes themselves are slow. If the yields are also very low then they will not be acceptable, then fermentation has to be rapid.

Product whatever is formed that should be easily recovered and then purified. After the process what happens actually let us say you have the raw material and then microorganism are there, so then you are reacting together to get the product plus impurities or byproducts may also be there, in general it is possible. Then plus unreacted raw materials, obviously these microorganisms would definitely would be there in the mixture because they are growing their numbers. So, this has to be removed from this mixture and this removal if it is taking in a more cost then again process may not be economically feasible.

So, here in fermentation industry also in general whatever happens in the chemical plant that is selection of proper raw material, economical raw material, sufficient or adequate rate of reaction and then purification or separation of products, these kinds of steps which are common for any chemical plants, they are also here in the fermentation and then fermentation is one type of a chemical process only actually though it is a natural process occurring, but it is occurring in the plants. So, all such kinds of steps are valid here also we can see. This we can realize from all these steps. Now, what are the critical factors of fermentation in general? In general not specific to any product, pH, temperature, etc., all these kind of things would be there, which are most critical in general in most of the fermentation process we are going to list them now.

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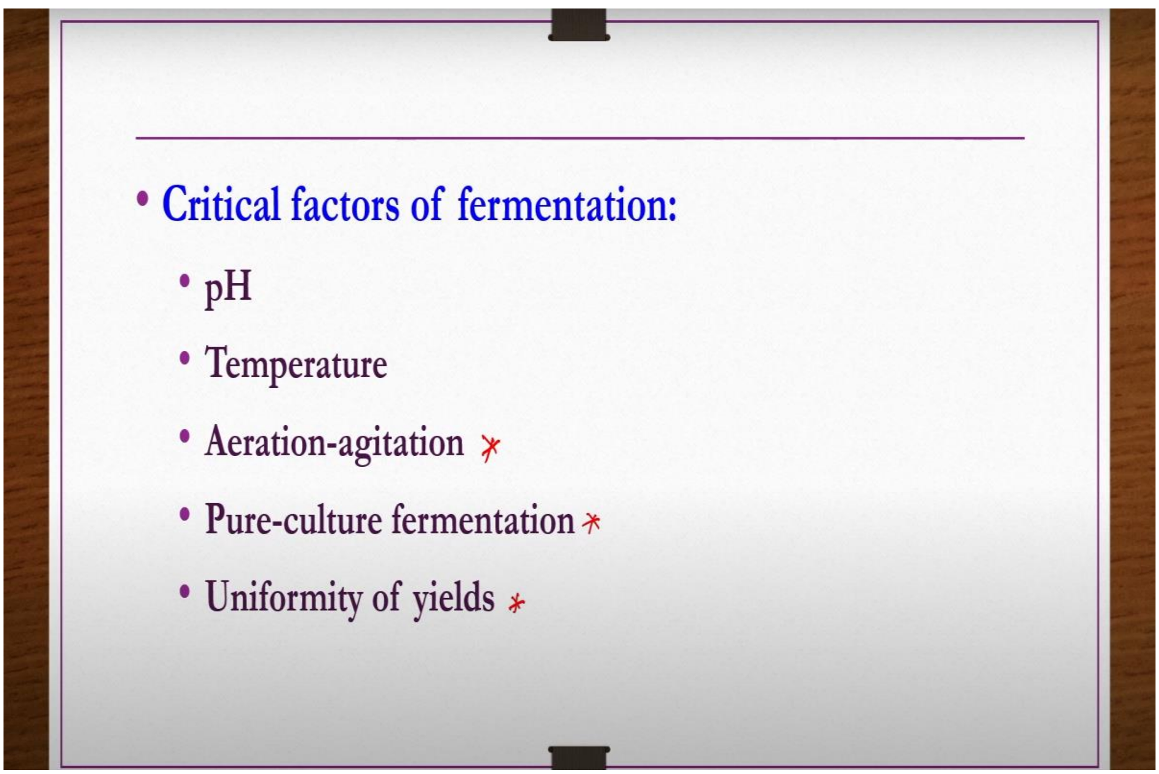

pH is very essential in fermentation process, then temperature is also very essential because it should be suitable to the growth of microorganism as well as for the conversion of the substrate into the product as well. Aeration, agitation, how much it is required, at what speed aeration should be done, at what RPM agitation is required, all these things are very essential crucial one. We are going to see in major engineering problems anyway how much it is important. Pure culture fermentation is required, there should not be any contamination. So, this is also one of the major engineering problem for most of the fermentation processes as we are going to discuss very soon. Uniformity of yields, whatever the yields that you get if it is changing every day or day by day or every fortnight also if it is changing then it is very difficult to maintain the product quality. So, that is also very much essential or critical factor of fermentation industry.

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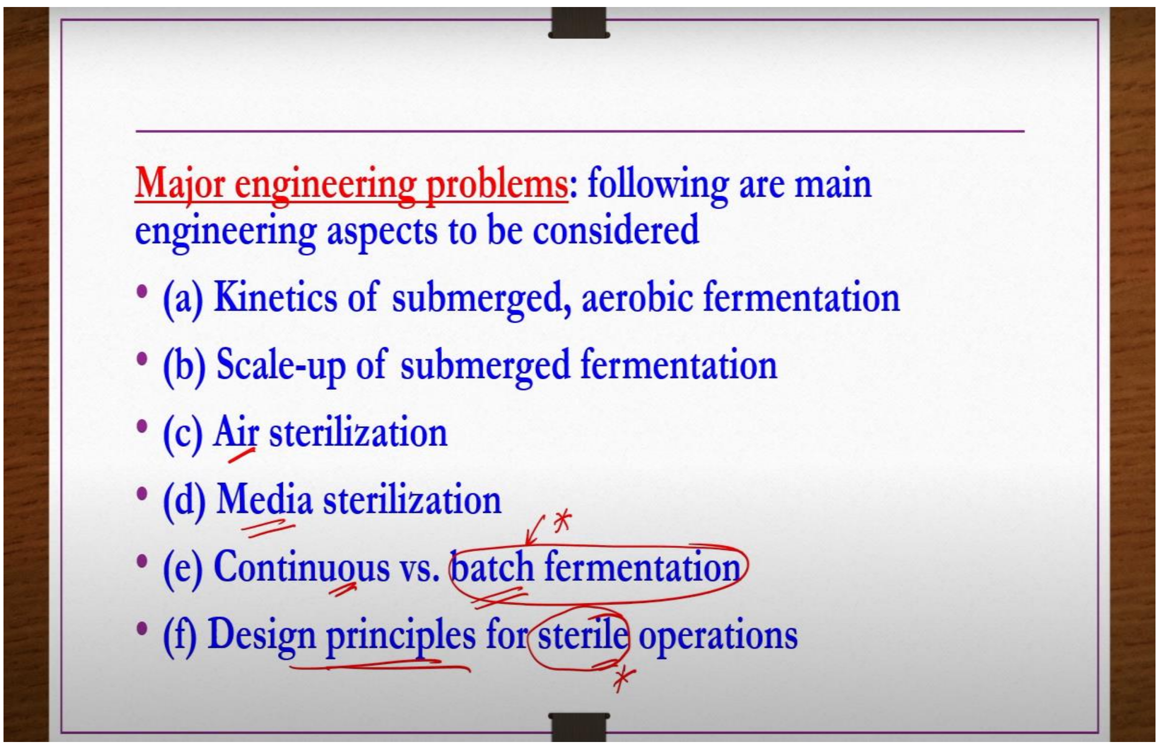

Now, we see major engineering problems associated with a generalized fermentation process not specific to any chemical production generalized fermentation process if you see. So, there may be certain kind of issues which may be applicable to almost all fermentation processes without any much deviation. There may be some additional engineering problems associated with the individual products development by the fermentation industry, but there could be in addition of whatever we are going to discuss because whatever the engineering problems that we are going to discuss they are very common to most of the fermentation process if not all for most of the fermentation processes.

So, what are the obviously the kinetics wherever there is a conversion is there then kinetics plays a very important role. So, kinetics of submerged aerobic fermentation process is one problem. Scale up of submerged fermentation, scale up is very much essential for any of the plant not only fermentation plant because you do at the lab scale, you do at the bench scale then you do at the pilot scale then you implement at the industry and then when you see lab to bench, bench to pilot when you move. So, the yield and the product purity etc.., all those things varies in general. Air sterilization in aerobic process air is very much important. So, it is sterilization is very much essential otherwise impurities may be there that impurities may be interacting with the culture or microorganism and then rather producing the desired chemical some other chemical may be produced. So, it is very much essential. Likewise media sterilization is also very much essential. If the substrate whatever is there that has to be sterilized properly then you know whatever the micro vegetative microorganisms are there the reaction or how they consume and then how they produce the product that would be very much controlled.

In fact, not only air and media each and every part of the fermentation plant should be properly sterilized because especially if you are applying the fermentation process in pharmaceutical industries where medicines antibiotics etc. are being produced then maintaining very much pure or clean environment is very much essential. So, there in such kind of fermentation processes even the connecting pipes etc. those things are also properly sterilized before the start of every batch. Then continuous versus batch fermentation which one should you go in general.

In general fermentation is a slow process. So in general batch process or batch fermentation is preferred. However, there may be a few processes which may be rapid. So, under such conditions you can go for the continuous fermentation, but majority wise batch fermentation is preferable because of the slow fermentation rates and then design principles of sterile operations. See sterilization is very much essential in the fermentation. So, design principles of sterilization operations is one of the major engineering problem of any of the plant any of the fermentation plant.

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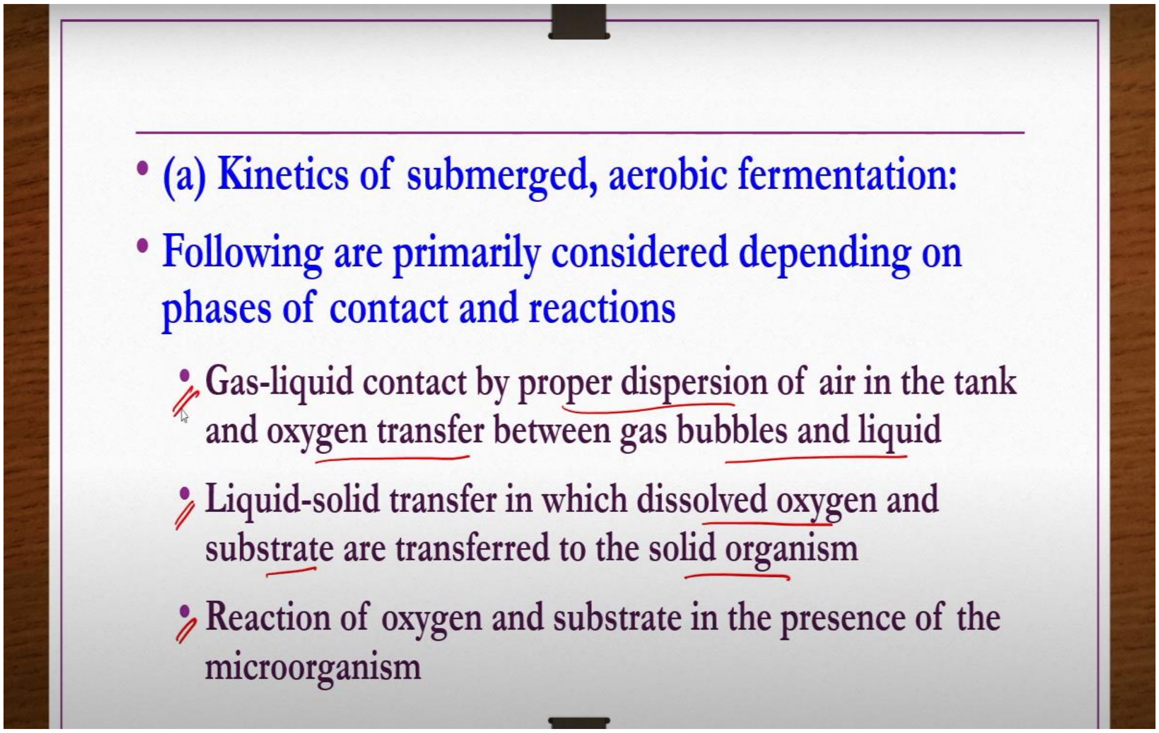

So, now we see details of individual engineering problems. Now, kinetics of submerged aerobic fermentation following are primarily considered depending on phases of contact and reactions. Let us say if you have gas liquid system then gas liquid contact by proper dispersion of air in the tank and oxygen transfer between gas bubbles and liquid are essential. One has to pay attention to such issues. If you have a liquid solid system then liquid solid transfer in which dissolved oxygen and substrate are transferred to the solid organisms. Then reaction of oxygen and substrate in the presence of the microorganisms these 3 are very important points and then one has to pay attention.

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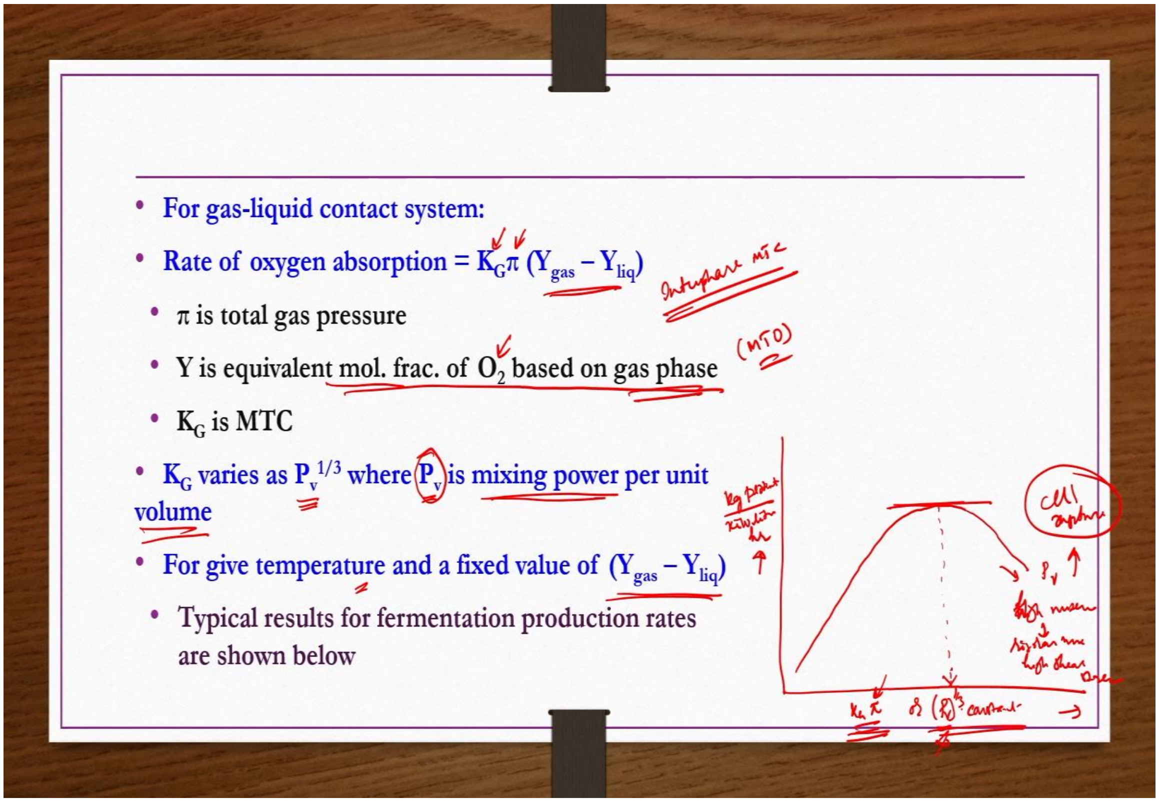

We take an example of gas liquid system here. For example, if you have a gas liquid contact system then rate of oxygen absorption is given by mass transfer coefficient multiplied by the pressure multiplied by the concentration difference. Here pi is the total gas pressure, kg is the mass transfer coefficient, y is equivalent mole fraction of oxygen based on the gas phase because the gas liquid interface would be there, interface mass transfer coefficients are coming into the role. So, whatever this y is there equivalent mole fraction of O2 based on the gas phase. So, what does it mean? This you can understand in mass transfer operation courses where you discuss about interface mass transfer, okay? So, here this mass transfer coefficient whatever is there that varies as cube root of PV where PV is nothing but mixing power per unit volume of the system whatever liquid that you have taken. PV indicates mixing power.

So, it is saying that mixing power so that means if it is increasing the rigorous nature in the mixing would be increasing that is what you can understand from the nature of this PV definition, okay? For a given temperature and a fixed value of concentration difference, typical results for fermentation production rates are so these for a fixed temperature and a fixed concentration difference. If you see the production rate, whatever the production rate is there that is nothing but kg of the product per kilo liter per hour. That one versus either kg multiplied by pi or PV or cube root of PV multiplied by this constant. This constant maybe depends on the system to system, right? It may be having only the size of the equipment related things or it may be having the constant related to the flow rates, etc. So that depends on system to system, but major role is coming from this PV or cube root of PV.

So, now this production rate whatever is there that if you plot against the kg multiplied by pi or cube root of PV multiplied by a constant, then what you can say this production rate increases gradually like this and then after certain x axis values, then it decreases like this. So, there should be a maximum like this here, okay? So, whatever your pressure and then PV values are there, you should be maintained such a way that the combination of kg pi or PV power one third and then constant should not be more than this value for a given fermentation process because after that production rate decreases.

You try to make the production rate maximum in general in your process, right? Why it decreases it here because PV increasing that means high mixing takes place. So, that means rigorous mixing leads to high shear stress, right? High shear stress, etc.., may be leading to the rupture, cell rupture will take place. So, if the walls of the cell get damaged because of the mixing, the cells whatever the microorganisms may not be doing their duty as effectively as they are expected to do, okay? So, this is one of the engineering problems. So, you can fix like this for your system, you can calculate and then you can fix what should be your maximum pressure, what should be your maximum mixing power per unit volume, okay?

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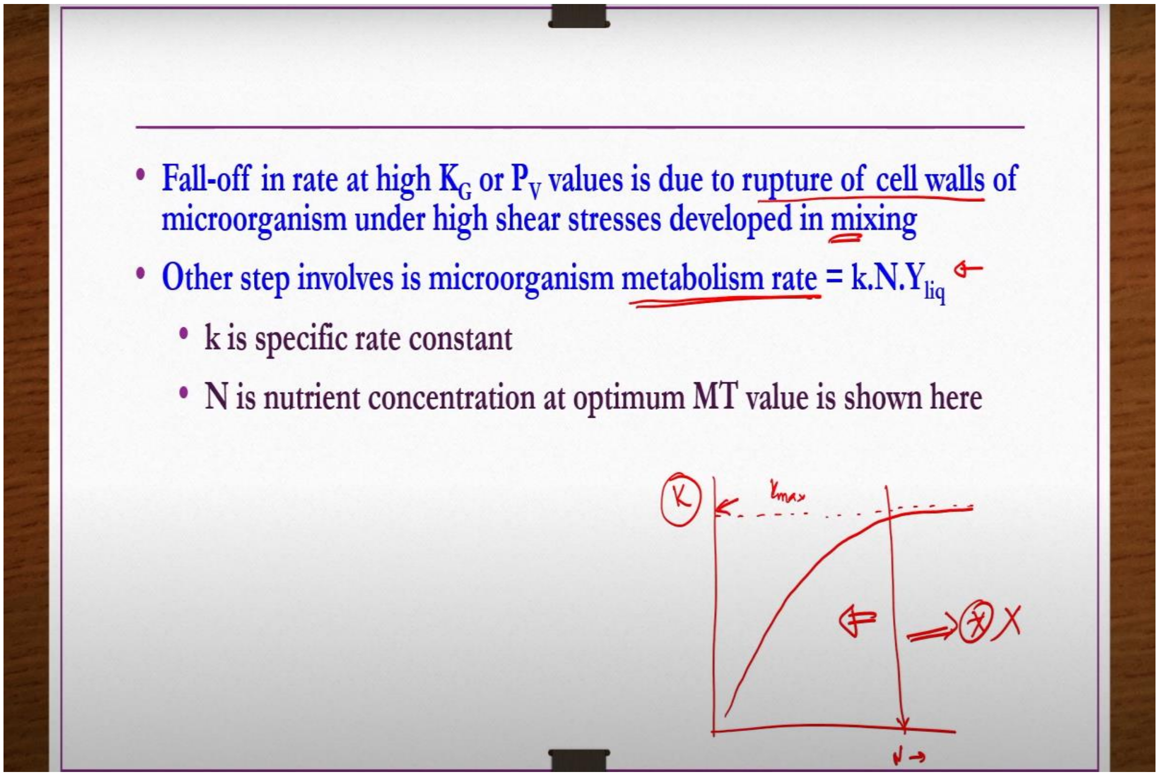

Falloff in rate at high kg or PV values in the previous picture drawn is due to rupture of cell walls of microorganisms under high shear stress developed in the mixing. If the PV increasing that means mixing is becoming more rigorous, right? When the mixing is increasing, so then high shear stress would develop. So, because of the high shear stress, a kind of strong collisions between the cells etc. will take place because of that one cell walls may be rupturing and then they may not be doing the desired duty whatever they are expected to do in the fermentation process.

Other step is microorganism metabolism rate, right? So, because that is important if the metabolism rate is there properly, then only the growth or propagation of the microorganisms will take place. So, this is the other important thing. So, this rate is given by k multiplied by n multiplied by y liquid. So, k is specific rate constant, n is nutrient concentration at optimum mass transfer value that if you see here let us say this k versus n, n is nothing but the nutrient concentration. For some of the processes, it is not just a substrate high energy content food and then microorganism but also nutrients are required.

Nutrients are required so that these microorganisms can do their work effectively or maybe rather quickly, okay? So, for that purpose nutrients are in general added. So, that nutrient concentration how much should be added that you can get by plotting this specific rate constant versus nutrient concentration capital N. So, what you can see it increases gradually like this and then after that it becomes almost constant. So, after this point, whatever the nutrient concentrations if you increase, it is going to be useless because it is not increasing the rate constant. So, it is better to maintain nutrient concentration below this value. It will not only avoid the wastage of nutrient concentrations, but also provide the maximum rate constant whatever possible maximum value, okay?

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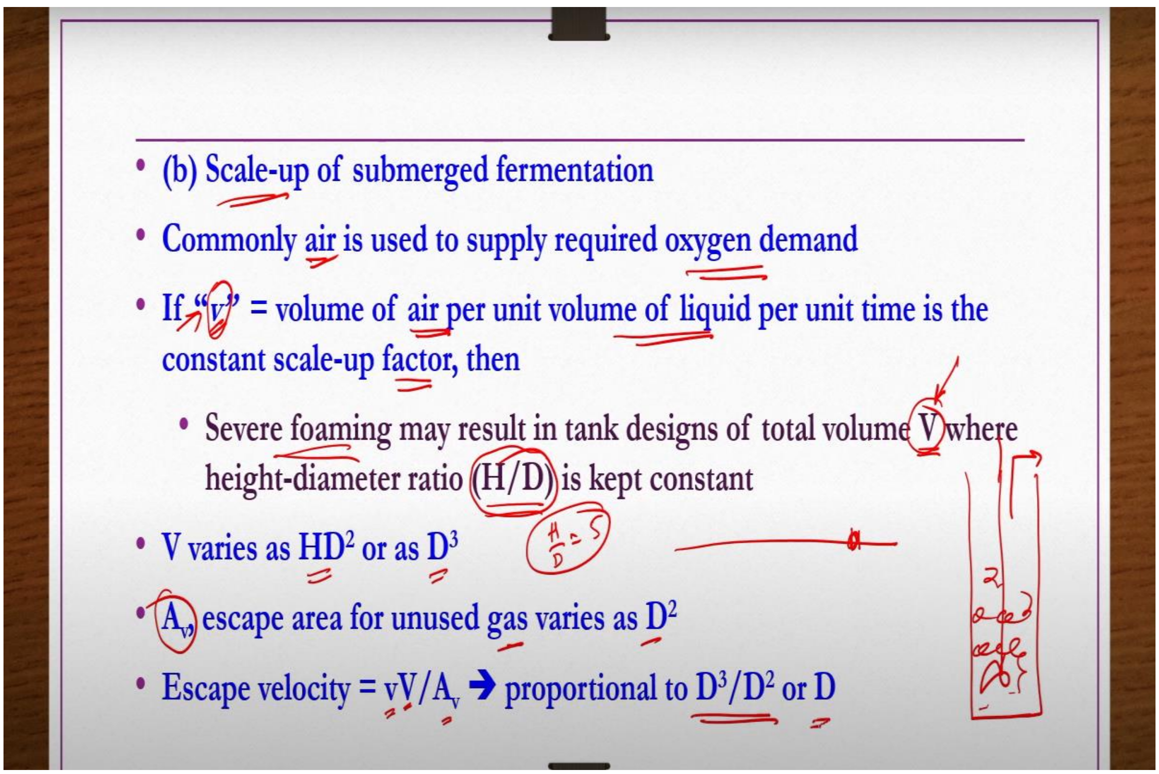

So, Scale-up of submerged fermentation. Let us say tank you have like this, fermentation tank. If you have fermentation tank like this, right? So, now here in this case what happened the liquid and then microorganism whatever the substrate etc. are there. So, more space is available for it to grow and then mix, right? But however, here you cannot do the thorough mixing because it is wider in shape. Otherwise, you have to insert mixers everywhere baffles or mixers everywhere like this, which is not possible. Let us say if you have a tall column like this, then mixing may be possible easily it is possible, right? But you know foaming whatever takes place because of the fermentation that may be very rapid that you may not able to control it may be going out of the reactor if it is open. If it is closed, then it may be increasing the pressure within the system and then that increased pressure again may lead to the rupture of the cells and then it may not do desired fermentation duty as expected. So, such kind of issues would be considered under the scale up.

So, what should be the optimum height, optimum diameter or optimum height versus diameter ratio value. So, these things should be considered under the scale up of fermentation process. Commonly air is used to supply required oxygen demand. If v is air volumetric flow rate per unit volume of the liquid and then this volumetric flow rate of air per unit volume of the liquid you take as a constant for the scale up because scale up when you do there should be some basis, right? In general for the aerobic process air is the one that is supplied to maintain the required oxygen demand. So, then air flow rate or volumetric rate of the air is taken as a scaling parameter. So, volumetric flow rate per unit volume of a liquid, then whatever that constant comes that if you consider as the scaling factor, what will happen? So, let us take that constant as v which is nothing but volumetric flow rate of air that is being supplied to the fermenter per unit volume of the liquid that is present in the fermenter. Then severe foaming may result in tank designs of total volume v where height diameter ratio h by D is kept constant.

Under such conditions, if the scaling parameter you take this one, you keep h by D ratio constant and then you keep changing different v, then what happens severe foaming may take place that is not good, right? So, what is a scaling factor in the sense you are changing you are trying to find out what is the total volume of the tank or fermentation reactor that you can afford. Technically how you can decide the volume of the tank should be for a given fermentation process that is what mean by the scale up. So, either h, either D or both you have to change these kind of things are required in general. Rather doing that one you maintain h by D ratio constant whatever fermentation you do in the lab scale, you do at the pilot scale or industrial scale with the equipment that you used in the lab scale. Lab scale equipment when you did let us say h by D was filed using the same ratio if you try to do reactor design for the pilot scale or the plant scale what happened it may lead to the severe foaming, right? So, that means, you know, total volume is defined such a way that you know accordingly you keep on changing the small value.

So, such kind of issues has to be carefully considered because this total volume v whatever is there that varies as h D square or D cube it is known depending on the shape of the equipment that you have taken. Escape area for unused gas whatever is there that is we called av. Let us say air is being supplied here there should be escaping which is not being utilized by this liquid that is present in the process, okay? So, that there should be provision for the escaping because this fermenters usually they are closed in general mostly, okay? So, escape area, let us say there would be some opening rupture or maybe the entire diameter is provided as far as opening. So, then that would be varying as D square because it is area so obviously D square some proportionality with D square would be there, right? So, then escape velocity whatever is there that is v which is nothing but the volumetric flow rate of the air per unit volume of the liquid and then V is the total volume of the equipment divided by the av is nothing but the escape area. So, this you calculate then what you can understand?

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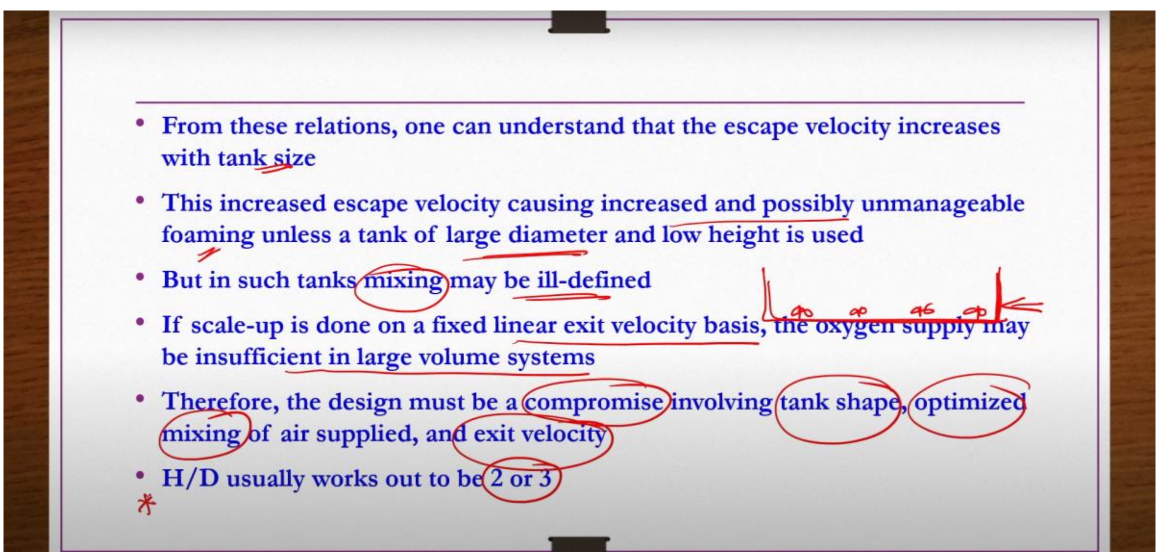

You can understand that it is proportional to D cube by D square or D that means one can understand that the escape velocity increases with the tank size. So, you cannot afford to have the very large escape velocity as well because if you increase the escape velocity then tank size will increase. So, then if the tank size increases your capital cost will increase and then later on operating and then managing problems would also be there. This increased escape velocity causing increased and possibly unmanageable foaming unless a tank of large diameter and low height is used. But in such tanks which kind of tanks if the diameter is very large but height is low something like this then mixing is not proper in general. You have to have the baffles or mixers at different location which is not good again from the proper technical design point of view. So, if you have the large diameter and then low height tanks then you can avoid increased escape velocity. You cannot have the increased escape velocity because if you have increased escape velocity there is a possibility of increased foaming that foaming you may not able to manage that much it will increase. So, you have to have the lower escape velocities for that you need to have the large diameter tanks and then low height tanks or the tanks with the larger diameter and then lower height. So, but if you have such kind of things then what happened mixing may be ill-defined it may not be take place properly like this. If you have columns like this then mixing is properly you can do without any difficult but if you have like this several mixers are required.

These mixers etc. may be easy to design and then do at the lab scale but industrial it is very difficult if they are broken down during the process then entire process would be shut down. If scale up is done on a fixed linear exit velocity basis then oxygen supply may be insufficient in large volume systems. So, design must be a compromise involving tank shape optimized mixing of air supplied and then exit velocity. So, you have to consider all of them and then do a kind of compromise which is best suitable for you to run plant economically. H by D usually works out to be 2 to 3 or the height has to be 2 to 3 times the diameter of the tank if you have such kind of tanks. So, it is better for the fermentation processes.

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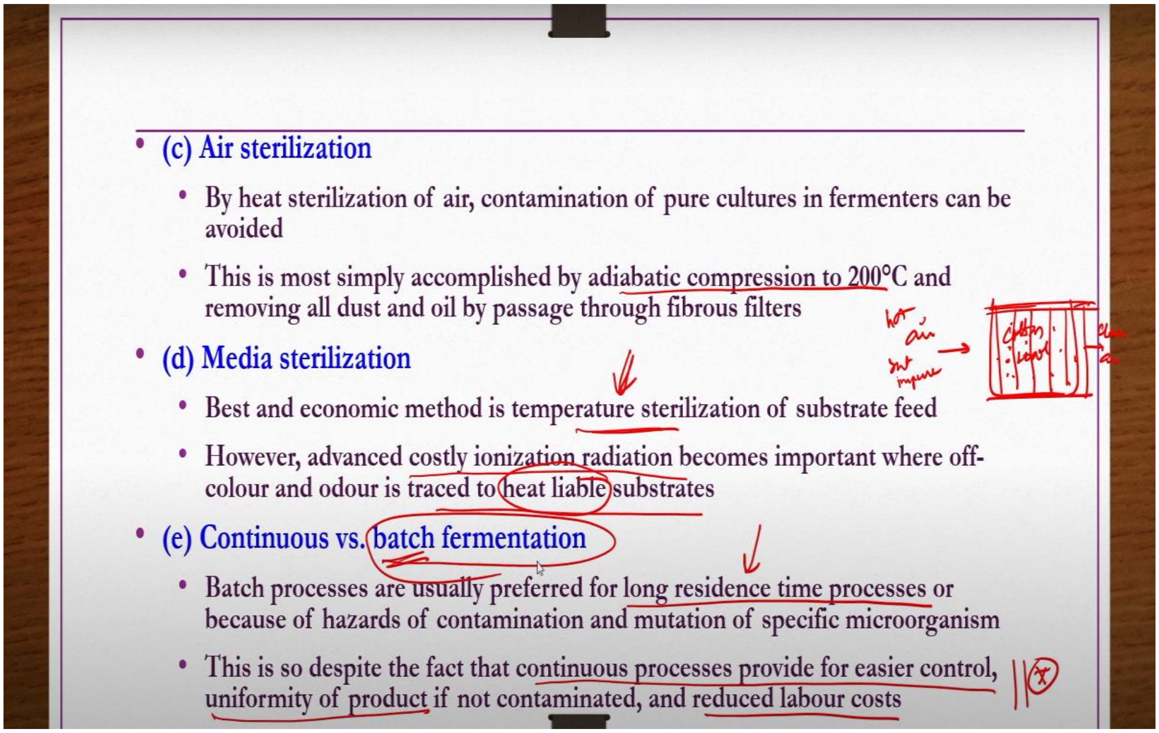

Next one is the air sterilization purification pure system is very much essential in fermentation industry because of the nature of the products as well as the micro vegetative microorganism that are involved they are very sensitive to the impurities. For that reason air not only air media but also the entire equipment that has been used for the fermentation they must be properly sterilized. How do you do the sterilization that also is important. By heat sterilization of air contamination of pure cultures in fermenters can be avoided and then this heating can be accomplished by adiabatic compression to 200 degrees centigrade and then after that air has to pass through filters. The filters are bag filters these are the bag filters like you know maybe a space which is filled with cotton or wool this kind of materials it is filled with and then this air whatever is there hot air but impure.

It may be having some kind of dust oil etc. when you pass through this one so whatever this oil dust particle etc. would be captured by this wool or cotton that is filled there within the filter and then clear or clean air you can get from the other side. This clean and hot air should be used as the sterilized air for the fermentation process. Media sterilization is also very essential and then best economic method is temperature sterilization. Impurities are there in the substrate feed then again microorganisms may be producing different types of chemicals than the desired chemicals.

However, advanced costly ionization radiation becomes important where off color and order is traced to heat level substrates. If the substrate is heat sensitive then you cannot go for this temperature sterilization process then you have to go for the costly ionization radiation processes etc. Continuous versus batch fermentation though continuous process provides the uniformity of the product proper mixing and then better yields etc. Batch fermentation processes are preferred because of a high residence time or high process time of the fermentation processes. Batch processes are usually preferred for long residence time processes or because of the hazards of contamination and mutation of specific microorganisms. This is so despite the fact that continuous process provide for easier control, uniformity of product and then reduced labor cost. Despite of these advantages in continuous process because of this long residence time requirement batch fermentation processes are preferred in general in fermentation industries.

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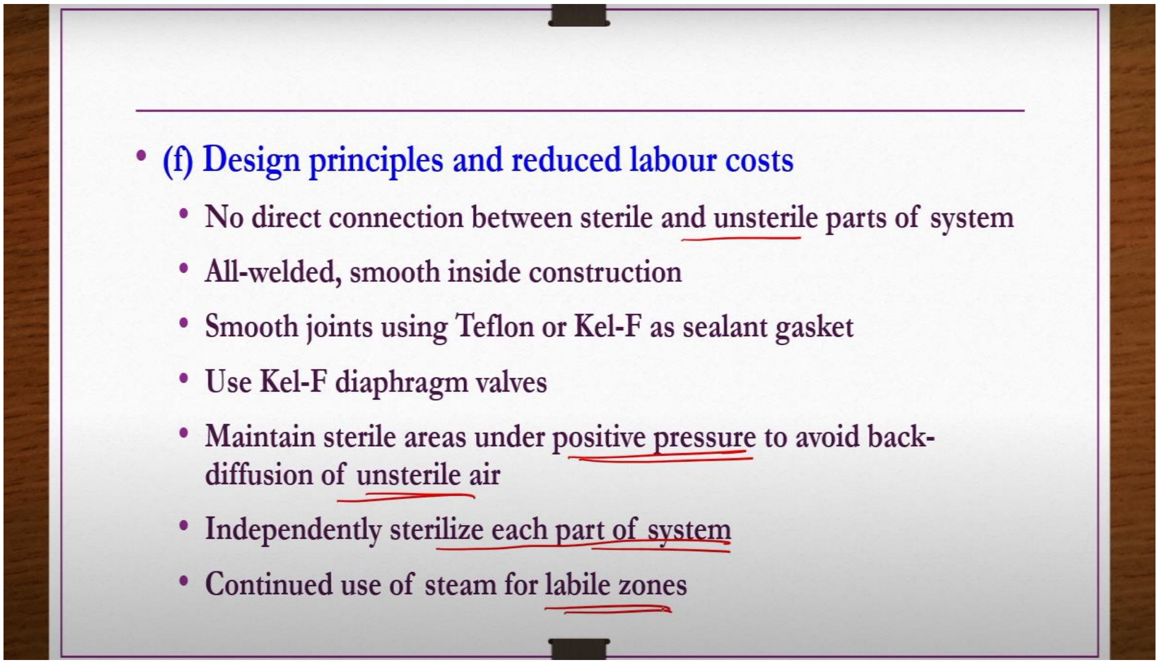

Last engineering problem of common fermentation process or fermentation industries design principles of sterilization operations and reduced labor cost. Sterilization is very essential not only the air media but also the parts of the equipment should also be properly sterilized. Otherwise impurities even small impurities found to be dangerous to the microorganisms because these microorganisms are specific specifically selected for a given operation for a selected chemical production.

So, if they are contaminated you not only producing the different product but also the growth or metabolism rate of these microorganisms may also decrease. So, that is the reason sterilization is very much essential in the fermentation industry. No direct connection between sterile and unsterile parts of the system should be there, they should be separated. They should not be direct contact between sterile and unsterile parts of the system.

All welded smooth inside construction also there, the inside the tank also roughness should not be there. If the roughness is there so then that may not good for the proper growth or propagation of the microorganisms. Smooth joints using Teflon or Kel-F as sealant gasket. Gas should not be leaked or should not be leaking because when the fermentation process takes place so many gases products would also be evaluating within the process and they may be increasing the pressure over the period of the fermentation process. So, because of that pressure there should not be any leakages. So, smooth joints should be there and then using and for that purpose Teflon, Kel-F as sealant gasket should be used.

Use Kel-F diaphragm walls as well. Maintain sterile areas under positive pressure to avoid back diffusion of unsterile air. So, this is another important thing with respect to the design principles of sterilization operations. Then independently sterilize each part of the system. Do not do the sterilization of the all parts you put together in one particular container and do the sterilization. That is not going to give required purification of the system or request sterilization of the entire system may not be possible if you do sterilization of all parts together.

Individual part should be independently sterilized. Continued use of steam for labile zones is recommended. So, these are a few basic general concepts about fermentation processes, different types of fermentation processes, what kind of reactions are possible in general, what are the major engineering problems in general to any given fermentation process those things we have discussed. The next class we will be discussing about specific to product fermentation processes specific to product like ethanol production, citric acid production, etc. We are going to discuss in the next lecture.

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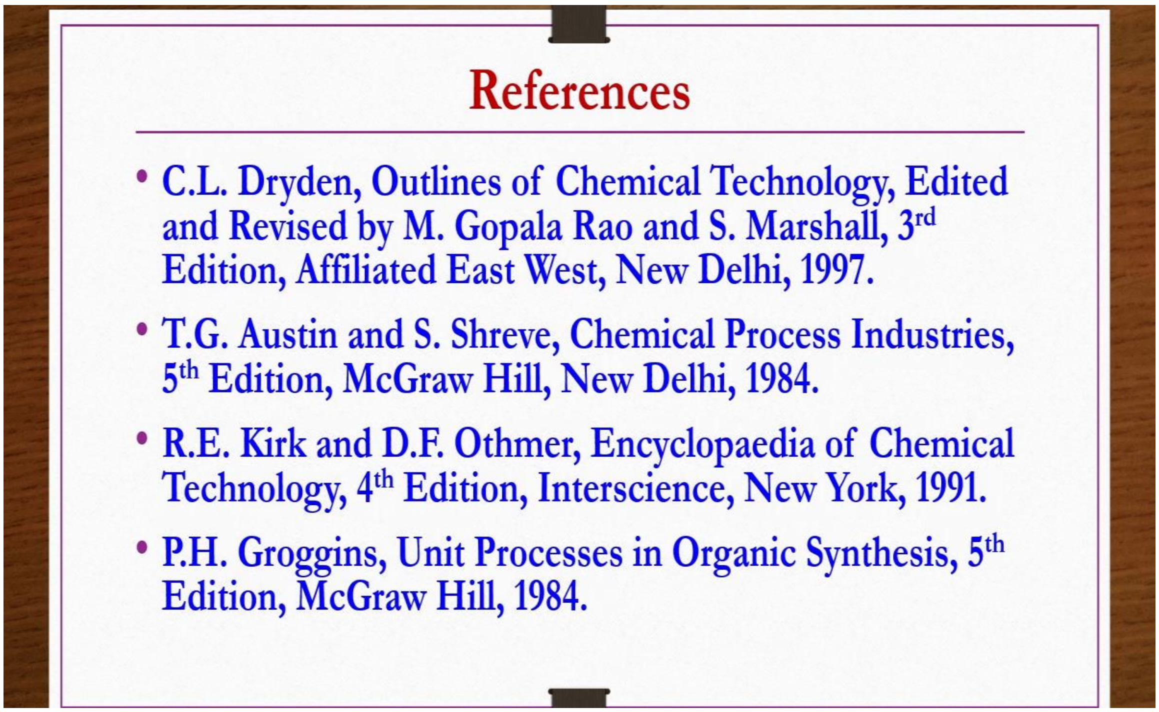

Reference for today's lecture are provided here. However, the entire lecture notes prepared from these two reference books. Thank you.