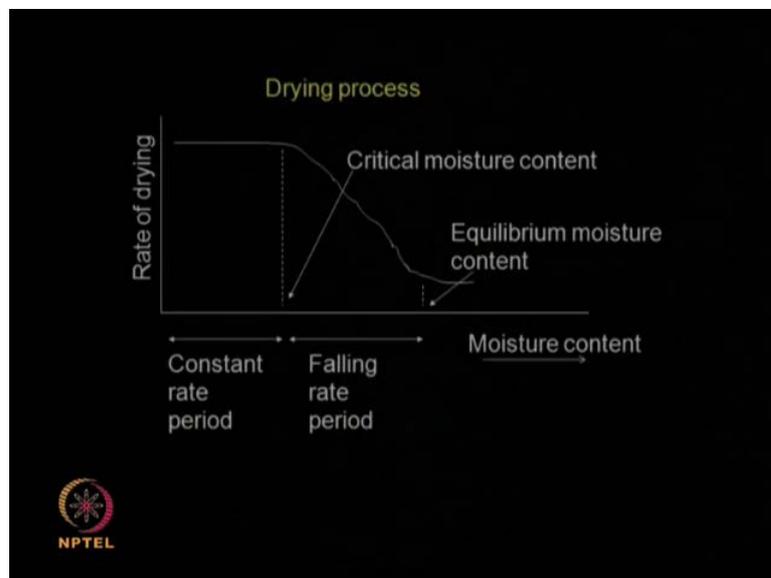


Downstream Processing
Prof. Mukesh Doble
Department of Biotechnology
Indian Institute of Technology, Madras

Lecture - 37
Drying and Distillation

We have been talking about the concept of drying and how important it is the most important picture in the drying process is this one.

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So, in the x axis we have the moisture content and in the y axis we have the rate of drying. So, initially we have plenty of water present on the surface of the solid. So, drying takes place as the liquid starts evaporating or the solvents starts evaporating. So, the drying is constant; that is why this is called a constant rate drying.

So, here the only factor that is limiting is how much heat you are able to supply. So, that the material gets dried that means or the liquid gets vaporized. So, the rate of evaporation is matching with the heat of vaporization, which is also equal to being drying force, which is the vapor pressure of water to the partial pressure of water at that temperature condition.

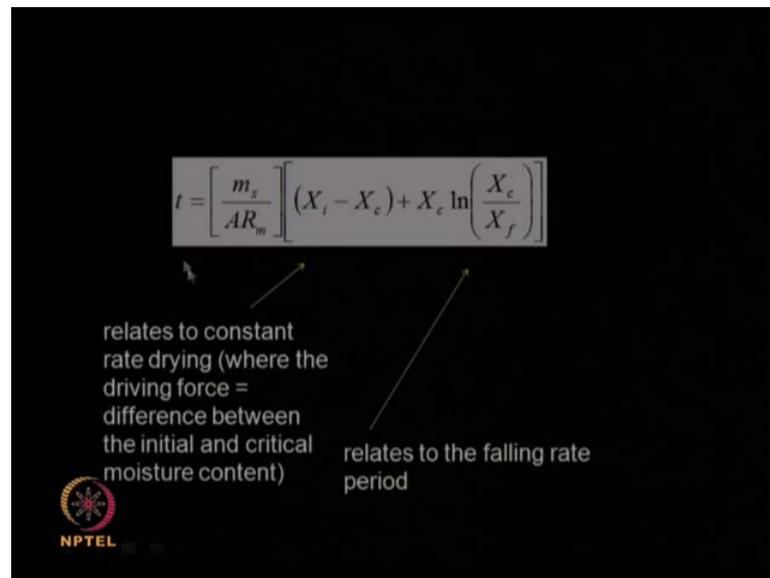
Now, once the water starts drying from the surface, the surface has only less amount of water more water is present in the interstices or in the pores, so there has to be some water, which needs to diffuse out of this pores comes to the surface and then its evaporated. So, what happens that time the rate of drying starts falling down and that is is, what is called falling rate period.

So, as drying process the water which are found inside has to diffuse out and then get evaporated. So, it becomes slower and slower and slower, slower and that is what is called the falling rate period here. So, initially we have a constant rate period and then the rate of drying falls down as a function of time.

Finally, the amount of moisture present in the solid reaches in a equilibrium value with the surrounding air. So, the surrounding air contains certain relative humidity. So, this particular moisture content is called the equilibrium moisture content. Some this equilibrium content is the concentration of water intact material present, which is in equilibrium with the amount of water present in the air at that particular temperature. Here you cannot dry the material below this water concentration, unless you change the relative humidity of the water.

Now, constant rate period and the falling rate period are separated by something called the critical moisture content. That is the moisture content until which the rate of drying is constant. Below which the rate of drying keeps falling down with the time, so that is called the falling rate period. So, we have a constant rate period, we have the falling rate period and in between you have the critical moisture content. Finally, you have the equilibrium moisture content.

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The slide features a black background with a white equation at the top center. Below the equation, there are two lines of text with arrows pointing to parts of the equation. The first line of text points to the term $(X_i - X_c)$ and the second line points to the term $X_c \ln \left(\frac{X_c}{X_f} \right)$. In the bottom left corner, there is a circular logo with a starburst pattern and the text 'NPTEL' below it.

$$t = \left[\frac{m_s}{AR_m} \right] \left[(X_i - X_c) + X_c \ln \left(\frac{X_c}{X_f} \right) \right]$$

relates to constant rate drying (where the driving force = difference between the initial and critical moisture content)

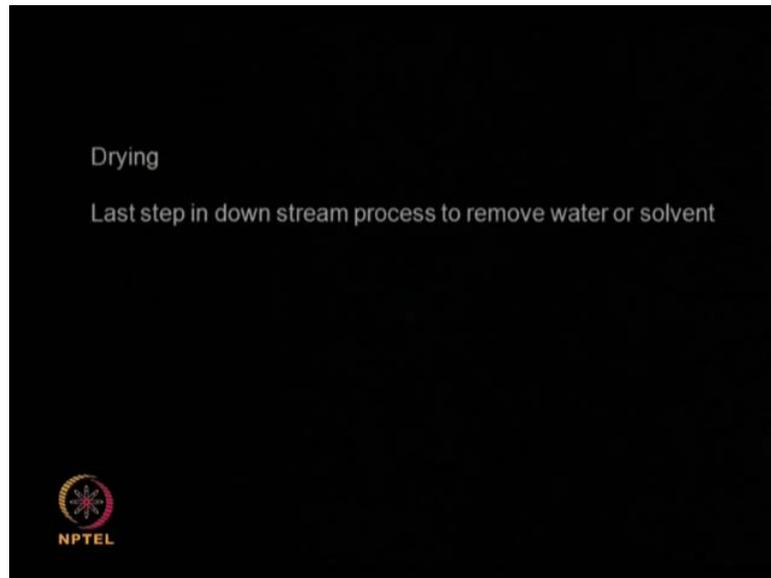
relates to the falling rate period

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Now, the time overall time required for drying a material starting from some initial moisture content to some final moisture content equation will look like that there are two terms. In this equation one is related to constant rate period other is related to the falling rate period. So, this corresponds to the rate of drying where the driving force difference between the initial and the critical moisture content where as this one related to the falling rate period. So, this is how the time required to dry a material can be calculated using this particular equation.

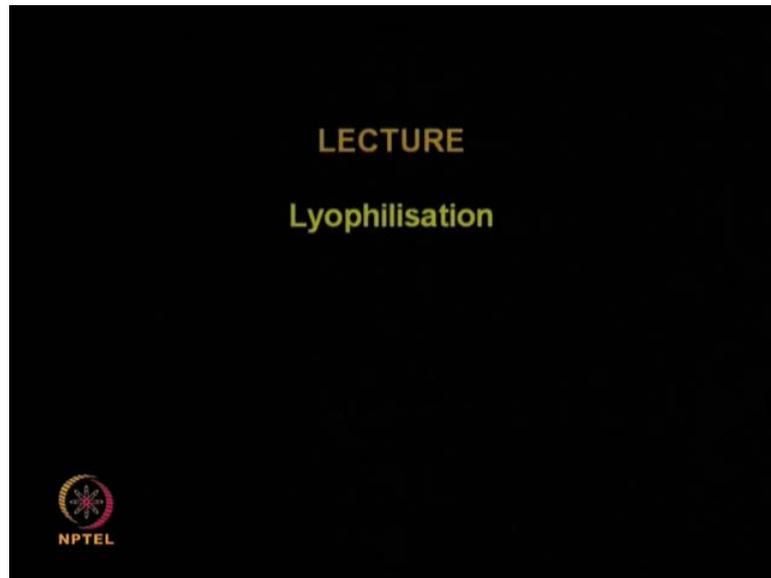
So, very useful equation if we want to design dryers and if we want to find out what will be the batch time for drying and materials starting from some concentration to some other concentration. So, you can see that if I increase the area here the drying time goes down, if the mass m_s is increased drying times goes up and so on actually. So, drying is a very important unit operation which is practiced chemical industry pharmaceutical industry biochemical industry and so on.

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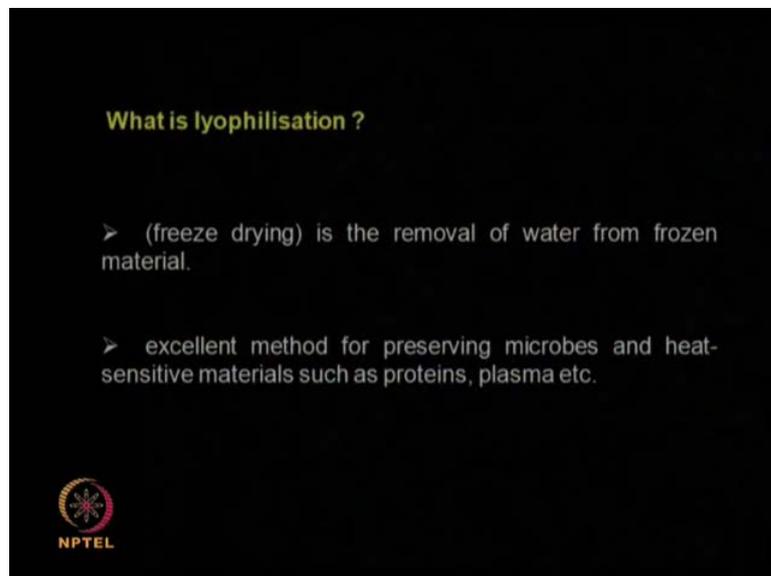
This is generally the last step in the downstream process. So, one important point which we need to keep in mind is the temperature sensitivity of the material with the material is very temperature sensitive. We cannot afford to increase the temperature so we apply vacuum, so that the temperature does not go up to margin. Now, analogous to drying using temperature, we can also remove water or moisture from a solid something called freeze drying or lyophilisation. This is practiced quite a lot in the area of biological systems, because there are highly temperature sensitive. So, that is called the lyophilisation.

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So, let us look at lyophilisation in detail and we look at also what are the parameters that contribute in this particular process.

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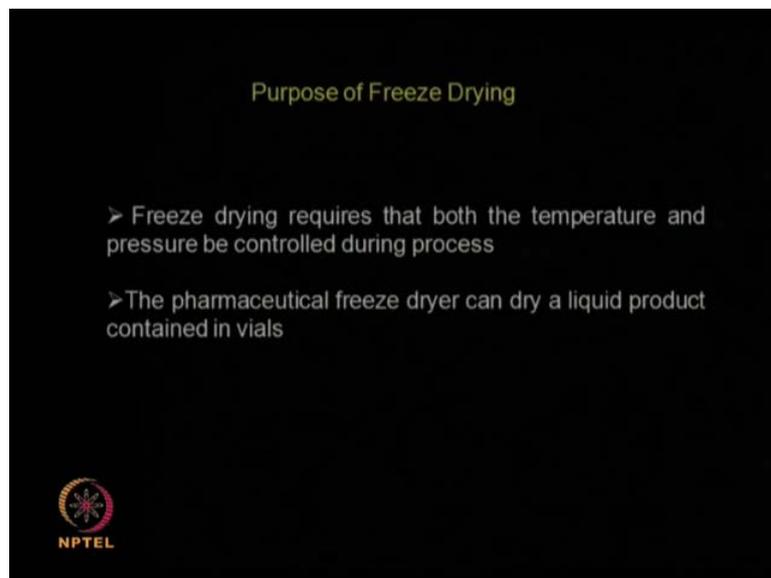


So, what is lyophilisation? It is also called freeze drying that means we are removing water from the frozen material, so if you freeze a material with the water present. So, what happens? The water becomes ices materials also gets frozen and then when you change the temperature or when you change the pressure the ice directly goes into the

vapor. It does not go into the liquid at all, so you select so that you select evaporating condition.

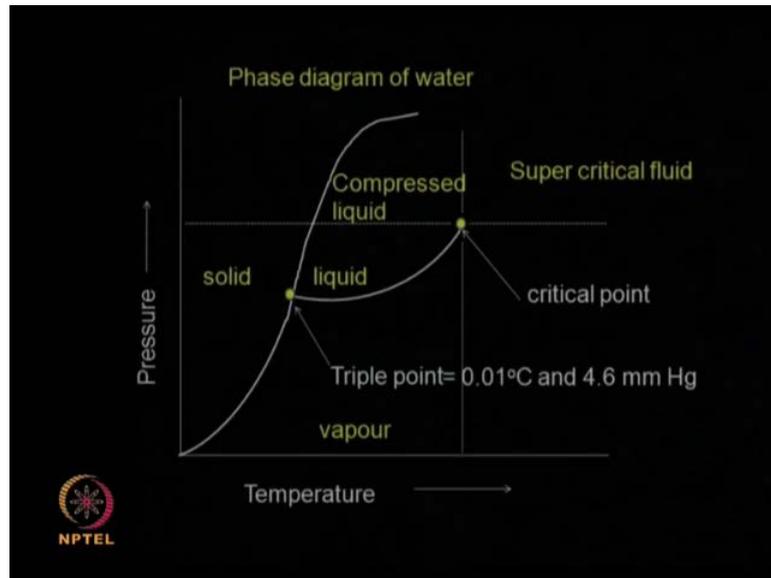
So, that ice directly goes into vapor and it does not go through the liquid phase that is what is called freeze drying. So, what you do in a freeze drying you cool it sufficiently, so that everything gets frozen including the water. Then you change the air pressure or reduce the pressure or increase temperature. So, that ice directly goes into vapor it does not become the liquid, so it is a very good method for preserving micros heat sensitive materials such as proteins plasma. For example, blood plasma I think like doing a freeze drying.

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So, in a freeze drying we control both temperature and pressure. So, for example, if I have some pharmaceutical product in vials, I can use diffuse drying technique to remove the water or moisture present at the same time keep the vials in a sterile condition. So, that is that the advantage of using freeze drying in pharmaceutical setup.

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Now, this is called a phase diagram for water, so in a phase diagram we can see where solid ice is present where liquid water is present and vapor is there water vapor is present so you have all three of them together. So, like you have the solid you have the liquid and we have the vapor.

So, as the pressure is increased you have the solid region and as the temperature increased you have the vapor region. Then in between you have the liquid region, now if you look at this there is something called the triple point where the solid liquid. The vapor meet this is called the triple point this is at 0.01 degree centigrade and 4.6 mm mercury point.

So, if you are evaporating here we have to if you want to move from solid to liquid to vapor like this, whereas if you are operating here, we can see that I can directly move from vapor to solid or from solid to vapor. I do not want to go through the liquid at all.

So, if you are here somewhere and you want to go to solid you have to go through liquid or if you are here from solid you have to go through liquid to vapor. Whereas if you are operating here, you can directly go from vapor to solid from solid to vapor. Now,, there is another point that is called the critical point where the liquid and the vapor meet and this region is called the super critical fluid.

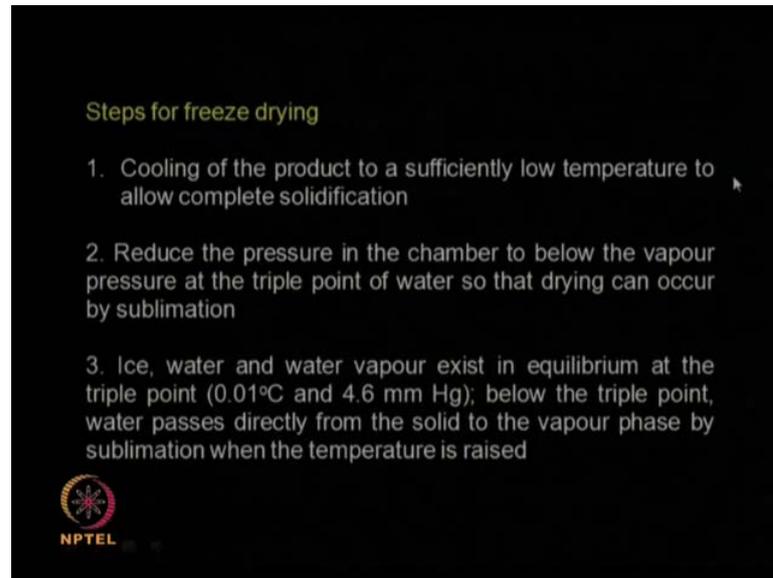
You must have all heard about super critical fluid super critical, C O 2 super critical water and so on actually. You know where the fluid behaves like a liquid or a gas, so it has got both the useful properties of the liquid as well as the gas.

So, super critical carbon dioxide has become very very important and we also talked about it long time back in the extraction process, where super critical carbon dioxide can be used very effectively for extracting natural product metabolites. A useful chemicals from phytochemicals, where you do not need to use high temperature, which may de nature or de activate such sensitive material.

So, super critical fluid region is this where you are operating above the critical point where the liquid and the vapor behaves like a super critical fluid. So, that is super critical fluid where as the triple point here we can move from vapor that is water vapor directly to ice solid ice or we can move from solid ice to vapor. So, if you are operating in this region if you are doing lyophilisation, all you need to do is you reduce the temperature. So, that the ice is formed and then you play around with temperature and pressure.

So, that the ice directly goes into vapor so by doing this alternatively. We can slowly remove whatever water is present to a vapor form, so in this process you are not increasing the temperature unlike drying. So, the material which needs to be dried is completely being operated at low temperature, so it does not get de nature. So, very useful technique especially for proteins especially for plasma and so on.

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Steps for freeze drying

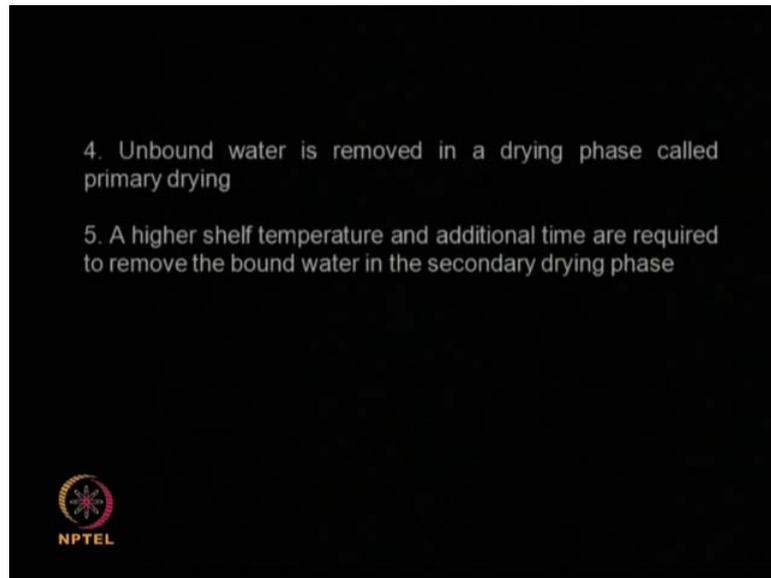
1. Cooling of the product to a sufficiently low temperature to allow complete solidification
2. Reduce the pressure in the chamber to below the vapour pressure at the triple point of water so that drying can occur by sublimation
3. Ice, water and water vapour exist in equilibrium at the triple point (0.01°C and 4.6 mm Hg); below the triple point, water passes directly from the solid to the vapour phase by sublimation when the temperature is raised


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So, what are the various steps in freeze drying? So, what you do is you first cool the product to a sufficiently lower temperature, so by doing that you are completely solidifying or converting the material into a solid form. Then what you do to reduce the pressure in the chamber to below the vapor pressure at the triple point of water. So, that there is sublimation. What is sublimation you are converting solid into vapor, that is what is called sublimation, right? So, you are converting the solid water into vapor water.

So, you what you do you reduce the pressure. So, initially you are reducing the temperature and then later on you are reducing the pressure so that solid ice becomes vapor. As I said that the triple point the ice water and water vapor exist in equilibrium at 0.01 degree centigrade and 4.6 mm mercury. So, below this triple point water passes directly from the solid to the vapor phase that is sublimation takes place, so no problem we do not the ice does not go as water.

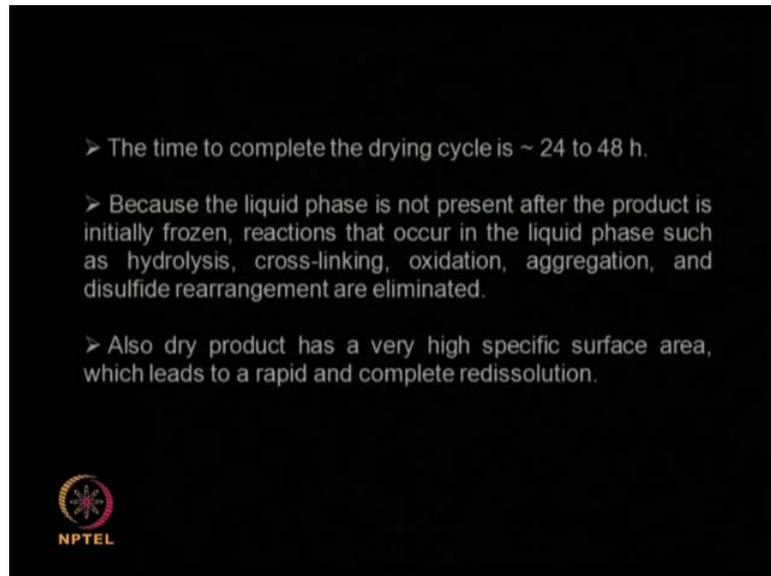
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So, by doing this we are removing all the unbound water, so that is called the primary drying. Now, later on we need to remove the bound water, so what do we do? We slightly raise the temperature and keep the pressure down, so by doing this we are removing the bound water that is called the secondary drying phase.

So, initially we have the primary drying phase where by reducing the pressure we are operating below the triple point so the solid ice goes into vapor. In the second phase, we are keeping the pressure down, but slightly increase in the temperature. So, that a bound water gets removed. So, these are the two steps, so we have the primary drying and we have the secondary drying remove with the unbound and the bound water respectively.

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So, generally in a super critical the time required to complete the drying cycle is about 24 hours even 48 hours laps, sometimes we take more than a day to completely remove of the solid. So, once you do this lyophilisation, there is no water present there is no liquid phase.

So, reactions like hydrolysis cross linking reactions oxidation reactions aggregation of the solid material disulfide rearrangement all these are prevented. Also, when you dry the product completely it has got much surface area for volume, so if you want to re redissolve it into some solvent, then it is very rapid and complete so that is the advantage of lyophilise product.

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Three steps in lyophilisation

1. Freezing. The sample is placed in a freezing vial/flask. The purpose is to completely freeze the sample.
2. Primary drying. Approximately 90% of the total water in the sample (essentially all of the free water and some of the bound water) is removed by sublimation.
3. Secondary drying. Bound water is removed by desorption, resulting in a product that has <1-3% residual water. This step requires 1/3 - 1/2 the time needed for primary drying.

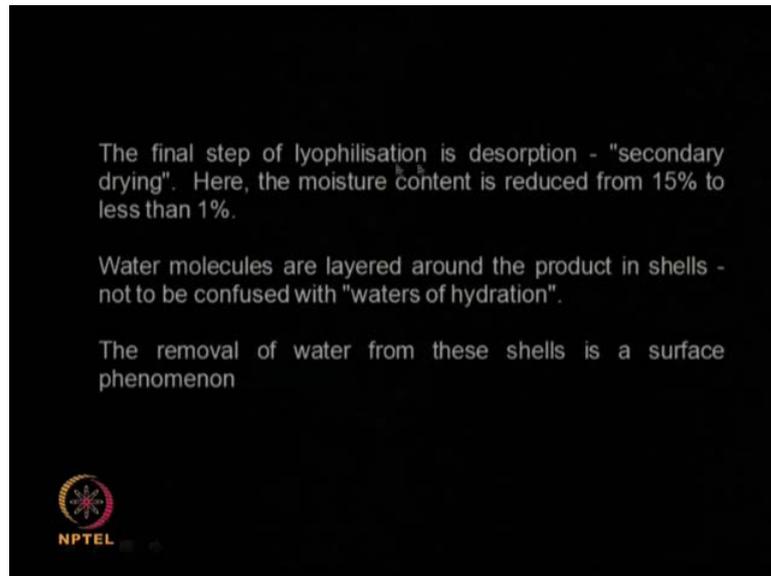


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Now so, the three steps in lyophilisation, we have the freezing sample is placed in placed in a freezing vial or flask. So, in a laboratory situation we take the material in a flask, if you are working in a pharmaceutical industry you take it in a vial. Let it become easier for you to completely seal it, once you have done the freeze drying. Then next step once you have frozen the material what you do? You are by sublimation you are removing the solid material into vapor, so 90 percent of that total water the sample goes away.

So, some of the free water and some of the bound water goes away. Then what do you do? We are now dissolving whatever the water is present by increasing the temperature. So, finally, by doing that you will end up with about 1 to 3 percent residual water, so this step also takes some time it almost 50 percent of the time it is taken for removing the unbound water, so you need some time for that.

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The final step of lyophilisation is desorption - "secondary drying". Here, the moisture content is reduced from 15% to less than 1%.

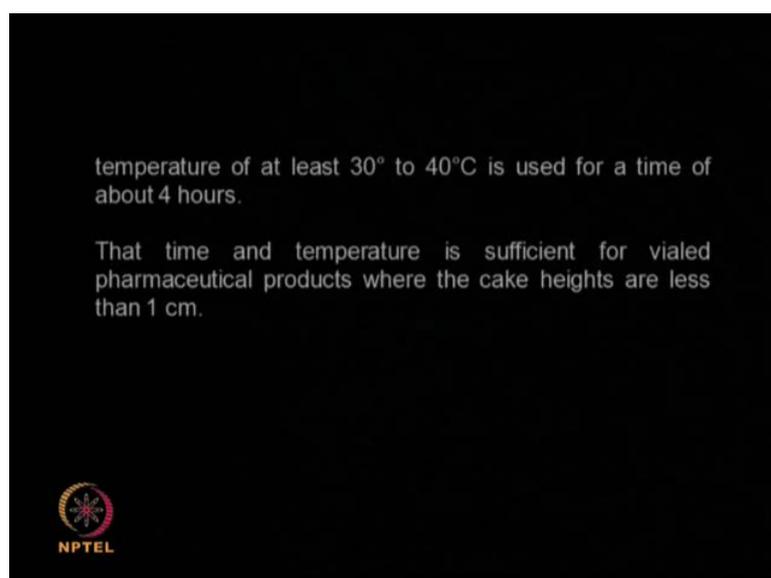
Water molecules are layered around the product in shells - not to be confused with "waters of hydration".

The removal of water from these shells is a surface phenomenon



So, the final step of this lyophilisation. We call it desorption or we call it secondary drying or drying to remove the bound water like that you know. So, you reduce the moisture content almost 1 percent. So, there is a lot of water which is present on the product in the form of shell, so it is a surface phenomenon it is not a water of hydration. But it is a more of a you should not confuse the removal of a bound moisture as water of removal of water of hydration. So, it is more like water present in the form of a shell.

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temperature of at least 30° to 40°C is used for a time of about 4 hours.

That time and temperature is sufficient for vialled pharmaceutical products where the cake heights are less than 1 cm.



So, you have to go up in temperature to about 30 to 40 degrees centigrade and may take about 4 to 5 hours. If you are if you have a vial pharmaceutical product, then you may slowly form ice cake like. So, generally the cake thickness may be of the order of one centimeter.

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Three formats for freeze drying:

1. **Manifold drying**
Drying flasks or ampules are attached to individual ports on a central manifold.

The samples frozen by the shell method, and are quickly attached to the manifold and placed under vacuum to prevent melting.

Room temperature provides heat for the sample.

This method is useful for relatively small volumes.



There are different types of freeze drying one is called the manifold drying.

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Three formats for freeze drying:

1. **Manifold drying**
Drying flasks or ampules are attached to individual ports on a central manifold.

The samples frozen by the shell method, and are quickly attached to the manifold and placed under vacuum to prevent melting.

Room temperature provides heat for the sample.

This method is useful for relatively small volumes.



So, we have a central manifold so you attach a many ampoules or drying flasks to the central manifold. Then the samples are frozen by the shell method first samples are frozen separately. Then they are attached to the manifold and then you are applying the vacuum prevent melting. Then you bring the temperature so there is a room temperature provides the heat.

So, generally this type of method is very good for small volumes, so first drying. I mean first froze freeze all the flasks separately and then they connect it to the manifold. Manifold is placed under vacuum to prevent melting and then you raise the temperature to the room temperature. So, this heat is sufficient to remove the moisture directly the ice goes into vapor.

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Three formats for freeze drying:

1. **Manifold drying**
Drying flasks or ampoules are attached to individual ports on a central manifold.

The samples frozen by the shell method, and are quickly attached to the manifold and placed under vacuum to prevent melting.

Room temperature provides heat for the sample.

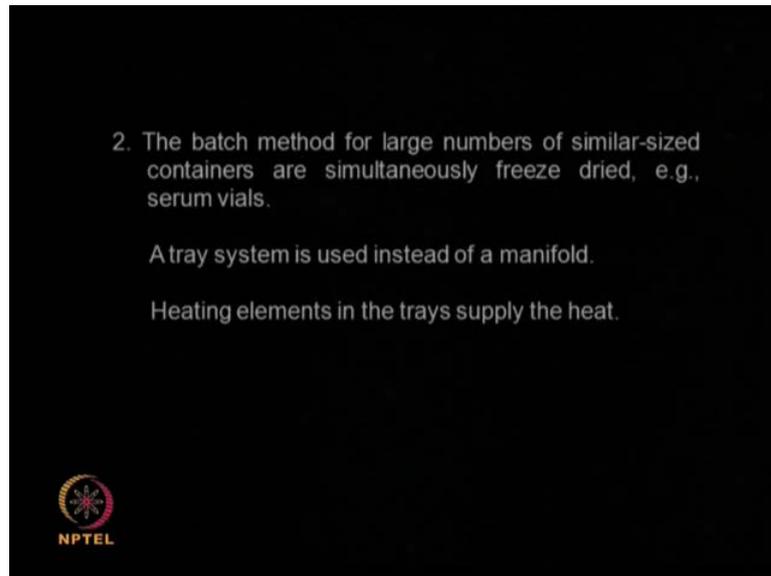
This method is useful for relatively small volumes.



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This is very good for small volumes.

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2. The batch method for large numbers of similar-sized containers are simultaneously freeze dried, e.g., serum vials.

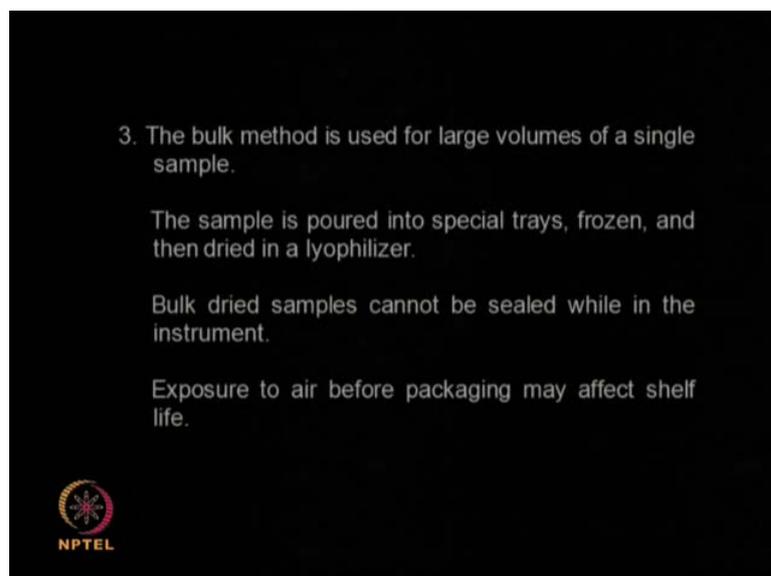
A tray system is used instead of a manifold.

Heating elements in the trays supply the heat.



If you are talking about bigger systems, then we can use a tray type of arrangement. Then they could be heating elements the tray supply the heat. So, we can have similar type of containers you can pool them all freeze it like serum vials and then keep it on the tray. Then you apply the heat and thereby you achieve the drying process.

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3. The bulk method is used for large volumes of a single sample.

The sample is poured into special trays, frozen, and then dried in a lyophilizer.

Bulk dried samples cannot be sealed while in the instrument.

Exposure to air before packaging may affect shelf life.

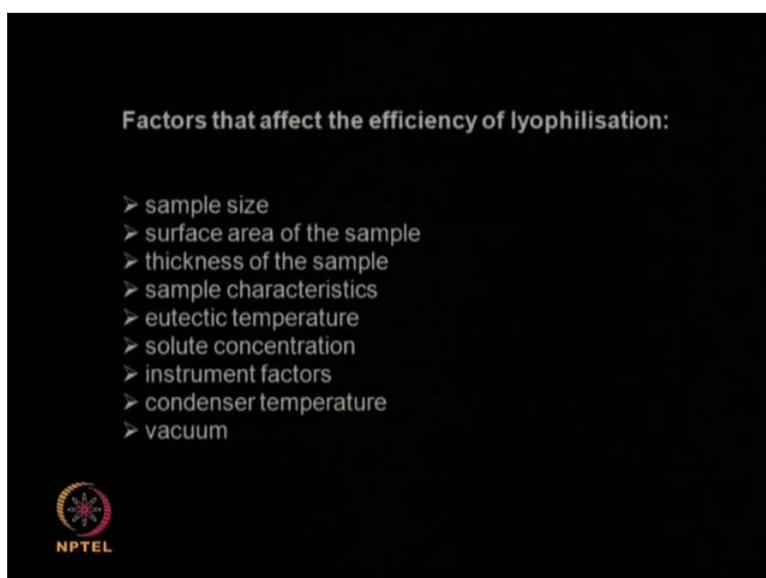


If you have large volumes of a single sample, then what do you do you can pour the material in special trays freeze it and then dried in a lyophilizer. But one this is you cannot take the samples and again seal it separately, because if you are if you are going

to do that and you are exposing it to air sometimes the oxidation may affect the product quality or product stability. So, if you are talking not exposing the material to outside atmosphere the best method is a manifold drying or a vial drying.

So, you take a samples in hundreds of vials and freeze it connect it to a manifold apply a vacuum slightly heat it up. So, all the moisture is removed and then you can seal the vials or flasks. So, that the advantage of that type of setup whereas, in this type you can handle a large quantity of material, but some amount of exposure after lyophilisation is inevitable here.

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So, what are the factors that affects lyophilisation, the sample size, how much material I am handling surface area of the sample? If it is having big area per volume or surface per volume is less thickness of the sample, because as you know the solid ice has to convert into vapor.

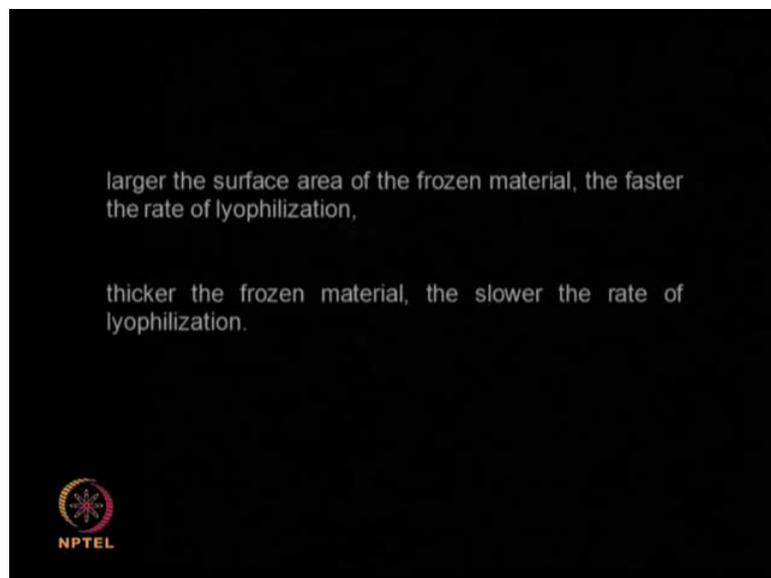
If you have a thick ice formed vapor has to diffuse and go up go out sample characteristics. That means physical properties physical properties viscosity density. So, on eutectic temperature, because what is eutectic temperature we are talking about solid ice and solid material.

So, these two can together combined to form the third blend of product it is very eutectic temperature comes into picture. Because you have ice going into solid you have the

actual material protein or any other chemical that is going to be frozen. So, both of them may dissolve and form an another third phase and that is where eutectic temperature comes into picture solute concentration. How much of solute is present in concentration?

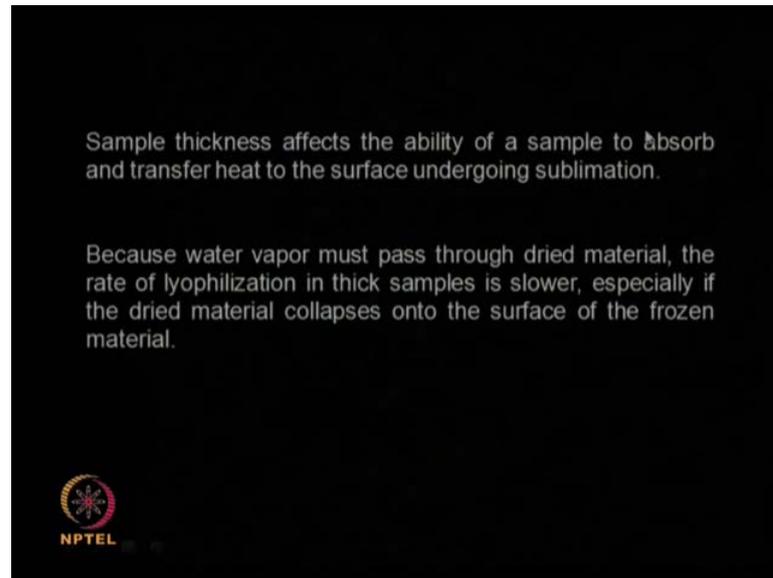
Then the instrument factors, what are the various instruments, which we are using? Then the condenser temperature, we are going into ultimately take out the vapor and condense it again. So, what is the temperature and how much vacuum you are applying? All this factors affect the lyophilisation process.

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So, larger the surface area of the frozen material faster will be the rate of lyophilization, this is obvious. So, if I have large lyophilizer area, then we can do the lyophilization process very fast thicker the frozen material slower the rate of lyophilization, right? Again when you have thick material the vapor that is formed when you apply vacuum and heat it; that vapor has to pass through the thick frozen material before it can be collected in the condenser. So, that process is going to be slow, so thicker the frozen material slower will be the rate of lyophilization.

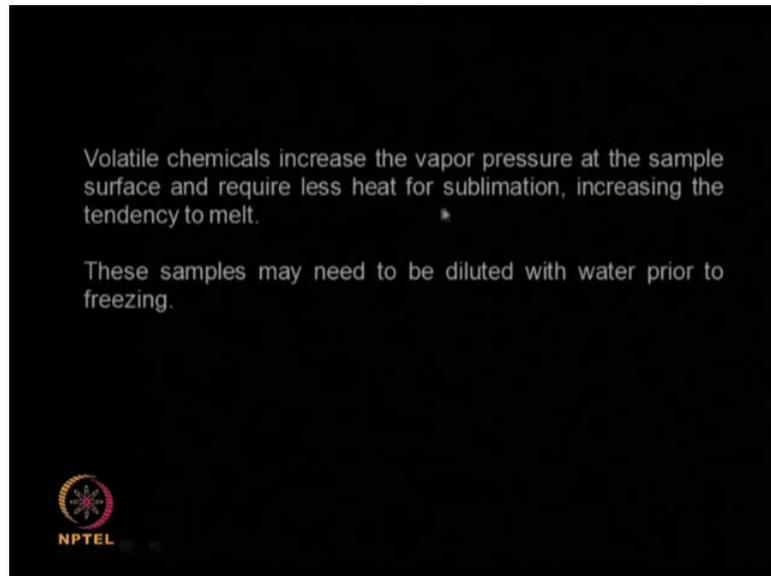
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So, sample thickness affects the ability of a sample to absorb and transfer heat to the surface undergoing sublimation. So, ideally I would like to spread it out on a large pan, so that when the lyophilization is fast the thickness is also less. That is the frozen thickness whereas, if I have a very small container the area for lyophilization decreases.

So, sublimation is slower because the vapor has to diffuse to the thick solid icy material, because the water vapor must pass through the dried material and the rate of lyophilization in thick sample is slower. Especially in the dried material collapses on the surface of the frozen material, suppose the dried material forms a shell like and as it gets dried it may just collapse. Thereby slowing down the diffusion of this vapor out into the vacuum region.

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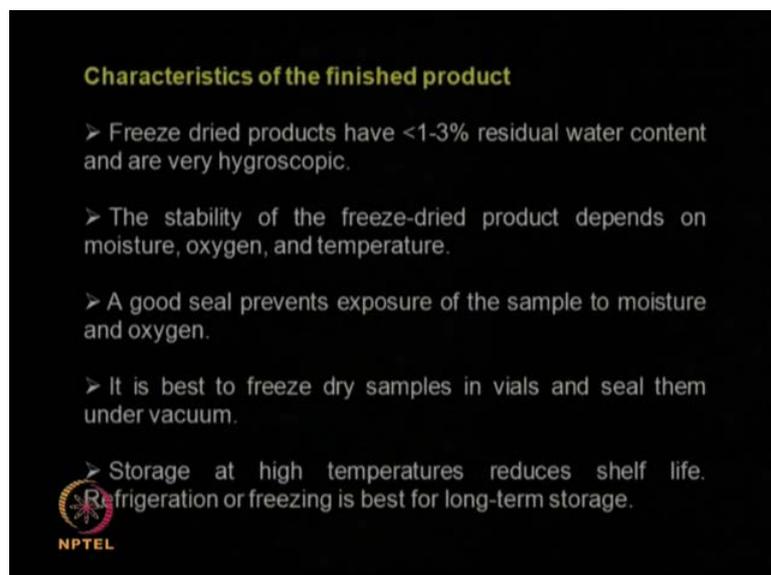
Volatile chemicals increase the vapor pressure at the sample surface and require less heat for sublimation, increasing the tendency to melt.

These samples may need to be diluted with water prior to freezing.



So, here volatile chemicals present then obviously it is going to increase the vapor pressure at the sample surface, so we need to have less heat of sublimation. So, the material is going to melt it is not going to form a frozen solid. If it forms a frozen, then it becomes for you to convert into vapor by applying heat, but if it is forming an ice, then it is not good forming a melted. So, we need to dilute it with water prior freezing, so by having water pour, water. We can form solid ice that is much better, so volatile chemicals always lead to problems in lyophilization.

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Characteristics of the finished product

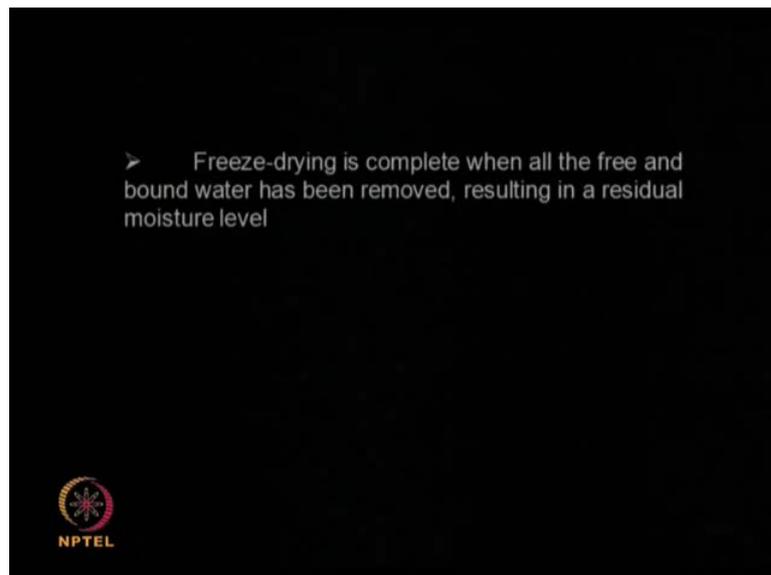
- > Freeze dried products have <1-3% residual water content and are very hygroscopic.
- > The stability of the freeze-dried product depends on moisture, oxygen, and temperature.
- > A good seal prevents exposure of the sample to moisture and oxygen.
- > It is best to freeze dry samples in vials and seal them under vacuum.
- > Storage at high temperatures reduces shelf life. Refrigeration or freezing is best for long-term storage.



So, what are the characteristics of the finished products? Once I have done some lyophilization and the amount of water residual water present may be in the order of 1 to 3 percent. So, the stability of the freeze-dried product it depends on the moisture present oxygen temperature, but if you have if you are freeze drying vials and you have a good sealing system. You are preventing exposure to moisture and oxygen, so it is an ideal to do small sample in vials.

So, we can seal them under vacuum. If you are storing material in high temperature, it will reduce the self life. So, ideally refrigeration or freezing is always good for long-term storage. So, if you want to store blood or plasma this thing is to freeze it or refrigerate it for a long-term storage and like storing it at high temperature.

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So, if you have finished removing all the bound water and there would not be any other water. It will have just very small amount of moisture present, which we call it the equilibrium moisture content, so we can call the freeze-drying being completed.

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Lyophilisation vs. Conventional Drying

- Advantage of lyophilisation is preservation of chemical and biological potency, homogeneity in the final product, and ease of dispensing/metering before final packaging.
- Protection from solution effects and chemical degradation
- Speed and completeness of rehydration compared with dry powder fills (e.g., for injectable penicillin)

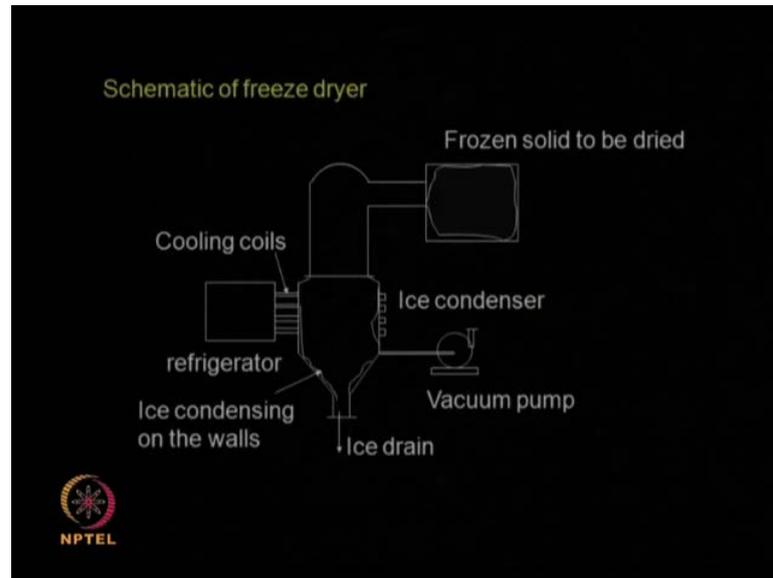


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So, what are the advantages of lyophilisation over conventional drying? So, conventional drying I have been talking about before like, so you apply vacuum, you apply temperature. So, the water vapor evaporates and goes where as in a lyophilization or freeze drying you freeze it. So, that the water becomes ice and then you keep the temperature, so that it does not go through the water phase. But it directly goes into the vapor phase, so you are operating below the critical point. So, advantage of a lyophilization is prevention of chemical and biological potency.

So, preservation of chemical and biological potency you are maintaining a homogeneity of the final product the product will be homogenous. The advantage is it ease of dispensing metering before final package. You are preventing it from chemical degradation. You can rehydrate it very, very easily. For example, if you have dry powder fills like injectable penicillin, it becomes very easy rehydrate it completely without any problems.

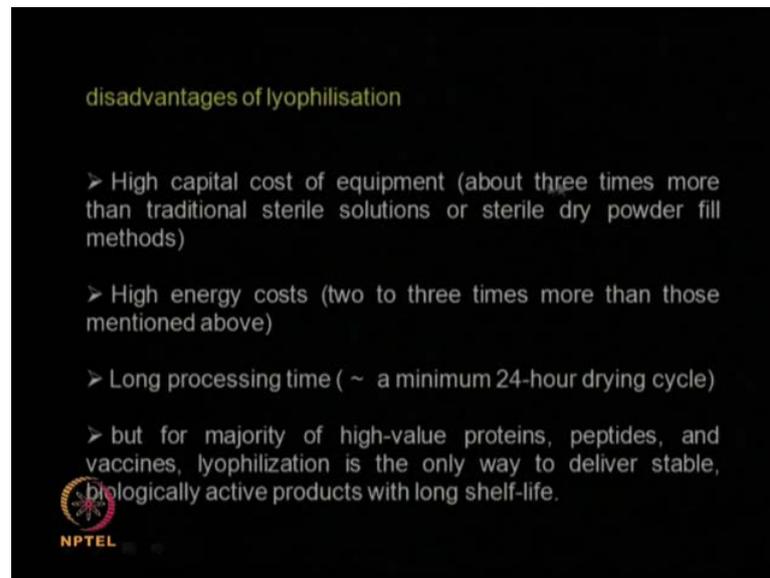
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So, these are the advantages of lyophilization. So, let us look at a schematic of a freeze dryer. How it looks like this is a freeze dryer? It is a large scale industrial scale freeze dryer. So, we have a frozen solid in a big container this to be dried, so we have solid is frozen ice is formed that is water has become ice. Then what do you do, if you have refrigeration system here? You have a vacuum pump here, so ice becomes vapor comes down it condenses here. Again it forms ice in the wall this is giving you the required vacuum. So, you are applying vacuum here and at the same time this temperature is high enough for the ice to directly go into vapor, which is condensed here and collect it here.

Here you have a refrigeration system, which keeps the temperature of the surface low this is how a large scale drying freeze works? So, we have seen an different types of drying the conventional high temperature drying and the lyophilization freeze freeze-drying type system, where you are at a lower temperature. Whereas, in the conventional drying you are drying by applying heat, so this is one of the very important downstream process. It comes almost an end of your downstream where you are reaching the finished products stage.

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disadvantages of lyophilisation

- > High capital cost of equipment (about three times more than traditional sterile solutions or sterile dry powder fill methods)
- > High energy costs (two to three times more than those mentioned above)
- > Long processing time (~ a minimum 24-hour drying cycle)
- > but for majority of high-value proteins, peptides, and vaccines, lyophilization is the only way to deliver stable, biologically active products with long shelf-life.

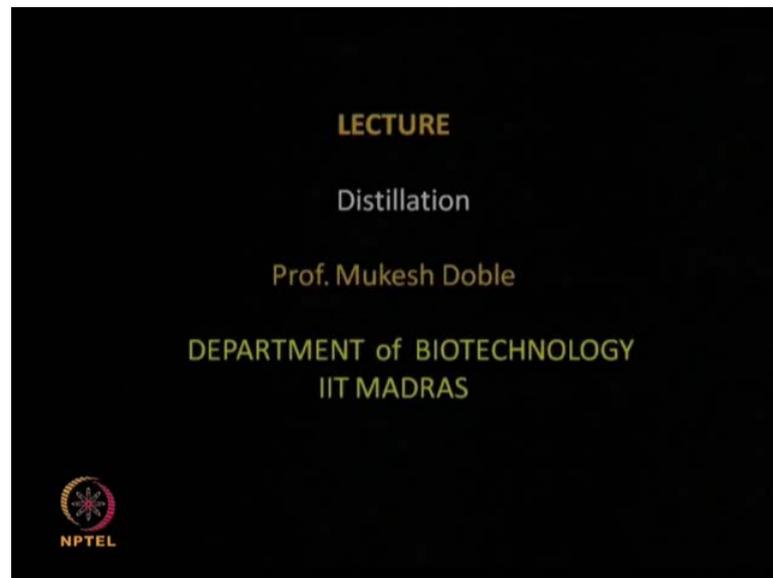
 NPTEL

So, what are the disadvantages of lyophilization? It is pretty expensive capital cost of the equipment is very high, 3 times more than traditional sterile solutions or sterile dry power fill methods, because you need refrigeration system you need a vacuum pump. So, many thing high energy cost 2 to 3 times long processing time you need long time. If I am going for a conventional drying where I am applying vacuum and heating material.

So, that the water becomes vapor I may finish it in few hours, whereas if I am going for a lyophilization or a freeze-drying, where I am freezing the material. Then I am increasing the temperature and changing the temperature and pressure to remove the moisture and so on. It may take 24 to 48 hours.

So, instead of 4 to 5 hours I may go to 24 to 48 hours. So, these are the advantages of a disadvantages of a lyophilisation, but then for high-value of proteins, peptides, vaccines, this is the only way to give stable biologically active products with long shelf-life. There is no other go you have to resort to this type of method, so far we talked about different types of drying; and what are the disadvantage and advantages of different types of drying? So, that completes the another downstream operation. Let us look at another one another downstream operation and this is called the distillation.

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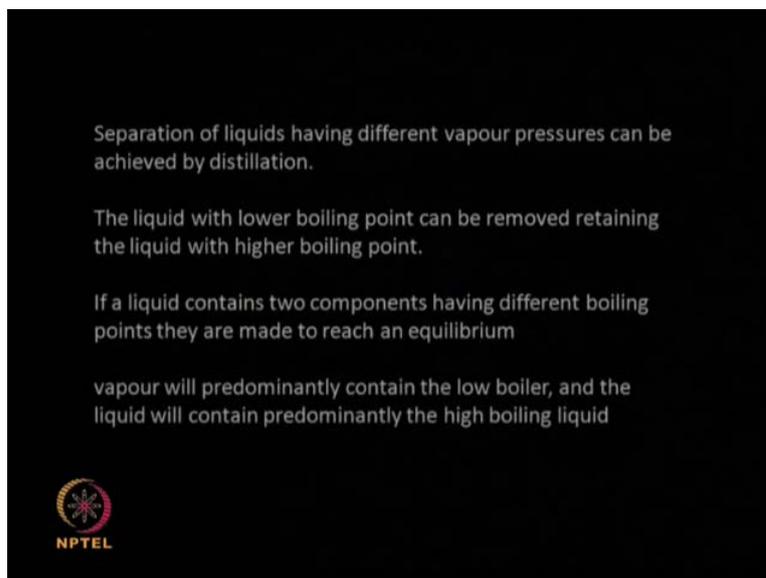


Distillation is also a very important downstream operation; if you want to separate metabolites or solvents mixed self. The most important point here we need to keep in mind is there are not temperature sensitive that means they can withstand higher temperature in chemical engineering chemical processes and chemical manufacturing distillation is widely used.

Because it is very fast quick very efficient and we can end up with high purity material, but in biochemical type of situation because we are worried about the temperature sensitivity of the products. We generally do not resort the distillation, but we do distillation when we want to recycle or recover solvents. For example, in extraction I am using solvents for extraction.

Now, I would like to recover that solvent, so that I can reuse. I cannot throughout all the solvent, so I need to reuse, so I need to recover the solvent. I am doing washing, so in such case chromatography, I am using lots of solvents. Then I would like to recover the solvent. So, that I can reuse this solvent, so in such situation in need to resort distillation there is no other go and it is. As I said it is the most efficient and best method where you can get very pure product. So, distillation has got many advantages especially for recovery of solvents, chromatography recover of solvents from extraction and so on.

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Separation of liquids having different vapour pressures can be achieved by distillation.

The liquid with lower boiling point can be removed retaining the liquid with higher boiling point.

If a liquid contains two components having different boiling points they are made to reach an equilibrium

vapour will predominantly contain the low boiler, and the liquid will contain predominantly the high boiling liquid



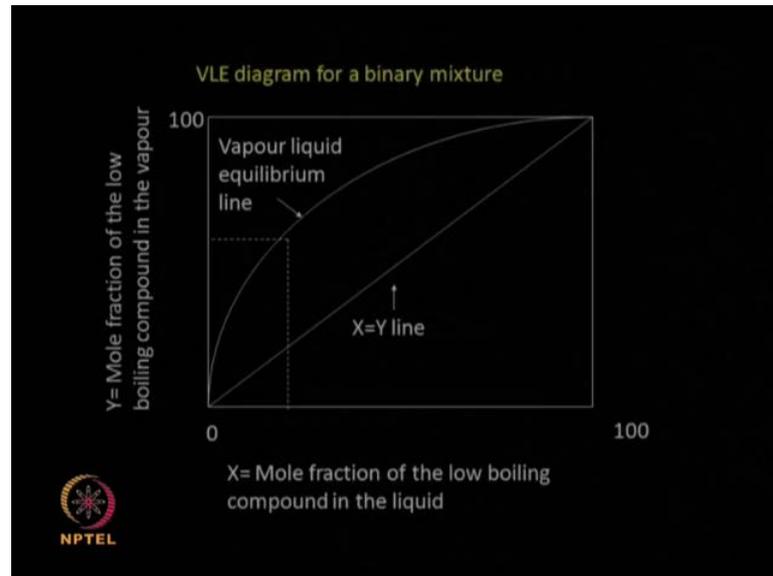
So, it is good if you want to separate liquids having different vapor pressure. So, the principle of operation is based on vapor pressure, so when I heat a mixture of liquid the liquid with lower boiling point goes into the vapor, whereas the liquid with higher boiling point remains in the solution.

By doing this I am creating an equilibrium between the vapor and the liquid phase I am creating in equilibrium between vapor phase and the liquid phase. So, the vapor will predominantly contain the low boiling and the liquid will predominantly contain the high boiling. So, if I for example, I have methanol water, I heat it up there is a vapor formed there is a liquid.

So, when I keep this two in equilibrium and if I analyze the vapor it will have more of methanol. If I analyze the liquid it will have more of water because methanol is lower boiling in water and more methanol will be there in the phase and more water will be in the liquid phase.

So, if condense the vapor I will have more methanol in that vapor. So, I can, I can once again take that mixture again heat it up condense vapor. I will have more methanol methanol and so on actually. So, that is I can recover all the methanol. So, as I said this type of distillation is very, very useful. If you are vacuum on a recovery of solvent from extraction recovery of solvent from chromatography h p l c's and so on actually.

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So, this is called vapor liquid equilibrium diagram for a binary mixture. Suppose, you have two components A and B like ethanol water methanol water. So, this is how a vapor liquid equilibrium diagram VLE, we call it vapor liquid equilibrium diagram for a binary mixture. So, the x axis you draw the mole fraction of the low boiling compound, so x axis 0 to 1 y axis mole fraction of the low boiling component in the in the vapor again 0 to 1. So, you will get a graph like this a curve sometimes may be like this or sometimes the curve may be going concave down.

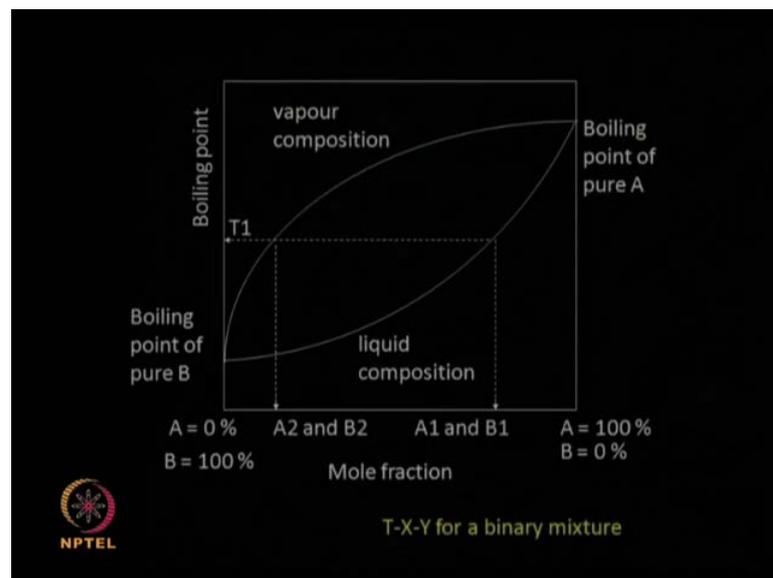
So, you may have a concave or you can have a convex. Now, this is called the x equals to y line, this is called the vapor liquid equilibrium diagram. So, if you take any point in this particular graph this tells you tells you the mole fraction of the low boiling compound in the liquid. This will tell you the mole fraction of the low boiling compound of the vapor. So, obviously because I said that you will have more low boiling component in the vapor than end liquid phase. So, if you take a point and project it to the x and y axis, you will have more of the low boiling component in the vapor phase, than in the liquid phase.

Whereas if you have a graph which is very, very close to this x equal to y line, the amount of component low boiling component in the liquid phase or in the vapor phase will be equal. That means it is called a constant boiling mixture. So, if you have this instead of this graph which is far away from the x equals to y line. If they are very, very

close than x will become equal to y ; that means concentration of the low boiling in the liquid phase or in the vapor phase is equal. So, that is called a constant boiling mixture. So, and ideally if I boil a binary mixture, I would like to have more of the low boiler in the vapor phase and less of the low boiler in the liquid phase.

So, that I can condense the vapor which will have more of the low boiler, whereas if the concentration of the component is equal in both the phases and I am not achieving this separation, so that is called a constant boiling mixture a constant boiling mixture. We cannot separate using a simple description at all. So, we have two components binary and this particular curves tells you the vapor liquid equilibrium for the low boiling. So, obviously because it is a binary 1 minus the other one gives you the concentration for the high boiling. So, generally we do not want to plot for high boiling, we always plot the VLE diagram for the low boiling point.

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Now, there is another picture which brings in not only the mole fraction for the two components, but we also bring in the concept of temperature into this. That is called T X Y diagram that is called a T X Y diagram. There we also bring in the temperature. Now, let us start from this side you know, so we have a is A 0, so B is 100. So, when you go to the other end, we have A equal to 100 and B is equal to 0.

Here on the y axis we have the temperature. So, you will have one graph corresponding to the vapor composition another graph corresponding to the liquid composition. So, here this corresponds to the boiling point for pure B.

This corresponds to the boiling for pure A, because here you have 100 percent A, correct? Here you have the 100 percent A, here you have the 100 percent B. So, this temperature corresponds to boiling point of pure B this corresponds to the boiling point of pure A. So, you can have the other way also that means in this particular picture.

We are showing that boiling point of pure A is higher than boiling point of pure B. But you can have another situation where the boiling point of pure A could be lower boiling point of pure B could be higher. Now, this graph corresponds to vapor this corresponds to the liquid composition.

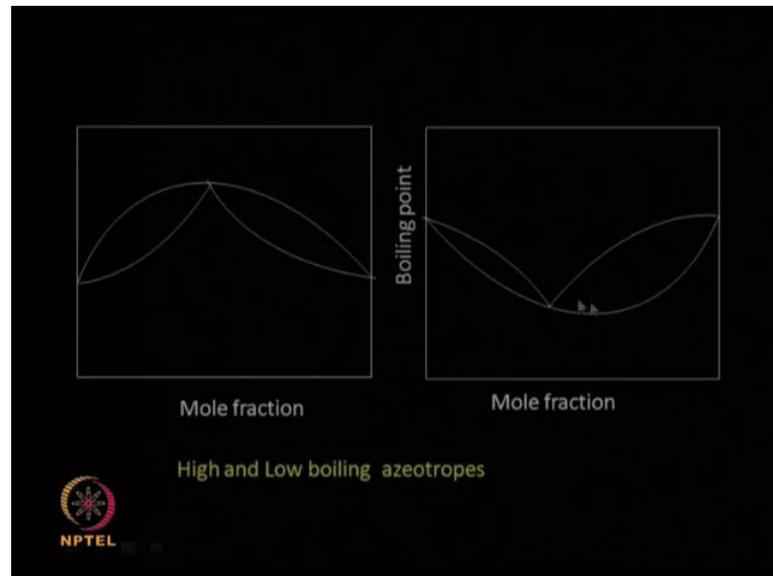
This is called a T X Y binary diagram. So, if you take one point here, so this is at a temperature T 1 and then you project it down and then go again to the liquid. Then project it down, so what does this mean? At a temperature T 1 there vapor will have A 2 percent of the species here A and B two percent of the species B, whereas the liquid will have A 1 percent of species A and B 1 percent of species.

Here, boiling point of A is higher, so obviously A should be more in the liquid and A should be less in the vapor, correct? Boiling point of B is less than A, so the vapor should have more B and the liquid should have less B. Because B 2 will be greater than B 1 and A 1 will be greater than A 2, so you see if you have a diagram like this, T X Y diagram then at any temperature all have to do is to draw lines horizontal. I can tell what will be the composition of A and B in liquid phase, what will be the composition of A and B in the vapor phase? So, this is also useful diagram.

Whereas if you have a VLE diagram, it does not bring in any temperature aspect into it, but it just brings in the compositions just in the compositions of A and B in the vapor and liquid species. So, as I said in this particular figure, we are saying that the boiling point of A is higher. So, A is a heavy material and boiling point of B is lower, so B is a lite material. So, more B is always found in the vapor, but as more A is always found in the liquid, in this particular figure. So, you can have a situation like this, so you can have this

up and this down. So, in that situation we can say B is a higher boiler and A is a lower boiler.

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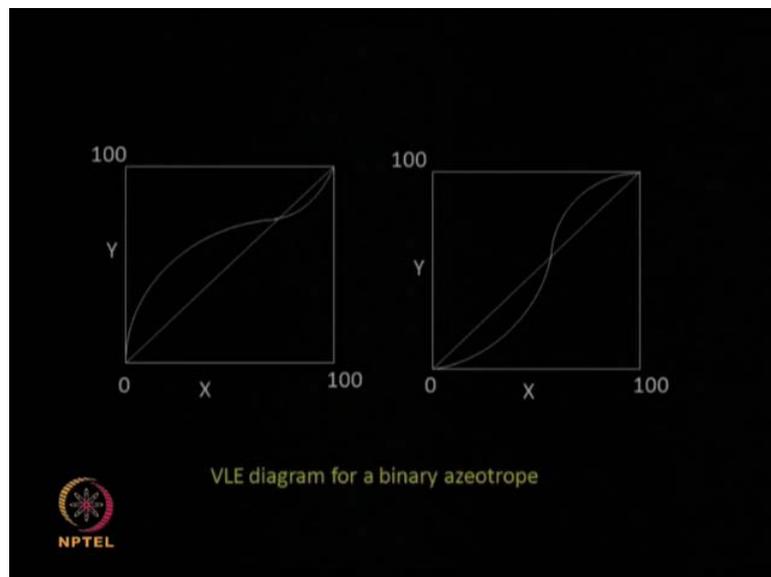


Now, this same figure you can have different types of combination you know? You can have the vapor like this, whereas the liquid may be going like this. You may have the liquid like this, vapor may be going up like this. So, if you look here or if you look here, the concentration in the vapor phase and in the liquid phase are the same. I some time back mentioned something, if they are same they are called constant boiling mixture or they are called azeotropes. That is the name for azeotropes. So, we have constant boiling mixture that is an azeotrope, so this is a high boiling azeotrope, this in an low boiling azeotrope.

If you see the boiling point of the mixture here is higher than the individual boiling point and the concentration in the vapor phase and the liquid phase will be same. Here the boiling point of the azeotrope is lower than the individual component pure component. So, that is why it is called an low boiling azeotrope. Again the concentration of this mixture in the vapor and in the liquid phase are same. So, we cannot separate out this type of binary system. They have a constant boiling region here. So, what do you do if you have azeotrope?

There are different methods, you sometimes change the vacuum and pressure conditions, so that azeotrope may go or you sometimes you add a third component, so that it breaks the azeotrope. Now, a days we are resorting to even a membrane type of situations where we can break azeotrope, because membranes do not work based on vapor pressure membrane just work based on either size or molecular weight solubility and so on. So, there are proactive operation membranes, which we talked about long time back where we can use that type of membranes for breaking azeotrope situations.

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So, how does azeotrope look in VLE diagram, the vapor liquid equilibrium diagram? So, the azeotropes will look like that x and y , so you may have instead of graph going all the time above the x equal to y line or all the time below the x equal to y line, it will just cut at some point. If this graph all the time goes above, no problem, if it goes all the time below, no problem, but if it goes like this. Then at this place, we have the composition of the low boiler in the vapor and the liquid are equal, because this is x equal to y line, similarly, here it will be x equal to y . So, it is called a constant boiling azeotrope.

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So, if you have the VLE diagram like this or if you have the T X Y diagram like this for a binary system you can say they are having a they are azeotrope. So, they cannot be separated by normal methods at all.

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Column may be

- Tray
- Plate
- Packed

In the bottom left corner, there is a circular logo with a star and the text 'NPTEL'.

There are different types of distillation columns, we can use you know they are called a tray columns plate columns packed columns. So, they can have packed material inside the distillation column. They can have plate type of material or even we can have trays type so all this help in mixing the vapor and the liquid together bringing them in close

contact to each other. Thereby you can get a better separation so these are the main advantages of that.

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An ideal mixture is one which obeys Raoult's law

mixture of hexane and heptane,
benzene and methylbenzene
propan-1-ol and propan-2-ol.

The Raoult's law states that the partial vapour pressure of a component in a mixture = vapour pressure of the pure component at that temperature \times its mole fraction in the mixture.



So, if you have a mixture two components an ideal mixture is the one which obeys Raoult's law. So, like hexane and heptane benzene and methylbenzene propan 1 ol and propan 2 ol, so they are called ideal. So, they all obey the Raoult's law state? So, what it says is the partial vapor pressure of a component in a mixture is equal to vapor pressure of the pure component at that temperature into mole fraction in the mixture, okay?

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For an ideal binary system

$$p_A = X_A P_A^\circ$$
$$p_B = X_B P_B^\circ$$

p_A and p_B partial vapour pressures of component A and B respectively.

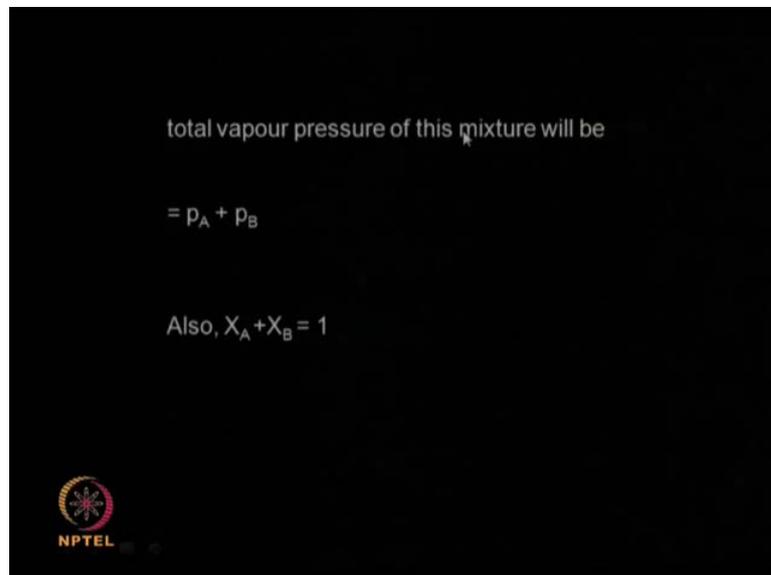
X_A and X_B are the mole fractions of component A and B respectively.

P_A° and P_B° are the pure component vapour pressures of A and B respectively



So, if you have a binary system the partial pressure of A is a vapor pressure of the pure component into mole fraction of that component present in the binary mixture. So, we need partial pressure for B will be equal to pure component vapor pressure of B multiplied by the mole fraction of B present in that. So, this is a very important law because it tells you that if partial pressure exerted by A component is a function of the mole fraction in that mixture binary mixture as well as its vapor pressure. So, if the mole fraction is high the partial pressure is high if the vapor pressure is high, then the partial pressure is also high.

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total vapour pressure of this mixture will be

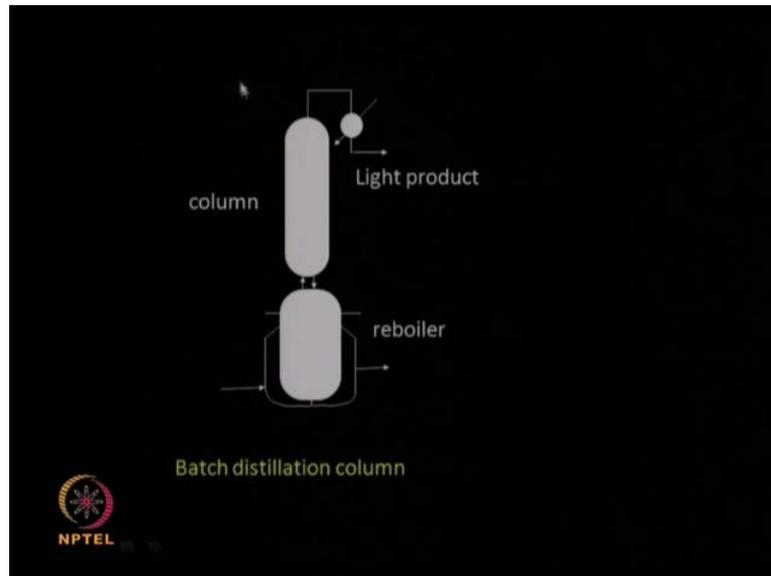
$$= p_A + p_B$$

Also, $X_A + X_B = 1$



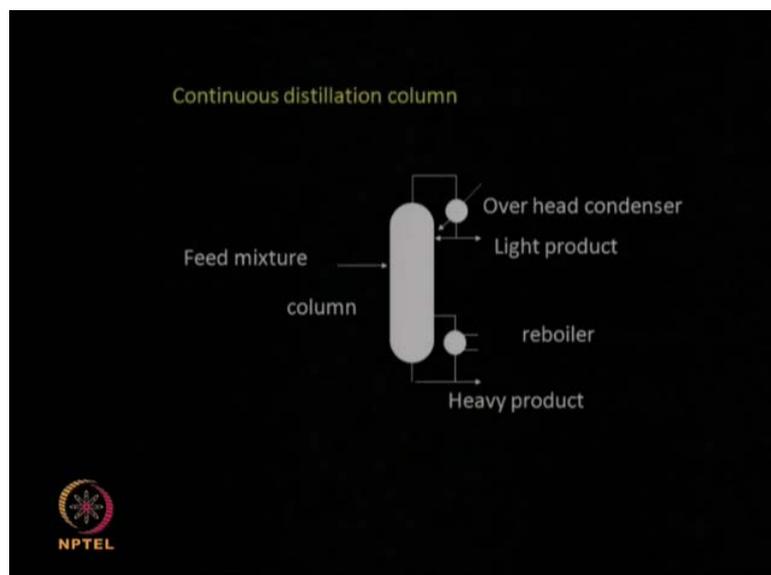
Now, at the same time the total vapor pressure of this mixture will be equal to P_A plus P_B , because P_A is the partial pressure offered by A and P_B is the partial pressure offered by B . So P_A plus P_B is equal to total vapor pressure, so if you are talking about operating at atmospheric pressure, so P_A plus P_B will be equal to atmospheric pressure and also x_A plus x_B . That is mole fraction of A plus mole fraction of B is equal to 1, if it is a binary system obviously this also should be true, okay? So, this Raoult's law tells that, if I know properties of 1, I can calculate what will be the partial pressure of that particular solute?

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So, this is a typical batch distillation column. So, what do we do? We charge material in a reboiler and then we heat it up. So, vapor travels up and then lighter product keeps coming up it gets condensed. It gets revolt sometimes, there is a lighter gets condensed here they may come down as a liquid vaporizes. So, this is a column we call it a column it can be a packed material inside or it can be any type of material inside, which brings in a good and mixing between the A liquid. That is coming down and the vapor that is raising.

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Continuous distillation column, so as the name implies continuously you are feeding some mixture and the heavy material comes down it is heated up as a vapor. So, it raises the vapors gets condensed and then the light product is removed part of the condense is sent back that called the reflux. So, the liquid travels down the vapor travels up, so by this particular operation what do we do we are bring the liquid and the vapor in contact with each other, so by bringing in this particular contact we are achieving the movement of the vapor and into the liquid phase.

That means movement of the low boiling that is present in the vapor to raise and movement of the heavy material to come down to the column. So, by doing this operation we will have more of the heavy's here that means high boiling material. We will have more of the light material here that is the low boiling material. So, we can play around the reflects and achieve very good separation, but then if we reflects too much of the vapor down into the column. We are slowing down our distillation, we are increasing the energy requirements and so on actually.

Whereas if I reduce the reflects, then my separation efficiency goes down. So, I have to keep playing with the both these factors, so that I achieve good separation and at the same time my energy cost does not go up. So, that is where we play around with the reflects. We can have different types of packing materials inside, like I mentioned before.

We can have tray column, we can have packed column and we can have seen plates different type of plate. So, we can bring in a good mixing between the vapor that is raising and the liquid that is falling. So, that the efficiency of separation is also enhanced. So, these are different ways by which we can bring in a purification and recovery of a solvents or other liquids, which we want to recycle it back into the process.

So, distillation is a very useful technique to practice especially as I said in a chromatography for recovery of the solvent, which we use in the continuous phase or in the extraction process. If you are interested in recycling, the solvent which we use for extraction. So, you need to understand, how the distillation system works and distillation has been there in chemical engineering for almost 70 80 years. So, the technology is well established, so it is a easily and quickly adapted in the bio chemical industries as well without adding any extra research effect into it.

As I said if you are handling thermally labile material, then obviously distillation cannot be resorted to because when you are operating at higher temperature. Then the material gets a either deactivator or becomes a become a (()) type of product. So, having talked about distillation having talked about drying lyophilization, we will in the next class we will see, what are the various types of downstream that are still pending?