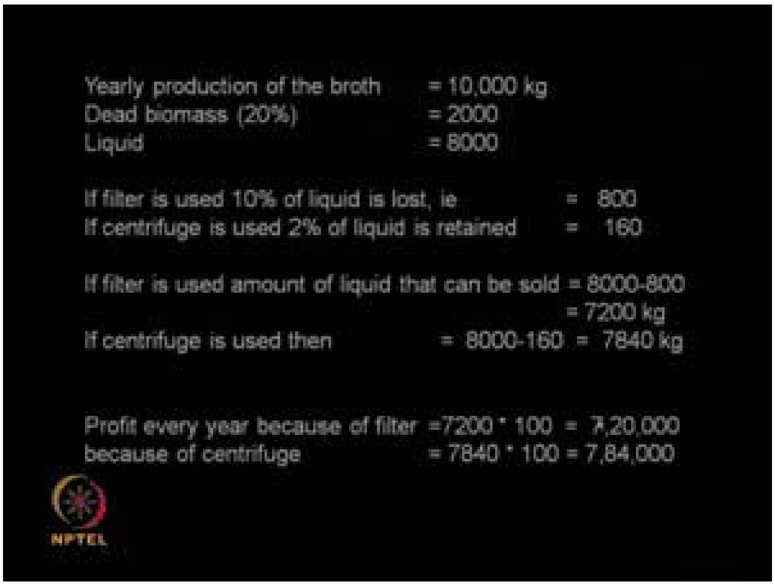
Downstream Processing

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

Lecture - 4
Costing (Continued), Physical And Chemical Principles In Downs stream

(Refer Slide Time: 00:21)



Previous class, I introduced something called net present value and cash flow. And I also gave an example how to make use of this particular concept in making a decision. It was related to a filter and a centrifuge; you can use a filter for removing the solid or you can use a centrifuge for removing the solid. Centrifuge of course is a very advantageous because it retains less amount of liquid, whereas filter will retain more amount of liquid. So, if liquid is your desired product then if you use a filter you will lose 800 kg of the liquid. And if you use a centrifuge you lose 169 kg of the liquid. So, profit every year because of filter will be 7.2 lakhs and profit every year, because of the centrifuge will be 7.84 lakhs, because you get more liquid when you use a centrifuge. So, you make more profit because liquid is your final product.

(Refer Slide Time: 01:13)

		YEAR				
		0	1	2	3	4
Purchase	Filter	-100000				
	Centrifuge	-150000				
AMC	Filter	-158493	-50000	-50000	-50000	-50000
	Centrifuge	-253589	-80000	-80000	-80000	-80000
Profit	Filter	2282303	720000	720000	720000	720000
	Centrifuge	2485175	784000	784000	784000	784000
DCF	Filter	2023810				
	Centrifuge	2081585				

Centrifuge is advantageous (= 2081585 – 2023810 = 57,775)

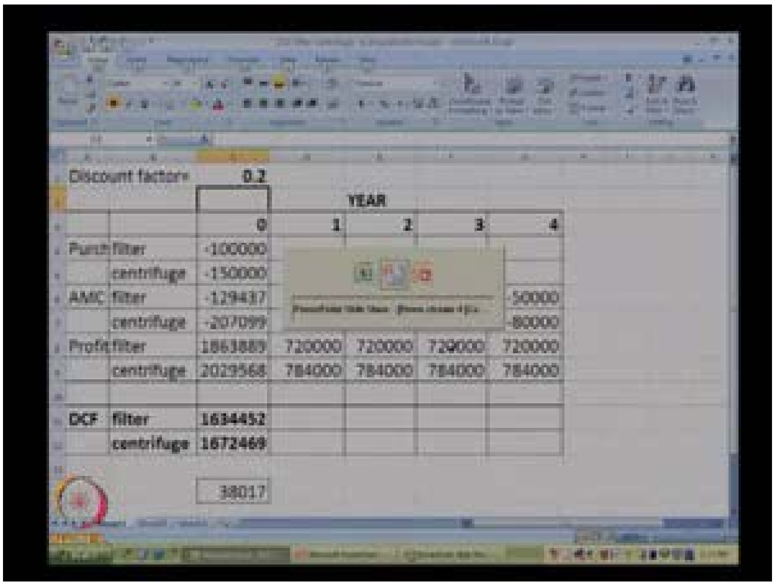
So, I showed you this same table last class if you are purchasing a filter it is 1 lakh and if you are purchasing a centrifuge it is 1.54s lakh. We put a negative term here because we are spending when we purchase the item. And we will put a positive term if it is a profit or if the cash is coming to us. It will be a negative if the cash is going away from us. Now, you have the annual maintenance contract filter will be 50000 rupees every year and the centrifuge will be 80000 rupees every year. That means, we have to spend more in maintaining the centrifuge every year. So, what happens if you look at the net present value for each of these 50000? That means, 50000 divided by 1.1 where this 0.1 comes because of the money value. And the this one the second years will be 50000 divided by 1.1 raise to the power 2; and the third year will be 50000 divided by 1.1 raise to the power 3, and fourth year will be 50000 divided by 1.1 raise to the power 4.

So, if you add up all these you will end up with this particular number, understand. So, it is not exactly 50000 into 4; 50000 into 4 will be 2 lakhs but actually the net present value for the AMC is only 1.58493, understand. So, that comes because the value of the money which you have in the first year is much less than the value of the money you have it today. Now, if you look at the centrifuge same thing your AMC is 80000 every year and if you calculate the net present value by dividing this 80000 by 1.1; this 80000 by 1.1 square 1 square; this 80000 by 1.1 cube; and this 80000 divided by 1.1 raise to power. And if you add up all of them you will end up with 253589. So, it is not exactly 320000; if you actually multiply you will get that. Now, the profit for filter as I showed in the previous slide every year you will get a 7.2 lakhs profit and because of the centrifuge every year you will get 7.84 lakhs.

But when again you calculate the net present value the cash flow then these are the numbers you get. So, you take all the positives and you take all the negatives together and subtract. So, if you have a filter you are going to have this much amount of profit. That means 2023810; if you have a centrifuge the amount of profit you are going to make is 2081585. So, of course centrifuge is better than the filter because total amount of profit in the 4 years the cash flow. And you subtract the annual maintenance contract and you subtract the purchase pie price as of today that is year 0; this is the difference we get.

So, that means you will make a profit of 57775; if you have a centrifuge better than a filter. So, it is a advantageous to have a centrifuge. So, you see but although there are the cost of the centrifuge is more the AMC is more; you are going to get more profit every year because of the centrifuge. And if you bring down all of them and today's value then you end up with a advantage for the centrifuge in the order of 57775 I have got a excel of the same thing.

(Refer Slide Time: 04:39)



Now, this is the excel sheet of the same problem. So, same table, filter this is the cost of the filter, cost of the centrifuge then the AMC for the filter, AMC for the centrifuge, profit for the filter, profit for the centrifuge. So, total discounted cash flow for the filter 2023810 and for the centrifuge you have 2081585; the difference for the centrifuge is

57775 that is for a discount factor of 10; percent that means 0.1. So, the advantage of doing a excel is we can change this number; if the discount factor is 5 percent. That means difference between this current year and the next year the difference is only 5 percent, unlike the 10 percent which I have it here. So, if I put in that 5 percent and have a look at this number. So, if you put in 5 percent received the difference comes out to be almost 70562.

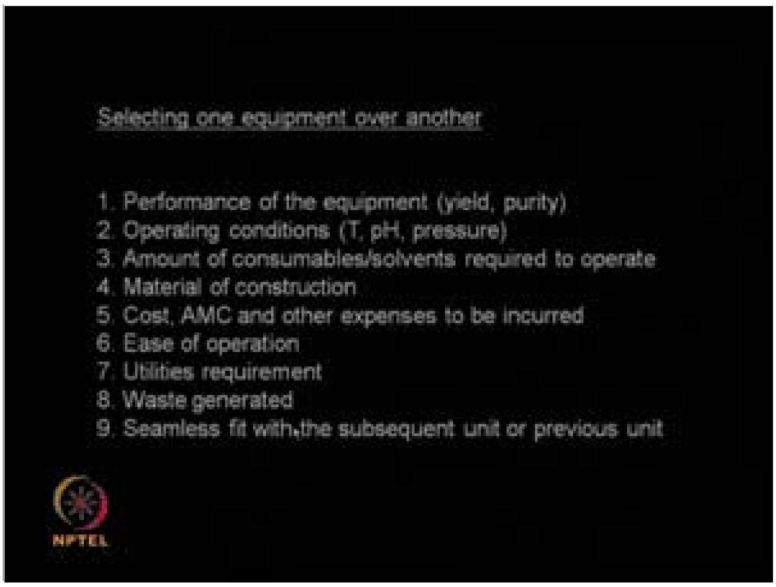
So, depending upon the discount factor the advantage between the filter and centrifuge changes understand. So, if the discount factor is less instead of 10 percent if the discount factor is 5 percent; you see that it is more advantageous to have your centrifuge rather than the filter. So, instead of 10 percent if I put it as 15 percent the discount factor of 15 percent then you see the difference between the filter and the centrifuge goes down; from 57000 when it was 10 percent, it becomes 47000 if it is 15 percent.

So, you see if the discount factor is larger; that means the value of the money is going down much more than the difference between the filter and the centrifuge is less. Because the amount of money which we get because of the profit from the filter and the centrifuge keeps going down much more. Because you are dividing by the that 15 percent comes in the denominator. So, that is why you are having much smaller number. So, if instead of 15 percent as a discount factor if I take it as 20 percent see the number has still come down dramatically; it is come down the difference between is only 38000.

So, if the discount factor is larger than the difference between the advantage of having a filter and a centrifuge keeps coming down. If the discount factor is much smaller the difference between the advantage of having a filter and a centrifuge gets enhanced. That means, it bet get us magnified because as you can see the profit in a centrifuge is much more 784000 every year whereas the profit in a filter is 720000. So, you have around 60000 every year having a centrifuge than a filter; and if the discount factor keeps coming down this difference gets enhanced in today’s value.

So, depending upon the discount factor the difference between a profit we make out of a centrifuge. And the profit we make out of a filter can vary from a very small number right up to a very large number. Let us go back to our problem. So, you see that the efficiency between a centrifuge and a filter is different, the cost of the centrifuge and filter is different, the annual maintenance contract between a centrifuge and a filter is different, the profit you make between a centrifuge and a filter is different. So, we make use of all these together in deciding on whether I should buy a centrifuge or whether I should buy a filter.

(Refer Slide Time: 08:53)



So, when you select an equipment in your downstream you always face such doubts, you will always face these types of problems; which equipment should I buy, filtration should I buy this or should I buy that, chilling plant should I buy this type of chilling plant or should I buy this type of chilling plant, heater should I buy this type of a heating element or should I buy some other type of heating element, should I go for a steam or should I go for a hot oil heating. So, you always face this type of doubts or this type of a worries when you are selecting equipment's or when you selecting you are utility strategies. So, selection of equipment's over another depends on several factors. So, this is what this particular slide tells; you performance of the equipment. How good the equipment is, what will be my yield of the product if I use this particular equipment? What will be the purity of my product if I use this equipment?

So, the performance of the equipment is one of the criteria in selection. For example, if I use a heating element the product may get charred; if it is very temperature sensitive. Sometimes you may go for a chilling equipment instead of heating for separating 2 different fluids if they are temperature sensitive then heating may lead to production of polymer or production of charred product. So, purity and yield of the product plays a very important role in selection of the equipment. Then comes operating condition; what temperature am I going to operate, what pH am I going to operate, what pressure do I need very high pressure or can I work at room temperature, do I require very high temperature if I require very high temperature I may go for steam or sometimes I may have to go for hot oil and so on? P H is it going to be very acidic pH conditions or is it going to be neutral pH conditions. If it is going to be acidic then your material of construction has to withstand the acidic condition. If it is a neutral then you can use very simple material of construction; mild steel is very cheap and it can withstand a normal condition in Ph.

But if you are going to have a very acidic pH you may have to go for some other special type of steel; then the cost of the material may be very high. Amount of consumable solvents require to operate. How much solvent do I require to operate this particular operation, how much consumable chemicals I will require to operate I need to consider that do I require too much solvent? If I require too much solvent then obviously my operating cost goes up; I may have to use the solvent, I may have to recover the solvent. So, again the cost is very high. So, how much solvent will I require can I do the operation in this particular downstream vessel with minimum amount of solvent; if so then that is very advantageous for me is it not?

So, how much solvents and consumables require that will decide on how I select the equipment. Material of construction do I can I operate with the mild steel; do I require stainless steel, do I require glass line steel, do I require titanium. So, each of these materials of construction leads to different total cost of the equipment; the cost of the equipment will depend upon the type of material I select. So, what material of construction am I going to use that is one of the important parameter when I am selecting an equipment. Then comes the actual cost of the equipment, annual maintenance, contract; and other expenses I will be incurring on the equipment.

So, I should find out for example if I am buying a BMW I will spend lot of money on maintaining, right. So, that is going to be a continuous expense if I have a Maruthi 800 no problem; the cost I will incur is very little. So, not only the original cost of BMW but maintaining BMW also I need to spend lot of money. So, you need to keep that point in mind. Ease of operation; how easy it is to operate do I require very complicated instrumentation and control if I want operate. Can I operate with the unskilled people or semi-skilled man power or do I require very complicated, highly trained man power? So, ease of operation is very important. Then comes utilities what are the utilities required? Do I require steam, do I require air, do I require nitrogen; what type of gases I require if I want operate? Do I require inert conditions?

For example, some motors may generate heat. So, I may require cooling water for the motors. So, I need to keep all those points into mind that is the utilities requirement. Because as I said longtime back it is not just enough to have an equipment if you want make the equipment running; you may require lot of support services. Then waste generated; how much waste is it going to generate? Because waste generated is something I have to send it to a effluent plant and treat it; I cannot just throw it out in the gutter. So, whatever waste I generate I spend money on treatment. So, is this equipment going to produce lot of waste or is this equipment going to produce little amount of waste? So, you need to consider both the aspects depending upon the amount of waste generated by the equipment you may select; your final choice of downstream. Seamless fit with the subsequent unit or previous unit. Because I showed you many flow sheets where you have 1 unit operation which goes into another unit operation which goes into another.

So, when I buy a downstream equipment how will it fit into next downstream? So, if I am heating a downstream and if the next downstream is cooling; then obviously from the high temperature I need to bring in to the low temperature. So, it is not exactly matching with each other. If I am doing an unit operation at a high pressure and the next equipment is at low pressure; I need to bring the pressure down. So, that I can do it in the next equipment; so that is not very comfortable fit. So, that is why it means seamless fit; if the pressures in the subsequent units are similar, if the temperature in the subsequent units is almost similar not exactly. Then I need not spend extra energy to bring down the temperature or change the pressure that is what it means a seamless fit.

So, you need to see how much what are the operating conditions in the next unit, what is the operating conditions in these unit? And together how they fit with each other that is called seamless fit. So, you need to consider so many factors when you are selecting an equipment. And it is not only the performance that the performance item one but it is several other factors you need to keep in mind before you select a equipment. So, you need to keep that point very important actually.

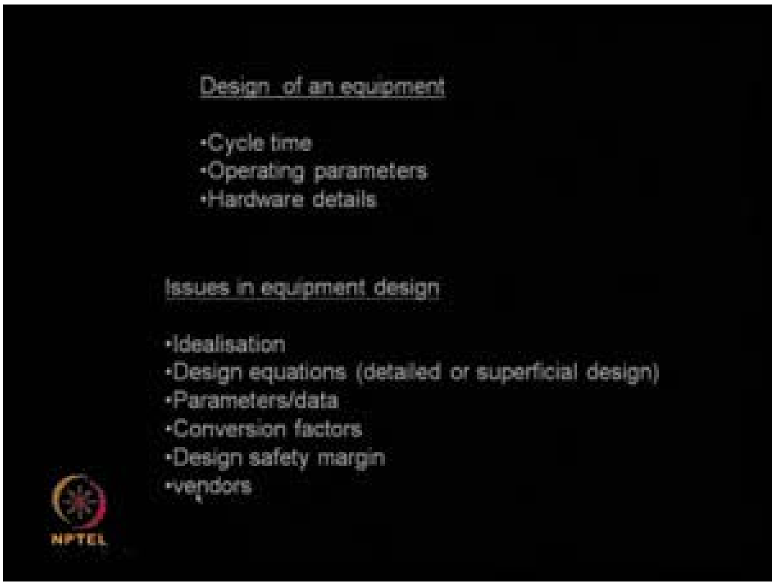
(Refer Slide Time: 15:53)

There is one more cost factor which I forgot to mention it is called payback period. We talked about the equipment cost, we talked about operating cost, then we talked about net present value, then we talked about cash flow there is something called payback period. It is how the amount of time I will take to pay back whatever investment I made. For example, if I borrow 1 lakh from you and I pay 50000 rupees this year and 50000 rupees next year I will be paying back your 1 lakh in 2 years is it not? Because you will be asking how long you will take to pay it back that is the first question you ask; whenever somebody comes to you for loan how many years you take or how many months you will take that what is called payback period. And that is very important because if you go to the bank and take a large loan for setting up a factory; bank would like to know how fast you will pay the money back? It tells you how good the investment is; if the payback period is very small that means the investment is very lucrative.

So, the banks also will be interested if you are going to tell the bank that I will take 10 years to pay back they will not be happy. If you go and tell the bank I will pay the money in one and a half to 2 years they will think yes; this project is very good. So, they would rather support this project rather than the other project which will take a very longtime for payback. So, payback period how do you calculate? If a suppose cost of setting up a plant is thousand crores and every year I make profit in the plant, correct. So, imagine I make fifty crore profit after tax; so this amount I pay back to the bank. So, 1000 by 50 that comes to 20 years. So, the thousand crores I brought from the bank as a loan I will paying the bank back in 20 years all the amount, assuming that every year I will make a profit after tax as 50 crores; so the bank will be interested in this particular number.

So, they will know that you will take 20 years to pay it back. So, if there is another project and if that project the payback period is 10 years; bank will think that project is better than this project. So, they would rather fund that project rather than this particular project. So, that is why payback period is important number and it also tells you how long you will take to clear all your debts? Because you have borrowed thousand crores and after 20 years there are no debts for you. So, it tells you or gives you an idea of how long you will take to clear your debts? So, payback period is also important parameter which tells you the soundness of your investment, it also tells the bank the soundness of the person who is borrowing the money.

(Refer Slide Time: 19:02)



So, when you go for a downstream equipment and when you talk about designing a downstream equipment; you need to consider several factors. So, what does the design means 1 important parameter is called cycle time. Suppose if you are designing a filter; how long the filtration will take place that is the cycle time. If you are designing a drier how long do you require to dry the equipment to reach the moisture content to some value to some other value that is called cycle time. If you want to heat a material from room temperature to 100 degrees how long it will take to heat that is called the cycle time. So, if you are doing a heating and cooling how long you will take to heat the material, how long you will take to cool the material? So, together that is called a cycle time. So, if you are trying to settle solids in a slurry; how long do you need to keep the liquid stationary; so that the solids will settle down that is called cycle time.

So, cycle time is a very important parameter you need to design. Next is operating parameters; what will be the temperature, what will be the ph, what will be the pressure? And if it is a fermentor like what will be the dissolved oxygen these are called operating parameters. Next is hardware details that means the size of the equipment's; how much will be the diameter, how much will be the length all these parameters actually. So, hardware we are not going to do any hardware design. We go to the vendors and then vendors will suggest certain equipment's for us and we can select from them. So, we need mechanical engineering expertise if you want to design hardware. That means, a diameter of the vessel length of the vessel, thickness of the flange, thickness of the vessel, radius of curvature and so many other parameters which are very mechanical engineering. And we are not going to do any of those generally we go to a vendor.

Now, when you are designing a equipment there are many issues which need to consider; one is called the idealization. That means we generally consider whatever we do in a vessel at ideal condition. That means if you are considering a gas and the liquid; we assume that the gas gets mixed completely with the liquid that is an ideal condition generally it will not. But we will consider it as completely mixed. Suppose if I am saying I am going to heat a liquid of a thousand liter from 30 to 80 degrees; we will assume all the thousand liter is uniformly getting heated up to 80 degrees. So, we do not assume any difference in temperature inside the liquid. So, that is an ideal condition agreed; if you assume we are mixing a solid and a liquid thoroughly. So, that the solid gets dissolved we assume that the solid completely gets mixed and dissolves; that is an ideal condition.

So, generally it becomes easy for us to do a mathematical calculation, designed using ideal conditions; we will not going into non-ideal conditions. Because it complicates the design equation, it complicate the equation which we need to solve. So, in generally we assume ideal conditions. Then type of design equations are we going to do mass balance type of equations or we going to do heat balance type of equations or are we going to go very deep into the equations and calculate the velocity of flow inside a stored vessel? So, what type of designs we are going to perform? So, that is the next step; third step is parameters and data. For example, if I am going to do settling I need to know the density of liquid, density of the solid, the viscosity of liquid, the surface tension; so many parameters I need to know. Same thing I need to know all about the solid properties; the size of the solid, size distribution of the solid and so there are lots of parameters we have to know; when we do this types of a downstream calculations.

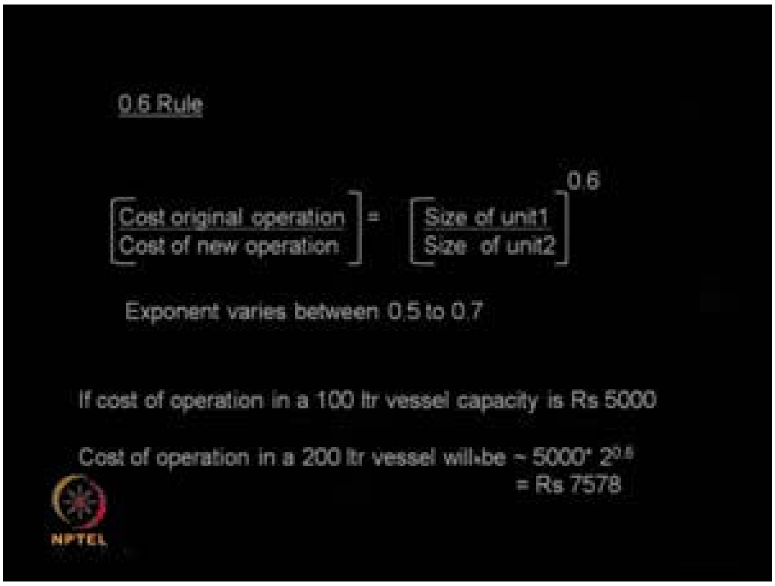
For example, if I am doing a distillation separating 2 liquids; I need to know the vapor pressure data for liquid 1, I need to know the vapor pressure data for liquid 2, I need to do know the viscosity of both the liquids, I need to know the surface tension, I need to know the where these 2 liquids mix are they miscible or are they are not miscible. So, all these parameters I need to know. So, collecting data is big challenge for downstream process calculations; many times we do not find data many times. So, what do we have to do we sometimes approximate, we sometimes assume we go to the net, we go to the books and try to locate data.

So, sometimes we may have to do experiments in the lab to collect data. So, if you are very serious about the data you may have to go to the lab and collect data; if you want to know the viscosity of a liquid you go to the lab and get the viscosity data for the liquid. If I want to know the surface tension either I assume some value from the net or I actually calculate surface tension. If you want to know viscosity effect as a function of time and temperature; we may have to do the experiment or you may assume approximate like linear change between temperature and viscosity.

So, data is a big challenge; collecting data is a very big challenge getting it from books, literature, net, collecting your own data. So, this is going to be the main bottle neck and this will take you a long time. Next is conversion factors as you know you have FPS units, CGS units, SI units. So, many units are there and when we do some problems also you will come across. So, conversion factors you have to be very thorough in conversion factors; kilo calories, kilo joules ((Refer Time: 25:06)), meters, centimeters, liters, meter cube, gallons. So, each country has different units and converting them is going to be a big challenge for you also. So, you need to remember all the conversion factors. Next is the designed safety margin; when we assume ideal conditions and do a design you know it is very ideal, it is not real. So, we generally add some extra margin 10 percent, 15 percent, 20 percent. So, how much do I add is always a important point you have to keep in mind actually; should I add 10 percent extra or should I add 20 percent extra.

If you add 20 percent that means you are over designing. If you are over designing a vessel of course you are going to spend more money buying that vessel right. So, you need to think do I need to over design the vessel or 10 percent looks very good margin. But then the safety is not very high; the equipment may be not performing as good. So, it is a challenge between equipment performance verses extra design hence extra equipment cost. So, you need to select should we do 5 present extra margins or 10 percent or 15 percent or 20 percent. And finally vendors you should know who are the vendors manufacturing? If you want to buy a centrifuge I should know who manufactures centrifuge in India or if outside India. If I want to buy a distillation column I should know who manufactures various distillation column, various types of distillation columns. If you want to buy a motor for agitation who are the various vendors? So, you need to know the vendors available in India or outside India.

(Refer Slide Time: 26:53)



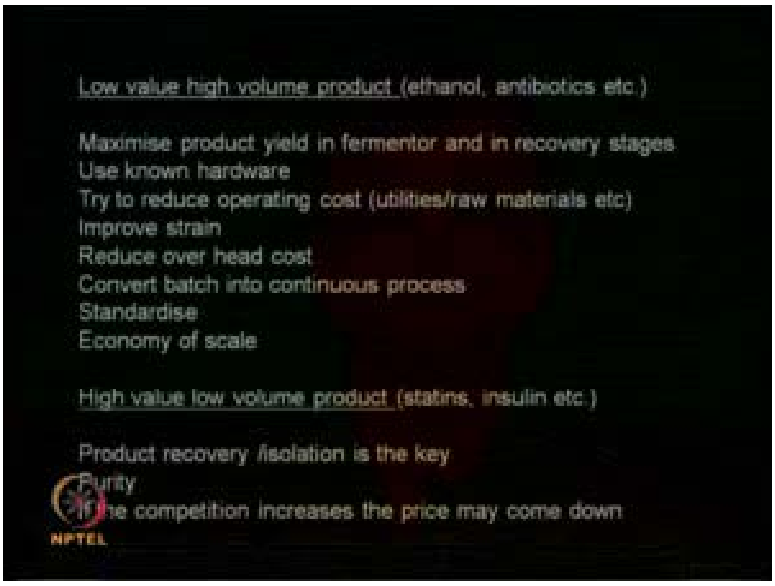
There are some few small rules which are very useful when you are doing design; one is called the 0.6 rule. It is very interesting rule which gives you a ball path figure of the cost. For example, if cost of the original operation is related to the size of the unit raise to the power 0.6. Generally this number is called the exponent it varies between point 5 to 0.7; do not ask me why you get 0.6 it is based on experience. And this number is of the order of 0.5 to 0.7. So, cost of original operation is directly proportional to size of the unit raise to power 0.6. So, if you have another cost of new operation and the size of unit is 2 times size of unit 1 and size of unit 2. So, cost of original operation divided by cost of new operation will be equal to size of unit 1 divided by size of unit 2 raise to the power point 6. So, for example if I have a 100 liter vessel capacity and I need the cost of operating this vessel is 5000 rupees. If I have a 200 liter vessel the cost of operation will not be 2 times 5000 that means it will not be 10000 rupees.

But it will be much less than 10000 based on this formula. So, original operation is 5000, original vessel size is 100, new vessel size is 200. So, cost of new operation; so I can calculate like this 5000 into 2 raise to the power 0.62 comes because of 200 by 100. So, it comes to 7578. So, what it tells you is; if I have to operate a vessel of 100 liter capacity and it cost me 5000 rupees. And if I want to operate similar vessel just the size is 200 liter the cost will not be 10000 rupees but it will be 2 raise to the power 0.6 extra rupees. So, it is 7578 rupees. So, it is not 10000 but less than 10000; but it comes out to be 7578. So, this 0.6 rule is very useful sometime depending upon the type of equipment; then this exponent may change. If it is a very complicated equipment it may go to 0.7; it is not so complicated it may become 0.5.

So, all it says is you cannot just because the vessel size is moved from 100 liter to 200 liter; you cannot just multiply by 2 5000 and tell it is called 10000 rupees; it will be less than that. Same 0.6 rule can be also used for getting a price of an equipment; this rule again tells you cost of equipment 1, size of equipment 1, cost of equipment 2, size of equipment 2; this raise to the power 0.6. So, if a cost of 100 liter vessels is about say 5 lakh rupees; a cost of 200 liter vessel will not be 10 lakh rupees; please remember. But it is 2 raise to the power 0.6 approximately. So, it will be around 7.57 lakhs rupees. So, this exponent can vary between 0.5 and 0.7. So, if it is 0.5 it will be much less right. So, it is not exactly 2 times 5 lakh which is 10 lakh rupees; but it is much less.

And, this exponent depends upon the how complicated the equipment is? The equipment is very complicated it will be 2 raise to power 0.7. If the equipment is not least complicated it can be 2 raise to the power 0.5. So, it will be in between. So, equipment of 100 liter capacity if it is 5 lakh equipment of 200 liter capacity will be 2 raise to power 0.6 into 5 lakh; that is what this 0.6 rule tells. It just gives you a ball path figure if you want to know the exact price you have to go to the vendor who is manufacturing the equipment and go and ask him? I want to buy a 200 liter vessel what is a cost, I want to buy a 100 liter vessel what is the cost? So, the final price if you want to get exact calculations done; you go to him. But you can use this type of formula; if you are doing it in your lab, in your office to just to get a ball path figure of the cost.

(Refer Slide Time: 31:30)



There are 2 types of products which are manufactured in bio process engineering; one is called low value high volume product. That means, the selling price is low but you make large amount of product; other one is called high value low volume product. That means, selling price is very high but you make only little amount of product. So, these low value high volume products like ethanol you know you makes large quantities of ethanol. But the cost of ethanol is cheap; same thing nowadays many antibiotics are made in large volume; cost is very cheap, all these penicillin and different types of a penicillin it is all made in large volume. Suppose you look at some pharmaceutical product like insulin statins. Statin is a cholesterol lowering compound; you might not make such a big quantity but the price is very large.

So, you may make only 10000 kg but each gram may be costing about 10000 rupees whereas, you make metric tons of ethanol but cost of ethanol will be only few rupees. So, you see the difference. So, that is why one is called low value high volume product, other one is called the high value low volume product. So, if you look at low value high volume product the goal of a downstream and the goal of a fermentation is very different; you all the time want to make large quantity of material. So, maximize product yield in the fermentor, in the recovery as much as you can get. Because you want to sell as much the profit is very little. Use known hardware do not go for new hardware. If you use known hardware the always you go to the vendor and it is cheap. If you want a very special hardware then the vendor has to make it specialized; so equipment is expensive.

Standard size right; so if you have a standard shoe size you go to a shop then it will be cheap whereas, you want a very specialized cut for your foot; then cost of that shoe is very high. Try to reduce operating cost; that means all the time keep seeing can I reduce the cost of the steam, can I use less steam, can I can I less use less utilities, can I use raw less raw materials? Because every time I need to improve on the profit because the value is very low. Improve strain; so you can do microbiology and see whether the strain can be tolerance can be improved.

That is how new ethanol tolerance strains have been discovered over the past few years. Reduce overhead cost because the value is very low you are selling the product at a very low price. So, obviously do not have too much of overheads; keep your overheads very low; see whether you can convert batch process into continuous process. Because if you can do continuously then you will be continuously manufacturing the product at the same purity and yield; without disturbing any of the equipments. That is why continuous process is very ideal for high volume or high quantity material.

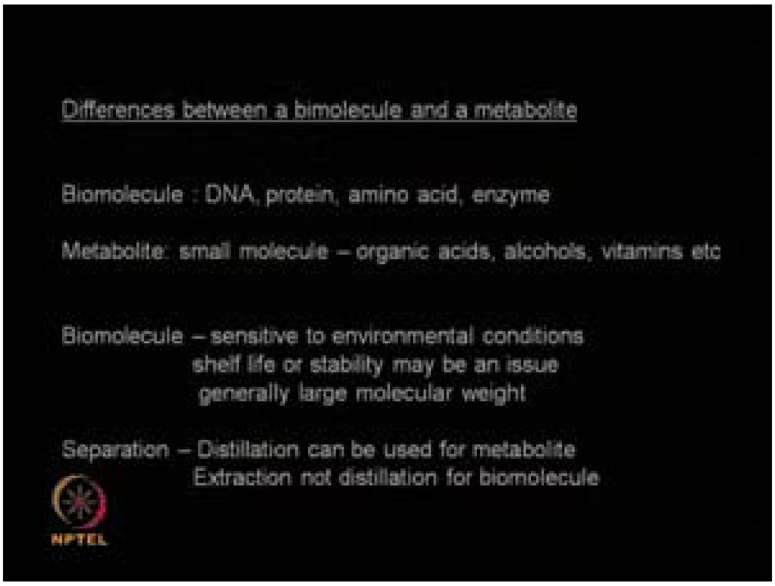
Standardize keep everything standard do not try nonstandard; as I said if you have a special shoe made for yourself it is very expensive. You use the shoe go to Bata and buy a shoe; it is very cheaper. Economy of scale you have a very large plant; and when you have a very large plant the overall cost will be also low. So, very large plants that is why high volume products will always be manufactured in very big factories; not in small factories. So, these are some of the approaches by which you can handle low value high volume product; on the contrary if you look at high value low volume product. Because here you are making only small amounts but cost of each kilogram or each gram is so high. So, you need to recover all the product because each gram you lose in the effluent; you are losing profit, you are losing money. Because it is a high value; each gram may be costing 1000 of rupees.

So, your product recovery and isolation is should be fantastic; the efficiency should be almost 100 percent; you do not lose any of your product in the waste. Purity is very important if you look at all these drug or pharmaceutical products; purity is a very important competition. Another very important point you need to remember is you will not be able to have the high value low volume product forever and ever; tomorrow another manufacturer comes. And they start of a company they become your competitor then the product cost, selling prize comes down. So, you have to always keep in mind I there is no monopoly for a very long time; this year I will have monopoly, next year I may have monopoly. But third year somebody else may be manufacturing that product; then you have to cut down on the cost.

So, what happens your high value low volume product will slowly end up like a low volume high sorry low value high volume product? We have to keep reducing the selling price of the product that is why for example; you know mobile phones are so expensive once upon a time; nobody could afford it about 7, 8 years back. But now practically it is throw away price because you have many competitors manufacturing mobile phones. So, obviously it has become almost like a high volume low value product. But about 10 years back it was like a high value low volume product; that is happening to everything not only mobile phones; even the service some of the services may be very high expensive 10 years back. But today same services are so cheap.

So, the type of strategy you employ depends upon the value of the product, depends upon the volume of manufacture. If the volume is very large you adopt some strategies. If the volume is very small you adopt some other strategies. If the selling price of the item is very large you adopt some strategies. If the selling price is very less that means your profit margin is also very less; you adopt some other strategies. So, depending upon the volume you manufacture, depending upon the price of the item you employ different strategies.

(Refer Slide Time: 38:45)



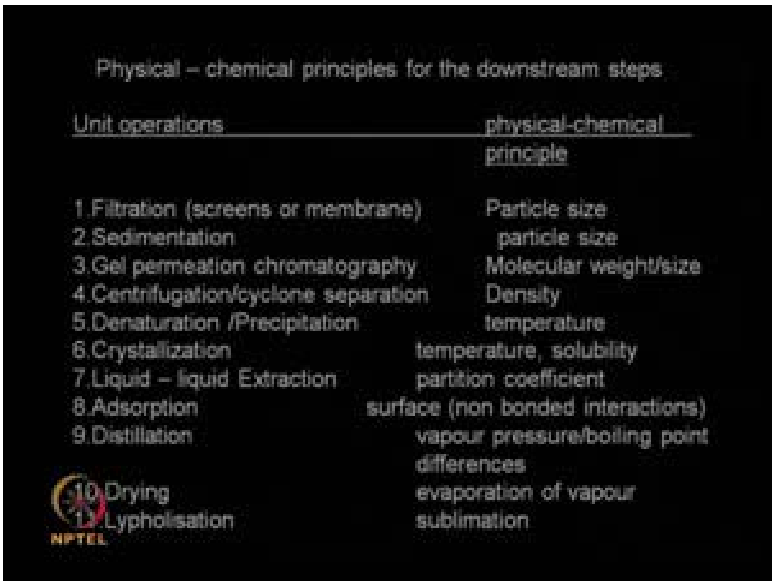
So, when you use a fermentor or when you use a bio reactor you get metabolites. Metabolites are small molecules or you get bio molecules; and the type of strategy of separation depending upon the type of molecule you get. So, you need to know some differences between the bio molecule and metabolites. So, what is a bio molecule it could be a DNA, it could be a protein, it could be a amino acid, enzyme. Enzymes have very large molecular weight, proteins have very large molecular weight. If it is a meta metabolite it is going to be a small molecular; it could be organic acids, alcohols, ketones, aldehydes, even vitamins they are all met metabolites. That means, these are produced during the fermentation process or during the bio transformation process.

So, bio molecules are generally sensitive to environmental conditions. Environmental means ph, temperature and the presence of impurities, presence of other toxins. So, you need to be very careful when you are doing a separation or when you are mixing a solvent; whether the bio molecule is tolerant to the solvent; can I add a butanol to a enzyme; butanol may be toxic to the enzyme. So, a bio molecule is always sensitive to the environmental conditions. Shelf life that means can I store these bio molecule for long period of time 3 months or 6 months. How stable it is going to be that is very important; that is why you need to have stabilizers after you purify a bio molecules; stabilizers could be anti-oxidants or anti ozonents and so on actually. And generally bio molecules have large molecular weight whereas, if you look at a metabolite generally they are much smaller molecular weight; they will not be very generally they are not sensitive to environmental conditions. You do not have to worry about shelf life also; you may be able to store alcohols for a very long time, you may be able to store many of the small molecule for a long time. You do not have to worry about toxicity or presence of other impurities which may reduce their activity.

Separation generally for metabolites we can use distillation columns. Because they are not a temperature sensitive whereas a bio molecule will have problem using when you use resort to a distillation column. So, what do we do we generally use extractions. So, in many bio molecule downstream you will use an extractor; once the extraction is done, once the bio molecule is removed. Then the solvent can be distilled for recovery and then sent back to the original extractor. But when the enzyme or when bio molecule is present you will not resort to a distillation whereas if you a just have a metabolite recovery you resort to distillation. For example, if you take a fermentation of sugar to alcohol; the very first step is filtration that is followed by distillation to remove the alcohol.

Whereas, if you have an enzyme after a fermentation; you will do a filtration and you will not do a distillation. What will you do? You will do an extraction understand you will not do a distillation. Because the enzyme present in the fermentation broth can get deactivated. So, what do you do? You do an extraction and the enzyme is taken up in the extractor. And then you separate the enzyme from the solvent using some salting out. And then you take the empty solvent and do a distillation when the enzyme has been removed; so understand. So, a fermentation of sugar to alcohol you can resort to distillation because ethanol is very stable at high temperature whereas if you have an enzyme in your fermentation broth what do you do? You cannot do distillation; you have to resort to extraction. So, you see the difference depending upon the type of downstream; which you want to do, you need to change the unit.

(Refer Slide Time: 43:19)



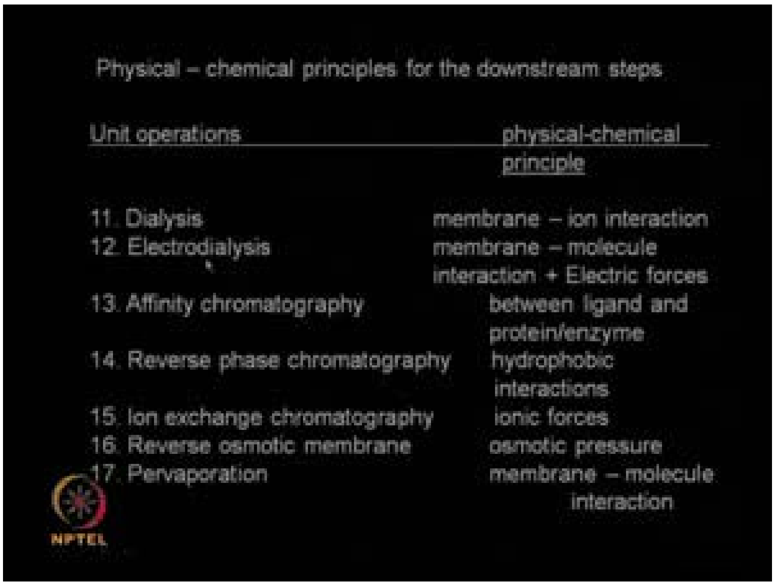
There are many downstream operations that are possible and we are going to talk about it in the next 30 or 35 lectures. And each one is based on a physical or chemical principle; irrespective of the downstream there is always a physical or a chemical principles on which it is based on. For example, if you take filtration or screening or membrane it is generally based on particle size. That means, a filter unit will separate particles of certain diameter and it will let particles of certain other diameter. So, it is based on the size of the particles; same thing with sedimentation. What sedimentation we are trying to settle large solids in slurry. So, again it is based on particle sizes agreed. So, you have large particles and the liquid is stationary. So, the large particles will settle down and the very small fine particles being may not settle down but the large particles will settle down. And this settling is called the settling velocity and there is something called terminal settling velocity.

And, this terminal settling velocity depends upon the difference in densities between the liquid and the solid. And it depends upon the viscosity of the liquid and depends on the particle size of the liquid. So, again particle size comes into the picture. So, sedimentation is also based on particle size. Now, let us look at something called gel permeation chromatography. So, this depends upon the molecular weight of the various components present. So, a larger molecular weights gets separated from smaller molecular weight; larger sizes get separated from smaller sizes. So, gel permeation chromatography is based on this contract. Let us look at centrifugation or cyclone separation that is based on density; the density difference drives the operation. If you look at again look at the denaturation or precipitation; so you have a something called the temperature. If you looking at crystallization again temperature plays a very important role and solubility of the material.

So, when you are crystallizing the least soluble material will crystallize out and the most soluble material will be retained. So, the solubility plays a very important role in crystallization. If you look at liquid-liquid extraction that is I am using a solvent to extract a liquid or a solid; the principle is based on partition co efficient; the solute gets partitioned between the solvent and the solution. So, if it has got a higher partition co efficient more of the solute will go into the solvent. And if it has got lesser partition co efficient less of the solute will go into the solvent. So, more of the solute will remain in the broth. So, that concept is called the partition co efficient. If you are looking at adsorption; adsorption is attachment of some material on some surfaces no solid surface. So, that is it is a surface phenomenon.

If you look at distillation it depends upon the boiling point difference between 2 liquids or vapor pressure difference between 2 liquids. So, a liquid which has got higher vapor pressure that means lower boiling point will move up of the distillation column. And the liquid which is got lower vapor pressure or higher boiling point will remain at the bottom of the distillation column. So, the separation is based on the vapor pressure. Then comes drying. Drying is nothing but evaporation of a vapor; vapor could be water or any solvent; lifealization is called sublimation. So, it is based on the sublimation because a solid directly goes into vapor; that means a solid ice will directly go into water vapor right. So, that is concept of sublimation. So, you see many of the unit operations on the side has or it is based on a physico chemical principle. Let us continue some more.

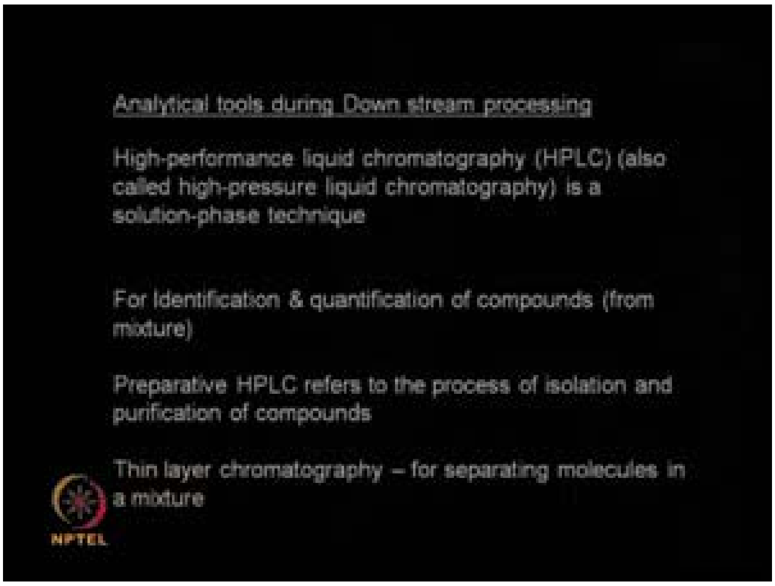
(Refer Slide Time: 47:34)



Dialysis there is a membrane ion interaction; there is a membrane and ions are interacting with that. So, the ions get separated; dialysis is very good for separating salts from a solution. Then we have electro dialysis where you are using a electric force. So, the separation is not only a membrane and a interaction but there is also a electric force applied. So, that positive charge material will give go the cathode and negative charged material will go to the anode. Then we have something called affinity chromatography; here it is based on a ligand and an enzyme or a ligand and a protein. So, there is affinity between the ligand and a protein or ligand and the enzyme. Then we have something called reverse phase chromatography; it is based on hydrophobic interactions. Then we have ion exchange chromatography; it is based on ionic forces.

Then, we have reverse osmotic membrane it is based on osmotic pressure; then we have pervaporation it is based on membrane and molecular interaction. So, here you see many membrane processes are there starting from dialysis, electro dialysis, chromatography then we have pervaporation, osmotic membrane; these are chromatography's and these are membrane based processes. So, we have interaction between the ions interaction between the ligands; which gives you the physico chemical principle of separation.

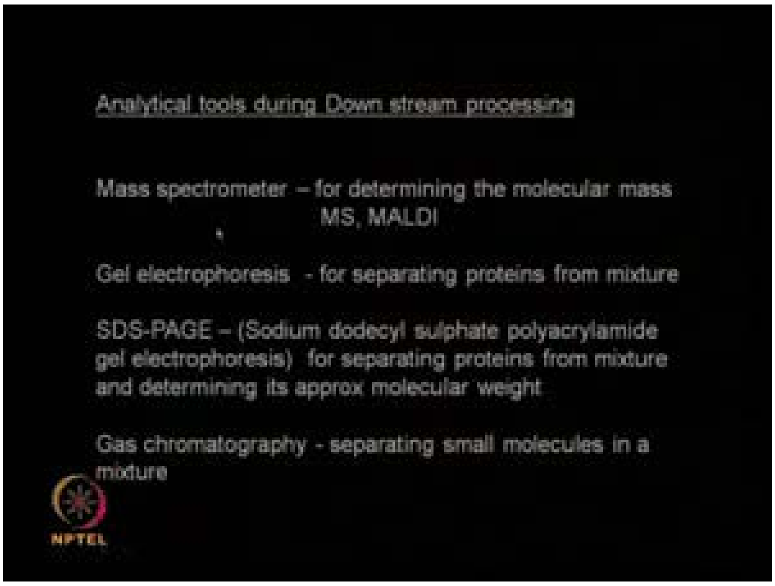
(Refer Slide Time: 49:03)



There are lot of analytical tools used in downstream processing I am just giving you an overview them. We will we will talk about it at the end of the course. We need many analytical tools for identifying what type of metabolites or bio molecules present in my mixture and what is the concentration of them? So, when I do a purification I can see whether it is getting purified; and the most important one is called the chromatography. HPLC you all have heard about the HPLC it is called the high performance liquid chromatography or high pressure liquid chromatography. So, it is a solution phase technique. So, what happens is there is a solvent flowing through and there is a stationary phase. And the solution containing a mixture of solutes or mixture of proteins get separated. Because they interact with the solid material and they come out in a separated form.

So, we can use it for identifying, we can use it for quantifying compounds from a mixture; there is something called preparative HPLC. So, I can use it for not only separating but I can use it for isolating also. If I isolate a protein from a mixture of protein; then I can use that isolated protein for other analytical jobs. That is why I use something called preparative HPLC. Then there is something called thin layer chromatography that is the TLC; this is a very simple technique using silica plate we can again look at mixture of metabolites or mixtures of proteins using this. And it can be very good for separating molecules from mixture. So, chromatography in various forms are very important for analysis in downstream; both for identification and quantification of compounds. Then we have something called mass spectrometer.

(Refer Slide Time: 51:14)

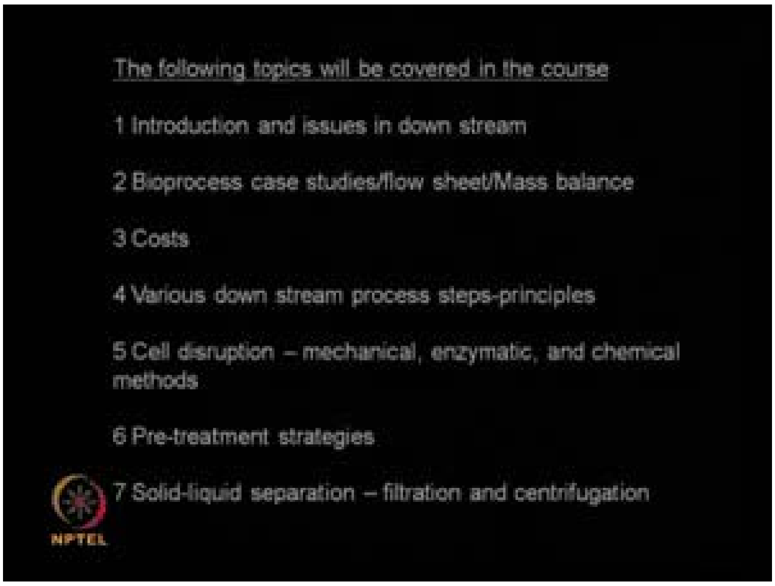


Mass spectrometer gives you the molecular mass; there are different types of mass spectrometer there is something called a MALDI mass spectrometer. Then we have the gas chromatograph mass spectrometer that is GCMS; then we have liquid chromatograph mass spectrometer that is LCMS; then we have ESI mass spectrometer, electron spray ionization mass spectrometer. So, there are large number of mass spectrometry minutes available or mass spectrometers available; each gives you the mass of the compound small molecule or large molecule. Then we have gel electrophoresis for separating proteins from mixtures. So, you have an electric field and you have charged proteins. So, the proteins get separated based on its charge based on the size or based on the molecular weight.

So, it is very good technique for separating out proteins from mixture; then we have something called SDS page. SDS means sodium dodecyl sulphate; it is a surfactant sodium dodecyl it is a sodium salt of dodecyl sulphate poly acrylamide gel so poly acrylamide gel electrophoresis. So, sodium dodecyl sulphate poly acrylamide gel electrophoresis; this is good for separating proteins from a mixture. And getting reasonably good molecular weight you can use marker molecular weight. And then we can tell what is the molecular weight of various components present in my protein mixture. So, it is a very good technique and you go to any bio chemistry lab; you will have find a SDS page unit there. So, SDS page is a very important instrumental technique in downstream operation. Then we have gas chromatography this is good for separating small molecules in a mixture. That means, when I have mixture of small molecules which can be easily vaporized I can separate the mixture. And I can find out what those components are I can get the what is the composition of this component.

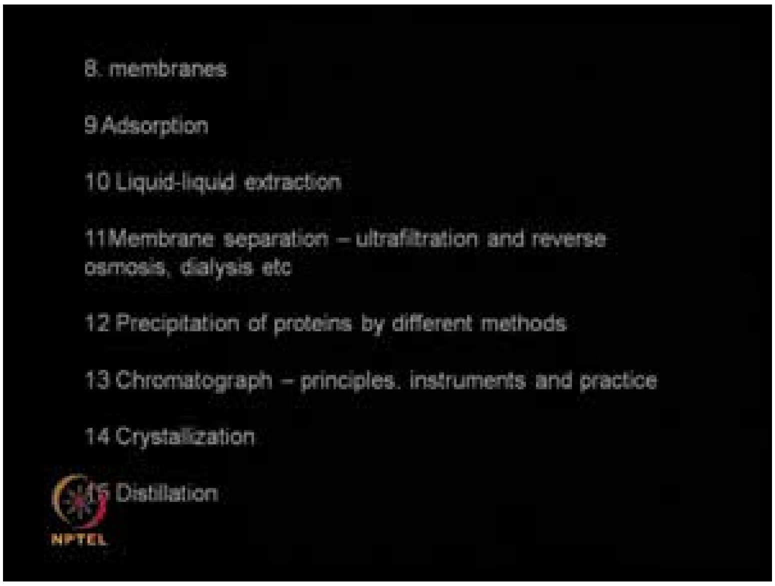
So, that a very useful instrument for small molecules it is not good for proteins. If I have a protein mixture I need to use HPLC; high pressure or high performance liquid chromatography please remember that. So, these are some standard instruments which you will find in any downstream lab. And without that you cannot do any downstream processing, laboratory or downstream processing manufacturing at all for measuring the quantity of proteins, for identifying quantity of proteins and identifying various metabolites. Metabolites mean small molecules and quantifying the metabolites; that are present in your mixture of mixture of metabolites that comes out from a fermentation broth.

(Refer Slide Time: 54:23)



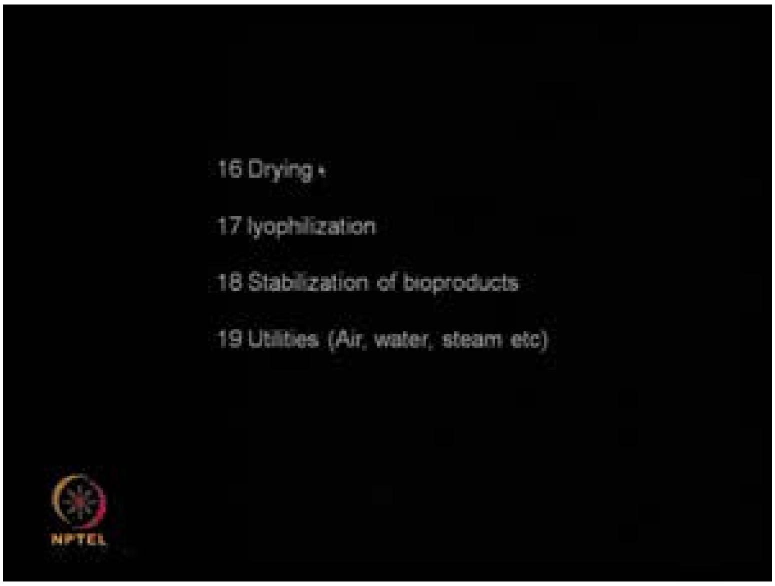
So, far we have been covering the concept of downstream. So, I talked quite a lot about introduction issues in downstream and I showed you some examples of flow sheet. And what will a flow sheet contain, what are the various units a flow sheet will contain? I also talked about mass balance. What is the importance of mass balance, how do you use mass balance and how do you use heat balance, what are the important parameters in balance? Then I also talked about cost the importance of costing. How do you select equipment based on costing? And then what are the various principles in different downstream steps? So, all these we talked about and in the next a course of time we are going to now get into serious downstream processing equipments or units things like cell disruption, free treatment strategies, solid liquid separations like filtration, centrifugation.

(Refer Slide Time: 55:22)



And, then membrane based processes adsorption liquid-liquid extraction, membrane separations, precipitations, chromatography, crystallizations, distillations.

(Refer Slide Time: 55:34)



And, then we will talk about drying, lyophilization, stabilization of bio product. And then finally we will look at utilities also because without utilities a downstream manufacturing unit has no meaning; utility is like air, water, steam, hot oil, chilling water and so on. So, if we talk about all these and if we understand how each equipment works? I think a we will have a fairly good idea about what are the various components in a downstream processing, how do you go about designing a downstream processing?