Membrane Technology
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Lecture-36
Perstraction, Membrane Chromatography and Controlled Drug Delivery

Good morning students. This is lecture 36 under model 12 and this is the last lecture of our course membrane technology. In today's lecture we will cover perstraction membrane, chromatography and little brief description about controlled drug delivery which is using membranes of course, which is running a lot of importance nowadays in the field of medicine.

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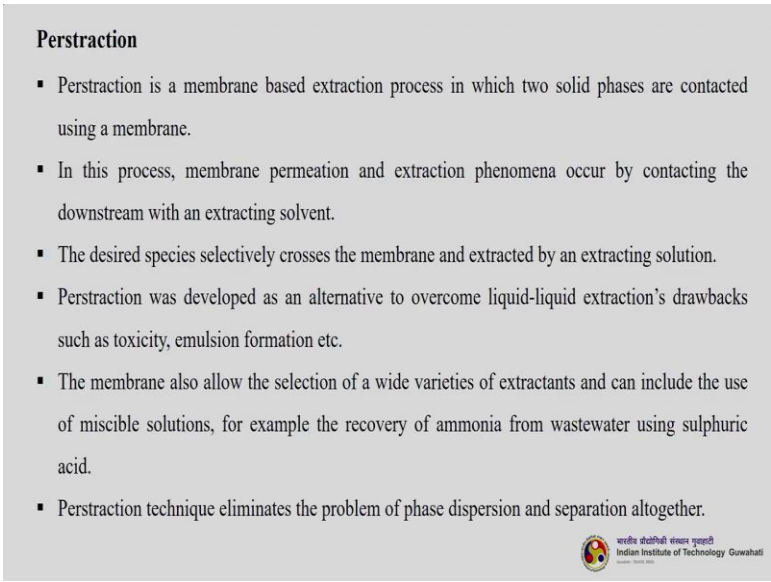

So let us understand actually, what is perstraction? Perstraction is something like liquid-liquid extraction. So it is membrane-based extraction process in which two solid phases are in contacted using membrane. So the membrane permeation and extaction phenomena occur by contacting the downstream within extracting solvent. So, basically in the permeate side little close to pervaporation. You can imagine that sense that in the pervaporation other downstream part is vacuumised so as to maintain a lower vapour pressure or partial pressure.

Here in this case we are in the downstream side you are using an extracting solvent. So the desired species selectively crosses the extracted by an extracting solution. So, Perstraction

actually was developed and conceptualised long back as an alternative to liquid-liquid extraction because liquid-liquid extraction in which we use and extracting solvent. Sometimes create some toxicity problem as well as form simulation with certain other types of solvents.

So to overcome these things perstraction in technology was conceived and developed. So in this case the membrane allowed the selection of a wide variety of extractants and so here since the extract and the phase from which extraction is being happening do not come in direct contact with each other, is in the case of liquid-liquid extraction, so that they are being separated by membrane therefore, we can use a varieties of extractant.

And those can include also miscible solutions for typical example is recovery of ammonia, from wastewater using sulphuric acid. So the perstraction technique eliminates the problem of phase dispersion and separation all together.

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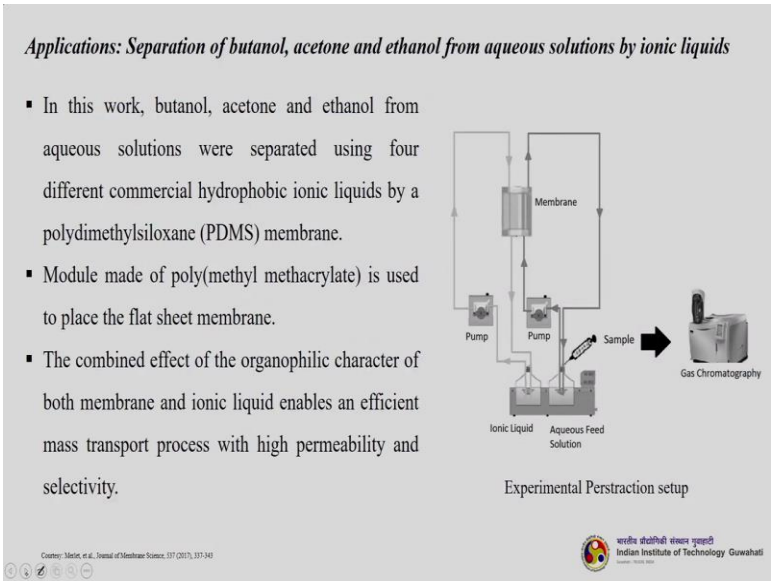

So, this is a good technique but as you know every technique some advantages and disadvantages. So this technical so as certain limitations will discuss later. So, let us use one of the application which is very classic application for prestraction is separation of butanal, acetone and ethanol from aqueous solution by ionic liquids. This is work that is been taken from one of the reference. So, you know ABE fermentation which is called Acetone butanol and ethanol fermentation it is strictly anaerobic process.

In which the anaerobes will degrade the substrate to various components so butanal, acetate ethanol are simultaneously formed but there ratio is of course different. So, many times what happens if you are trying for a butanol production, which is a very high grade liquid fuel. So, butanol beyond certain percentage in the fermentation broth proves to be toxic to the microorganism. So, the need is to remove butanal as it is being produced.

So here in this case perstraction also plays a very important role. But in this case what we are discussing today here ionic liquid are being used. We have discussed little bit in ionic liquid in some of our class exactly. I don't remember which one. Ionic liquids class of green solvent in which there is cation and there is anion that is why they are fused together to form a ionic liquids. So the important class are RTIL which are called room temperature ionic liquid.

At room temperature there liquids otherwise there are basically salts. So here for different ionic, liquids were used by using commercial hydrophobic ionic liquids and the membrane is a PDMS membrane. So the module is made up of poly methyl methacrylate. It was used to replace the flat sheet membrane. The combined effect of organophilic character of both membrane and ionic liquid enables and efficient mass transfer process with high permeability and selectivity.

So the schematic of the prestraction setup, which is used to remove butanol, acetone and ethanol from aqueous solution using ionic liquids. Excellent results were found actually and reported.

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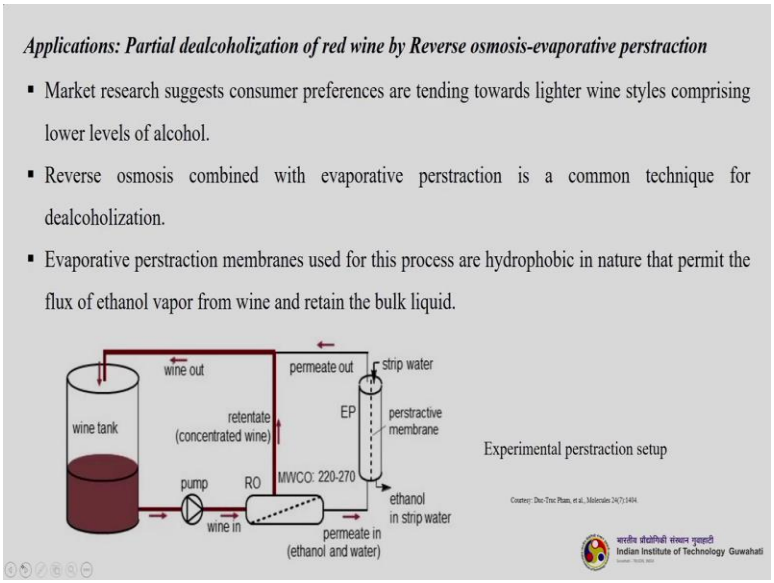

Another application is partial dealcoholization of red wine by RO and evaporator prestraction mechanism, you know, there is a huge demand of less alcohol beer or alcohol free beer especially in European markets. So on reverse osmosis combined with evaporator prestraction is a common technique for dealcoholization. See, you know, we have discussed this dealcoholization beer during our discussion on RO.

So, here RO is combined with evaporative prestraction. You can see this is the schematic representation actually from the wind tank wine is being pumped out to the membrane system, which is a RO membrane here. OK then the molecular weight perturbation around 200 to 250 then the concentrated wine which is being collected at the retentate because the RO membrane is selectively passing only ethanol and water ok.

So the concentrated wine is being recycle back into the wine tank, and the ethanol and water are being which is being collected from the permeate side and being treated to a prestraction membrane where ethanol is being collected in purified manner and the water is being circulated. So evaporative prestraction membranes used for this processor hydrophobic in nature is the permeate the flux of ethanol vapour from mine and return the bulk liquid.

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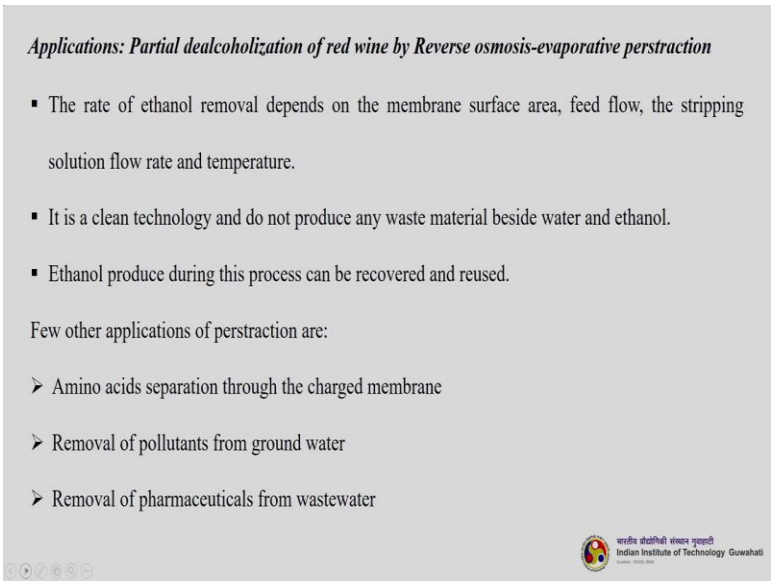

The rate of ethanol removal depends on the membrane surface area feed flow are the shipping solution product and the temperature. It is a clean technology and do not produce any waste material beside water and ethanol. Ethanol produced during this process can be recovered and reused. So, there are few other applications of prestraction also, amino acid separation through charge membrane, removal of pollutants from groundwater, removal of Pharmaceutical from wastewater.

But again as a I just talking about disadvantages, you know, the membrane cost also plays a very big role here and fouling needs to be taken care off. So which is very in have not any such membrane processes apart from that this is a good technology which is established footprint in event commercial scale.

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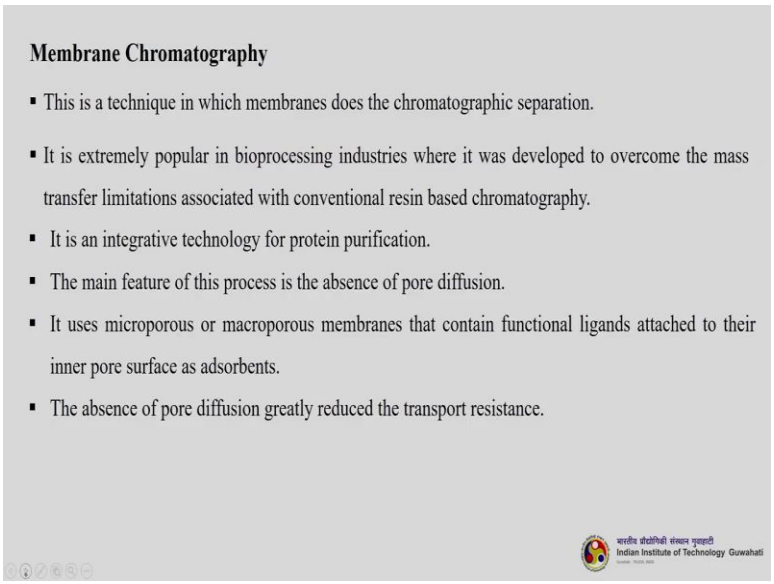

In today's lecture the next topic is membrane chromatography. So you can imagine if you know about chromatographic separation so you can imagine that a membrane is doing the chromatographic separation. So, it is exactly what the membrane does here. It is extremely popular in bioprocessing industries where it was concieved and developed to overcome the mass transfer limitations associated with conventional resin best chromatography, especially for the purification of protein products as well as antibodies.

So it is an integrative technology for protein purification. The main feature for this process is the absence of pore diffusion here so here there is no pore diffusion here. It uses micropores and macroporous membrane that content functional ligand's attached to their inner pore surface as adsorbent. So the absence of pore diffusion greatly reduced transport resistance. Now, as you know, one of the most important features in this bio-processing industry is the protein purification.

And anywhere going to use protein whether it is a therapeutic product or any even such as a food substitute also then you can understand that the type of purity that we eat that we need basically is almost 99%. As you know, no other separation method will give me high purity at chromatographic separation, whether it is adsorption, distillation, absorption liquid-liquid extraction. Just you name it any separation technique nothing will give so high purity than that of chromatography separation. However, the problem with chromatographic separation is cost.

So, chromatographic separation is basically you packed bed separations where separation is happening due to exhaustion, distribution coefficient plays a very important role apart from other parameters that affect that. So, to reduce the chromatographic cost the new techniques being adopted and membrane chromatography aims to do so which will try to address two things first, is this mass transfer limitations? Ok which are actually associated with this chromatographic separation where it is the pecked bed.

Basically, the ligands are there ok, which are packed inside the bed so they are pores in nature to avoid pore diffusion and their mass transfer limitations membrane has been conceived and of course prices also a factor.

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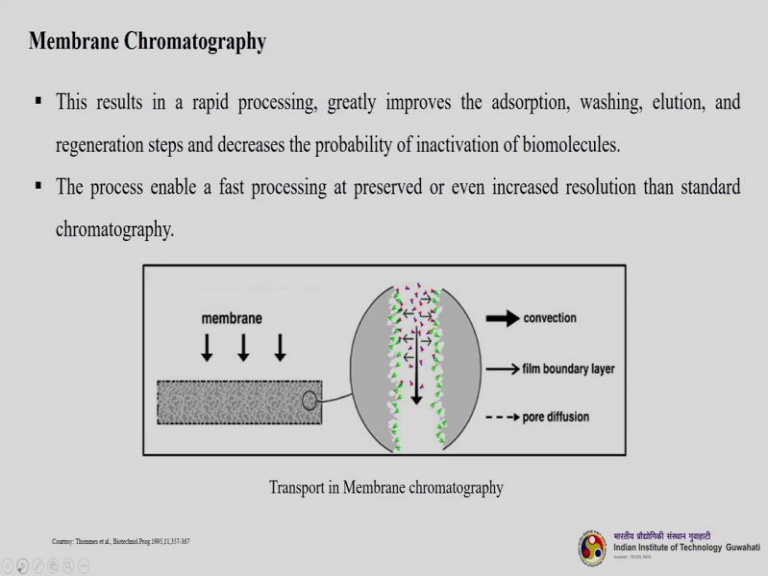

This results in Rapid processing greatly improved adsorption, washing, Illusion and regeneration steps and decreases the probability of inactivation of biomolecules. The process enable a fast processing at preserved or even increase resolution then standard chromatography. This is membrane you can just see and this is one of the pore you can see how different mechanisms are playing an important role. First is convection this is your convection OK then film boundary layer.

These are film boundary layer separation then pore diffusion ok so here pore diffusion is happening right.

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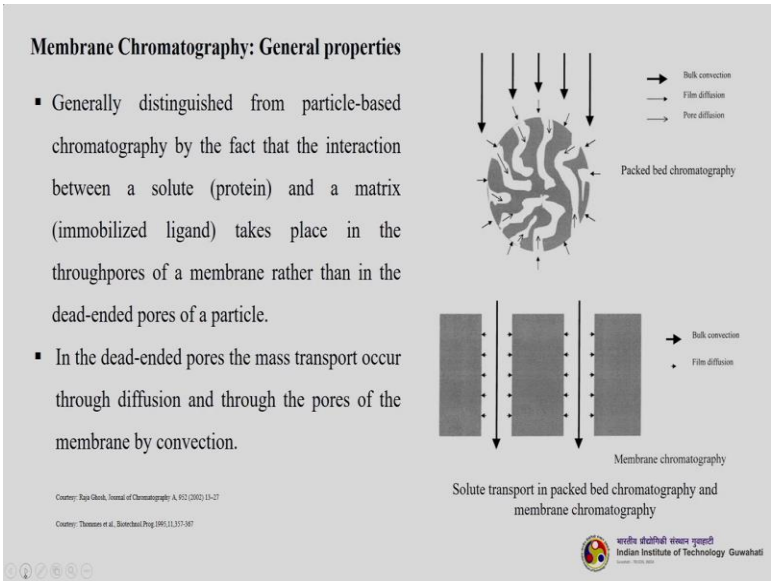

Let us discuss the general properties actually. Generally distinguished form particle based chromatography or we can say resin based chromatography by the fact that interaction between solute and a matrix that is the ligand ok takes place in the throughporse of the membrane rather than in the dead-end prose of the particle we will try to understand what is this meaning actually. So let us see this is here packed bed chromatography.

This is a throughpores that means the pore is open to both sides right whatever is coming this side is again getting out this side or in reverse direction, but you see this is a dead-end pore this dead-end pore, this is a dead pore and there are so many dead-ended pores. The membranes do also have dead-end pored but here we are not talking about that type of membrane. Here you can say that convection is happening ok through the pores only and the dead-ended pores not present.

So, in that sense your bulk convection and film diffusion both this are predominant there is no pore diffusion. This is the advantage if you compare membrane chromatography compared with their traditional resin based chromatography. So that dead-end pores the mass transport occurs through diffusion and through the pore of the membrane by convection. So, the elimination of

pore diffusion significantly reduces the mass transport resistance and fasten the process just increase the rate of the process.

The only transport resistance is due to the film diffusion from the core of the liquid to the membrane surface. So, the chromatographic interaction in the membrane are similar to those of occur in ion exchange hydrophobic and bio or pseudo-affinity interaction.

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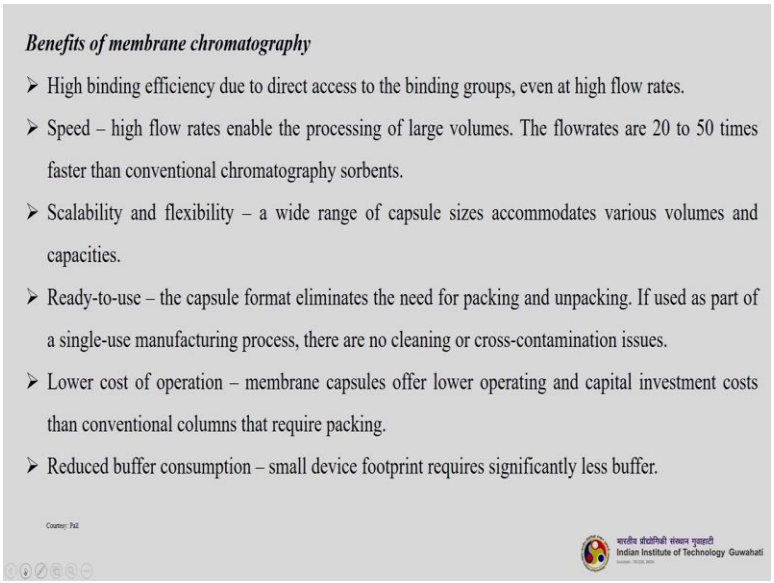

So let us understand the benefit of membrane chromatography. So, the membrane chromatography is having very high binding efficiency due to direct access to the binding group even at high flow rate. So, speed high flow rate enable the processing of large volumes. The flow rates are 20 to 50 times faster than the conventional chromatographic solvents. Scalability and flexibility a wide range of capsule sizes accommodates varies volumes and capacities.

Ready to use the capsule format eliminates the need for packing and unpacking. If used as part of a single use manufacturing process. There are no cleaning or cross contamination issues that is arises. So, lower cost of operation. This is one of the most important aspect in commercialization, the membrane capsule offer lower operating and capital investment cost than conventional columns that require packing.

Reduced buffer consumption that will small device footprint requires significantly less buffer. So these are all various benefits of the membrane chromatography.

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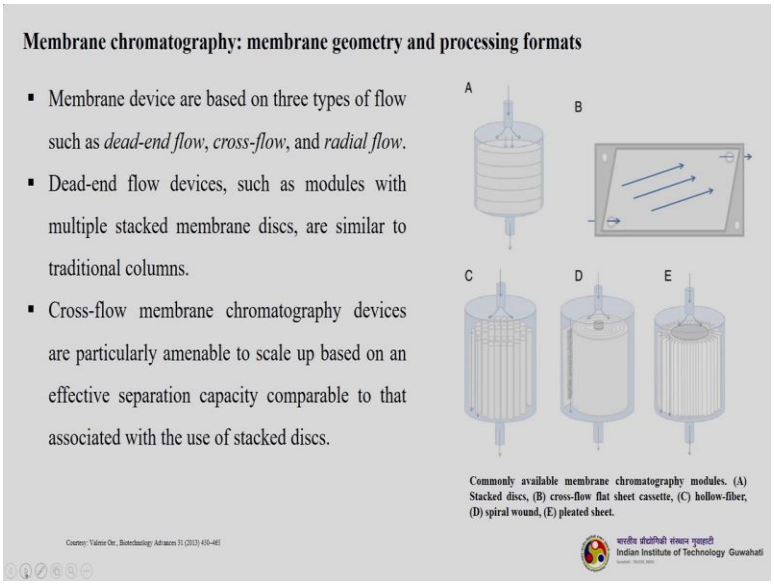

Now let us see some of the geometry and processing format. Let us see how are the different modules are available. So membrane devices based on three types of flow such as dead-end flow, cross flow and radial flow. Dead-end flow control devices such as models with multiple stack memory and disk are similar to traditional columns. So, this is your dead-end stack this ok just the different membranes are packed or stacked together similar to the traditional column.

The cross flow membrane chromatography devices at particular amenable to scale up based on effective separation capacity comparable to that associated with the use of stacked discs. So, we can have cross flow cassette. This is a cross flow cassette then will have hollow fibre systems. We will have spiral wound system. We have pleaded sheet system. Pleated sheet basically you can imagine that I am just trying to draw. It will look something like this.

If you see from the top view and these are the membrane sheets, so you can see this is the cross-section how it looks like right. So the sheets of membranes and stitch together and along a hollow pipe which you can imagine through which your permeates will be collected.

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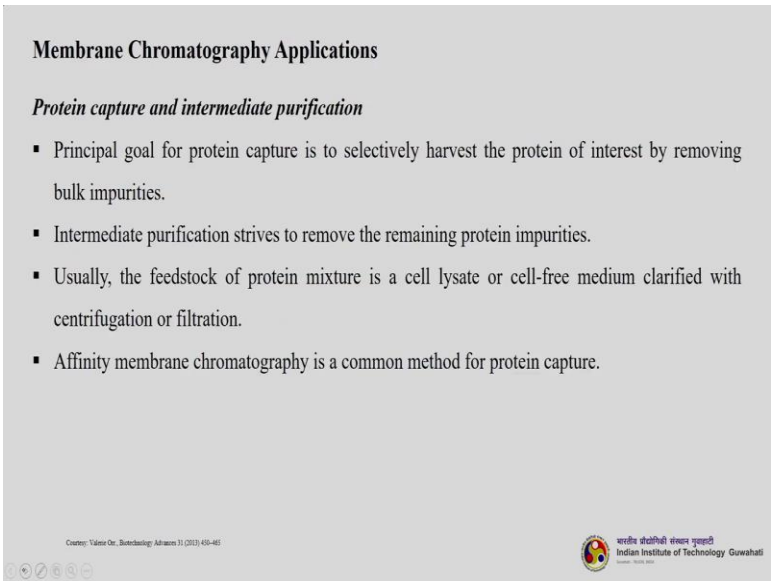

Let us see few application fore most and important applications, of course protein capture and intermediate purification. The principle a goal for protein capture is to selectively harvest the protein of interest by removing multiple impurities it may happened that the protein of our interest is present with various impurities along with other bigger proteins also, ok to selectively separate it. So, intermediate purification start to remove the remaining protein impurities usually the feedstock of protein mixture is a cell lysate or cell free medium ok clarified certification of filters. So, affinity membrane chromatography is common method for protein capture.

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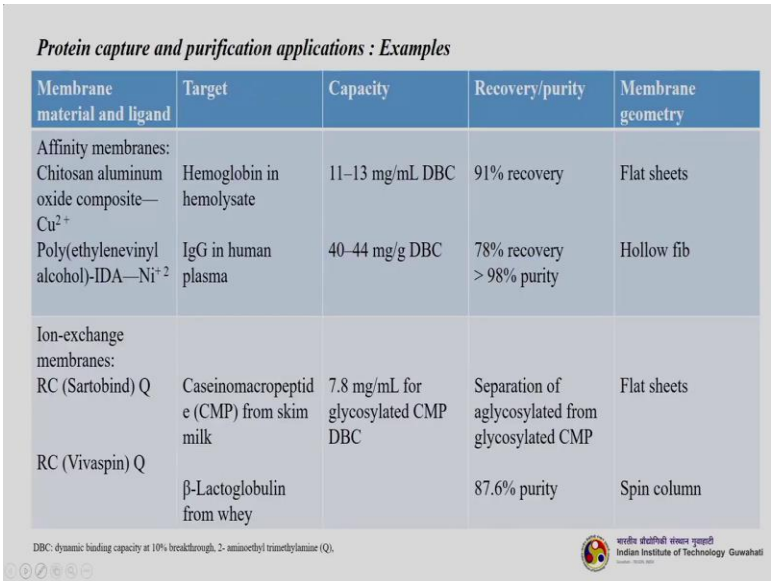

These are few examples given in this tabular format for protein captured purification applications. You can see the all the first column list of the membrane material and ligand, second is the target solute, third is the capacity then you have recovery and purity and membrane geometry. So let us see one, the affinity membranes chitosan Aluminium oxide composite ok. Hemoglobin in hemolysate is the target molecule air capacity is 11 to 13 milligrams per ml.

And 91% recovery flat sheet membranes similarly if you see ion exchange membrane ok, so let us say RC Vivaspin so beta-lactoglobulin from whey is the target molecule on target salute you can say 7.8 millions per millilitre for glycosylated CMP, separation almost 87.6% pure, Spin column is the geometry.

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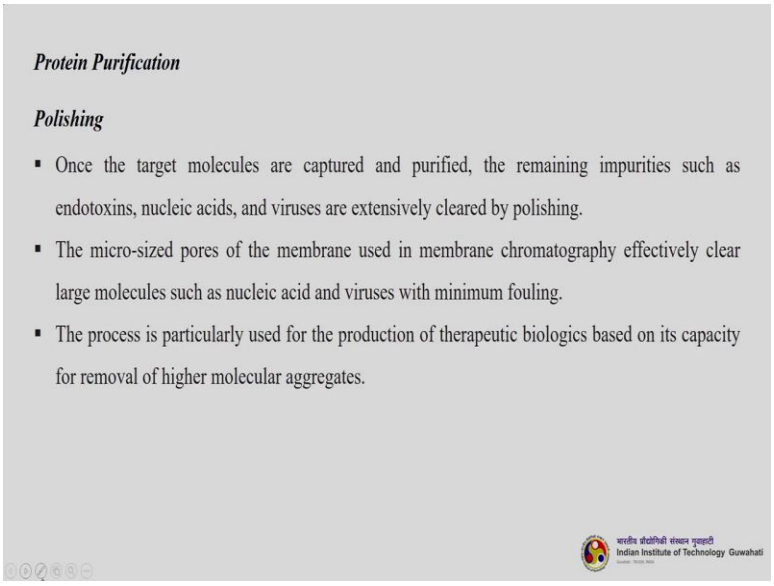

So, protein purification there is a polishing so once the target molecules are captured and purified the remaining imperative sentence endotoxins nucleic acids and viruses are extensively cleared by polishing. The micro size pores of the membrane used in membrane chromatography effectively clear large molecule such as nuclic acid and viruses with minimum fouling. The process is particularly used for production of therapeutic biologics based on its capacity for the removal of higher molecular aggregates.

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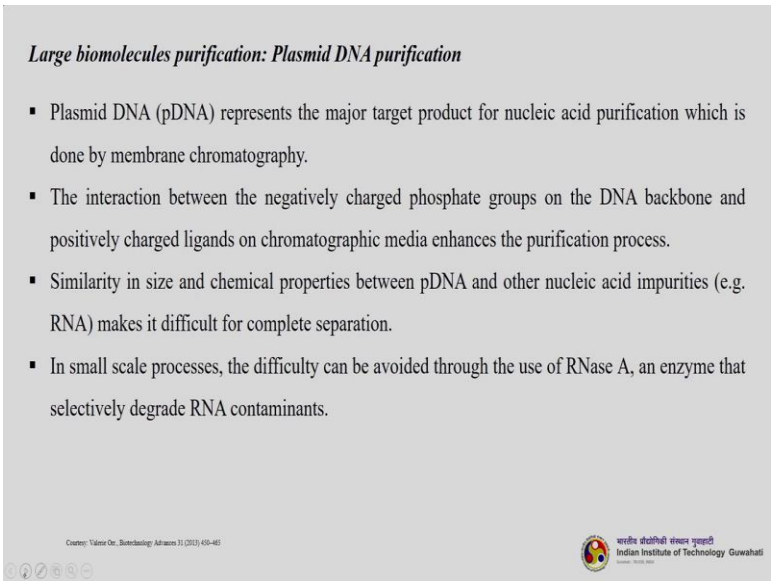

Large bio-molecules purification is for example plasmid DNA purification. Plasmid DNA are known pDNA represents the measure target product for nuclic acid purification, which is done by membrane chromatography. The interaction between the negatively charged phosphate groups on the DNA backbone in the positively charged ligands on the chromatographic media and enhance the purification process. So, you can see how the separation; if you see the ligands let us say this is one ligands ok which is bound to the membrane.

Basically it is positively charged and the DNA molecule let us say this is a DNA molecules and the packed bed side is negatively charged. So this will come and join with each other. They will get attached to each pDNA and other nuclic acid impurities as per example RNA also makes it difficult for complete separation. So, in small scale processes the difficulty can be avoided to the use of RNA is an enzyme that selectively degrades the RNA contaminants because you are only interested in purifying the pDNA.

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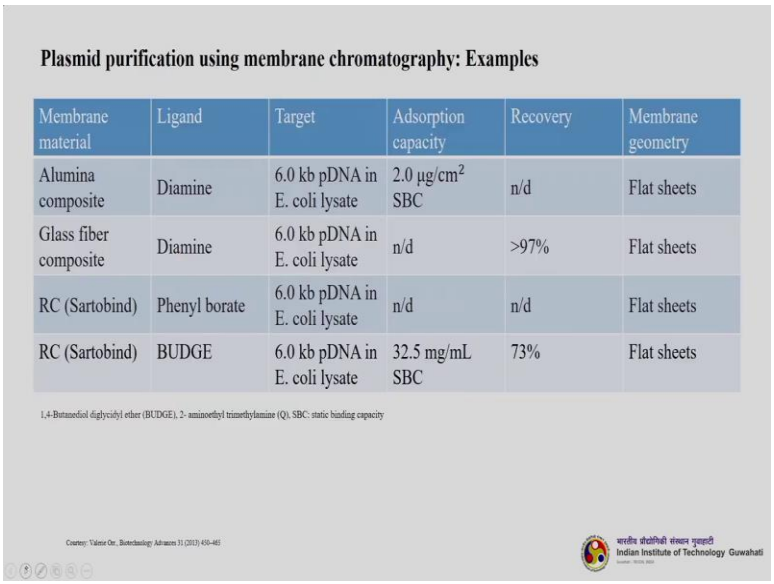

So, plasmid purification using membrane chromatography few example, so if the membrane material is aluminum composite the ligand is diamine target is pDNA in E coli lysite, adsorption capacity is almost 2 microgram per centimetre square recovery data is not given here in this case membrane geometry is flat sheet. So if you talk about RC Sartobind. This is actually the membrane material the brand basically the ligand is budge, target is 6 pDNA E coli lyset 32.5 milligrams per litre is the adsorption capacity, recovery is very good 73%. The membrane geometry is usually flat sheet there are others also.

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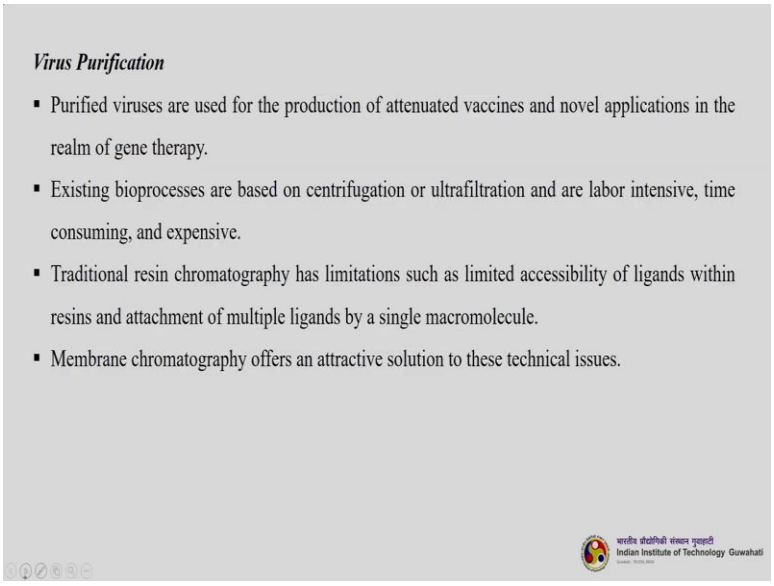

I hope you understand that what are the different types of membrane materials at the capacity? What are the recovery? What is the target solute? OK so the next when is virus purification.

Purified viruses are used for the production of vaccines and mobile applications in the realm of gene therapy. So you need purified viruses that is why the existing bioprocesses are best in usually certrifugation and ultrafiltration again membrane based process and labour intensive time-consuming and expensive too.

Traditional resin chromatography has limitation such as limited accessibility of ligands within resins and attachment of multiple ligands by single macromolecule. So, membrane chromatography offers and attractive solution to this technical issues.

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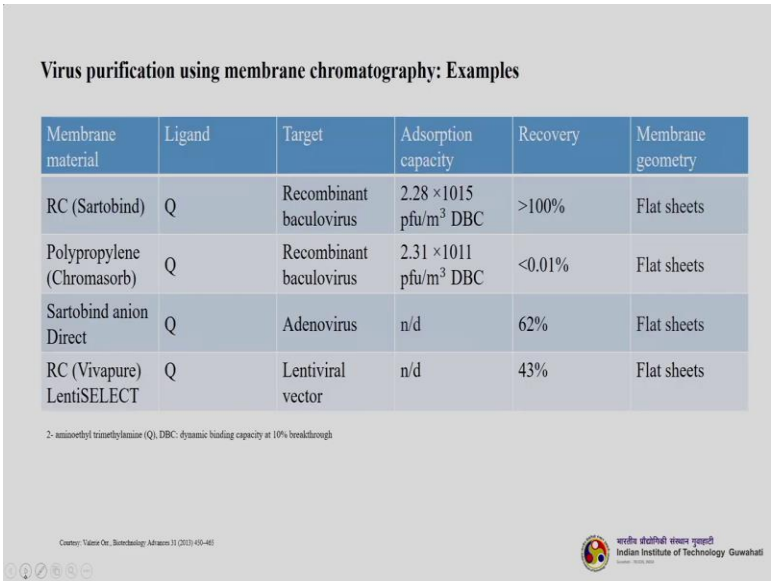

So, different virus purification using membrane chromatography few examples are given here. Again if you see RC the regenerated cellulose basically the ligand is Q target is Recombinant baculovirus adsorption capacity is 2.8 into 10 power of 1015 per metre cube greater than 100% recovery, flat sheet geometry. So, you can just go through it later on to see whether the different types of other viruses that are being removed using different ligands as well as membrane material.

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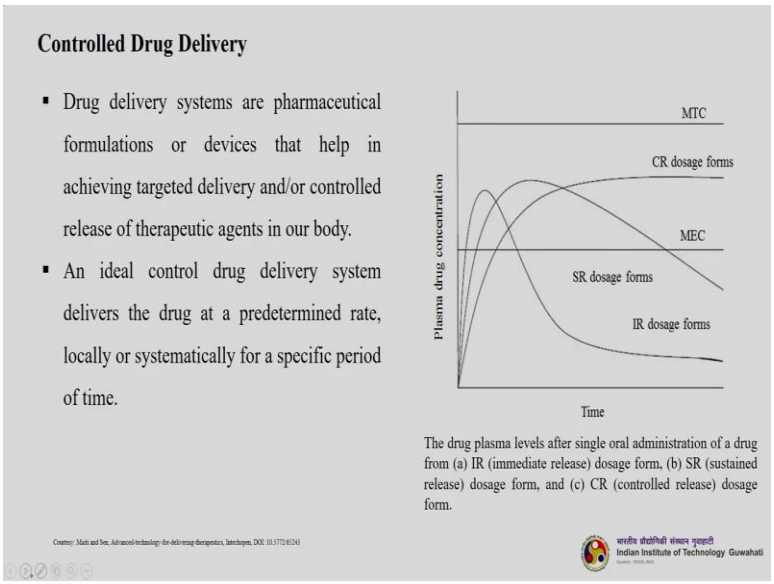

For the next section are that you are going to discuss today is controlled Drug Delivery as I told you in the beginning of the class of controlled Drug Delivery is nothing very new it has been practicing since few years. However due to its inherent advantages there is a huge interest of the scientist, doctors on this particular technology that how to improvise it and make it further beneficial for the human as well as other living organisms.

So drug delivery systems are Pharmaceutical formulations or devices that help in achieving targeted delivery and are controlled release of therapeutic agents in our body and ideal controlled Drug Delivery System delivers the drug at a predetermined rate locally or systematically for a specific period of time plus just have a look at this particular diagram. From this diagram is telling us also here the plasma drug concentration is being prepared with time.

Three types of things are there so the drug plasma levels after single oral administration of drug OK three different types of delivery was done. The fastest IR which is immediate release, this is second is which is called sustained release. This is your SR actually right and the third is controlled release, this is CR just see how the profile cell you see when it is instantaneous or immediate-release so you see that there is a huge speak here.

Ok immediately at the entire drug has been administered inside the cell and there is a huge decrease in the drug concentration with respect to time, sudden decrease and sudden increase

sudden decrease. Now sustained, slowly it is basically sustained release you can see how this is sustained release here little better then still it comes with respect to time, sudden increase then it is coming time is better than the higher, however this is also not very good.

Look at the CR control release. You can see how slowly the concentration is increasing and it is maintaining reaching the saturation almost after a certain time. And the concentration remains constant for a particular period of time. So this is called controlled drug delivery and it is always better than the IR and SR form of delivery.

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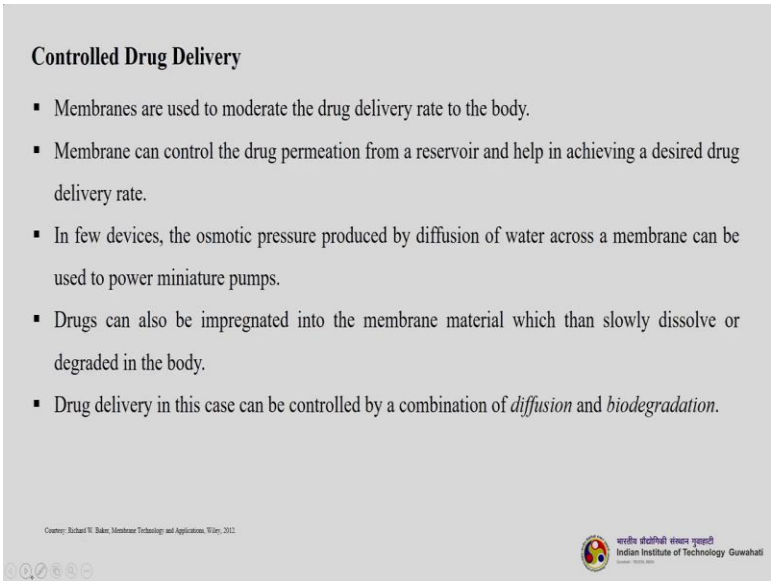

So membrane are used to moderate the drug delivery rate to the body that is the job of membranes actually. Membrane can control the drug permeation from reservoir and help in achieving a desired drug delivery rate. In few devices the osmotic pressure produced by diffusion of water across the membrane can we use to power miniature pumps. Drugs can also be impregnated into the membrane material which then slowly dissolves or degenerated in the body.

Drug delivery in this case can be controlled by a combination of diffusion and Biodegradation ok this is very important.

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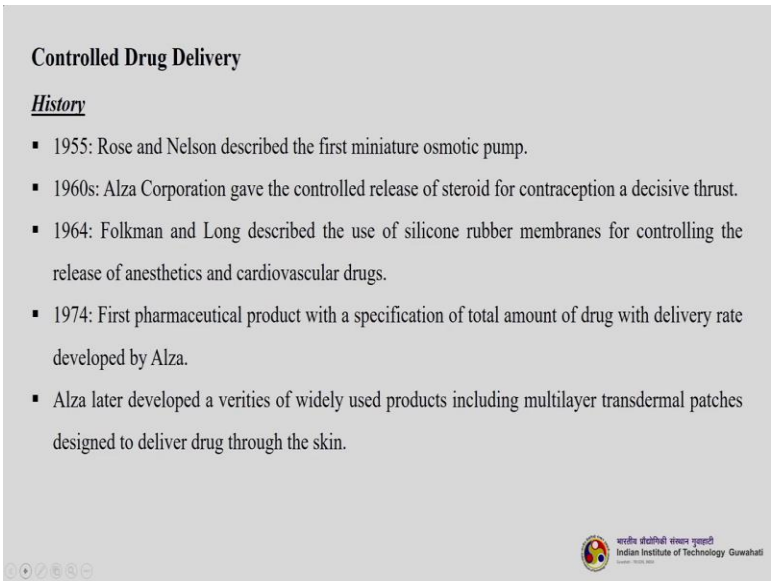

So if you look back little to the history of the drug delivery in 1955 Rose and Nelson describe the first miniature osmotic pump to deliver the drugs inside the human body. In 1960 Alza Corporation get controlled release of steroid for contraception a decisive thrust. In 1964 Folkman and Long describe the use of silicon rubber membranes for controlling the release of anesthetics and cardiovascular drugs.

Then in 1974 first Pharmaceutical product with specification of total amount of drug is delivery rate was developed by Alza. Alza is a leading pharmaceutical company later and same company developed varieties of widely used products including multilayer transdermal patches design to deliver drugs through the skin.

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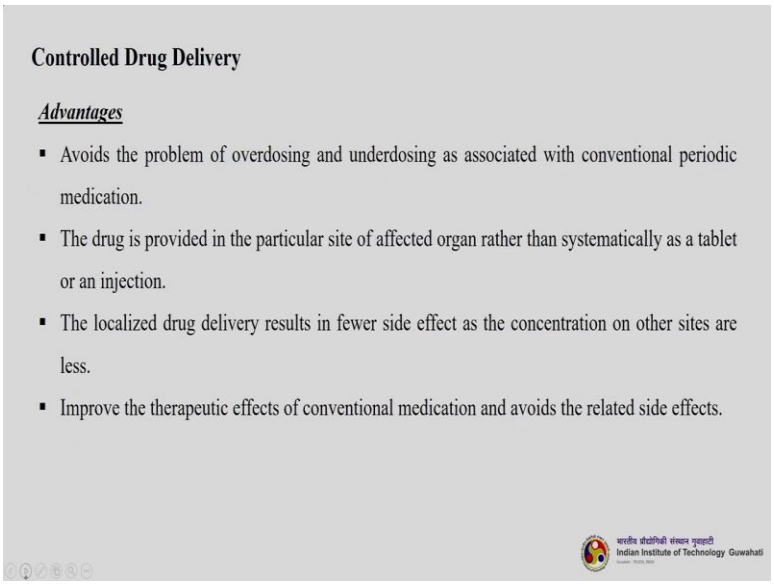

The advantages of drug control drug delivery. It avoids was the problem of overdosing and underdosing as associated with conventional periodic medication. The drug is provided in the particular site of the affected organ then rather than systematically as tablet or injection. The localised drug delivery results in fewer side effect is the concentration on the other sides are less improve the therapeutic effects of conventional medication and avoids the related side effects.

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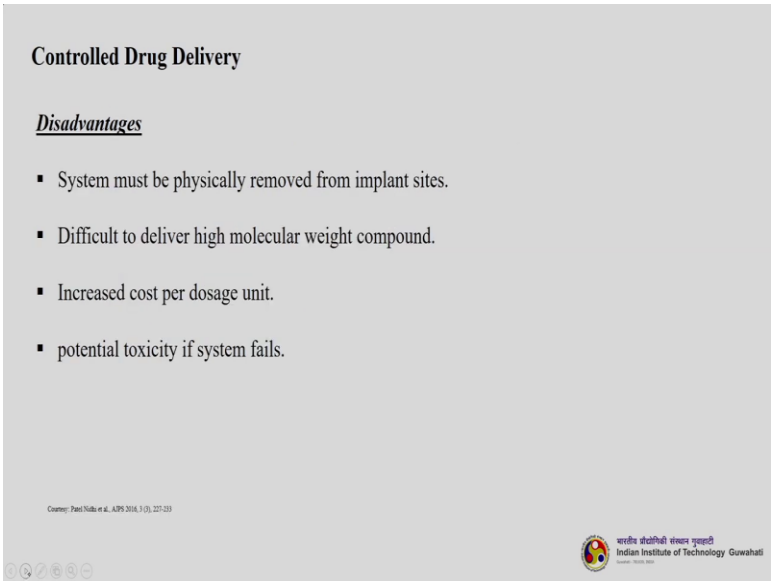

There are few disadantages also but system must be physically removed after it has done its delivery from the implant sites. So difficult to deliver high molecular weight compounds because the dispersion takes long time and do not get properly dispersal and few will remain inside the

capsule. Increased cost for dosage unit and potential text toxicity to the entire system body if the system do not work or it fails,

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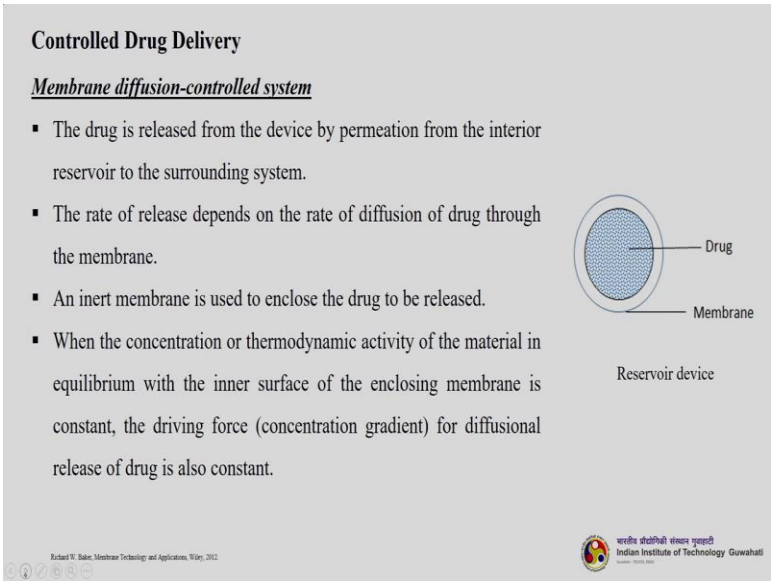

So, huge amount of work is still going on for controlled Drug Delivery will see one or two such very interesting works. So it is a membrane diffusion control system, so in this system the drug is released from the device by permeation from the interior reservoir to the surroundings system you just you see this particular think, this is the membrane ok and inside this membrane capsule your drug is being inserted or packed whatever it is you can say in that way.

So the drug will release through the membrane something like this to the tissue that the surrounding filed, so the rate of release depends on the rate of diffusion of drug through the membrane. So, here what is happening the rate of diffusion of the drug is the most important factor that is the driving force basically, so concentration difference is there and compared to here it will be more so obviously from higher to lower.

And inert membrane is used to enclose the drug to be released when the concentration of thermodynamics activity of the material in equilibrium with the inner surface of the enclosing membrane is constant the driving force that is concentration gradient for diffusional release of drug is also constant.

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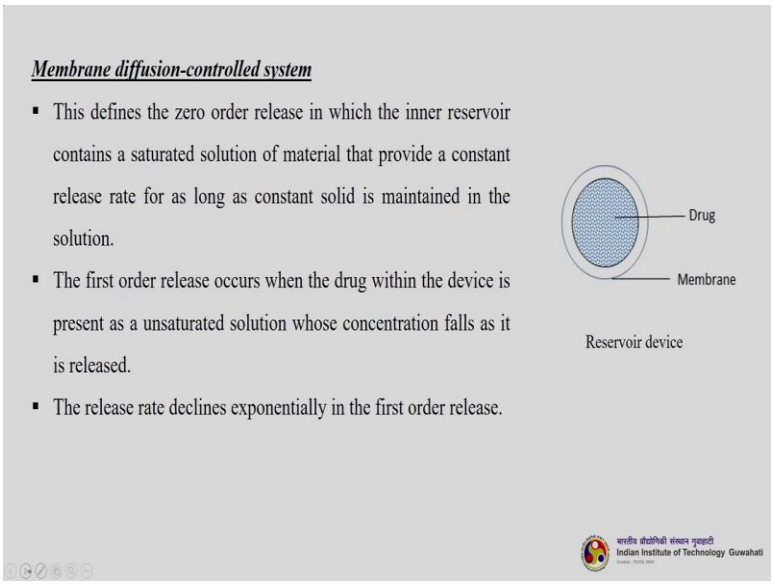

This defines the zero order release in which the inner reservoir contains a saturated solution of a material that provides a constant release rate for as long as constant solid is maintain inside the solution. So, the first order release occurs in the drug within the device is present as unsaturated solution which concentration falls as it is released. So the release rates the declines expontially in the first order release instantaneously it is releasing basically.

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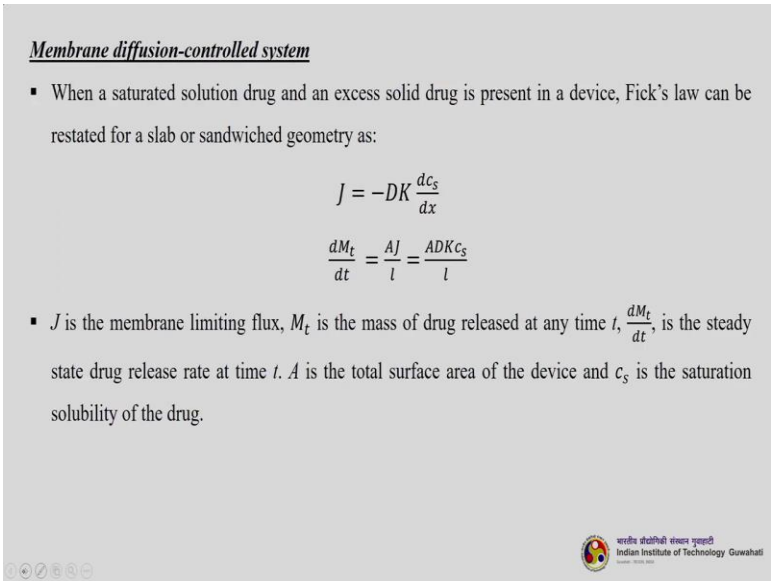

So when a saturated solution drug and excess solid drug is present in a device Fick's law can be applied. So, for a slab or sandwiched geometry J equals to –DK dc s by dx dM t by dt equals to AJ by l which is equal to A K cs by l again substituting J from here, right? So J is the membrane limiting flux M t is the mass of the drug release at any time t that is dM t by dt is the steady-state

drug release date at time t, A is the total surface area of the device and C s is saturation solubility of the drug.

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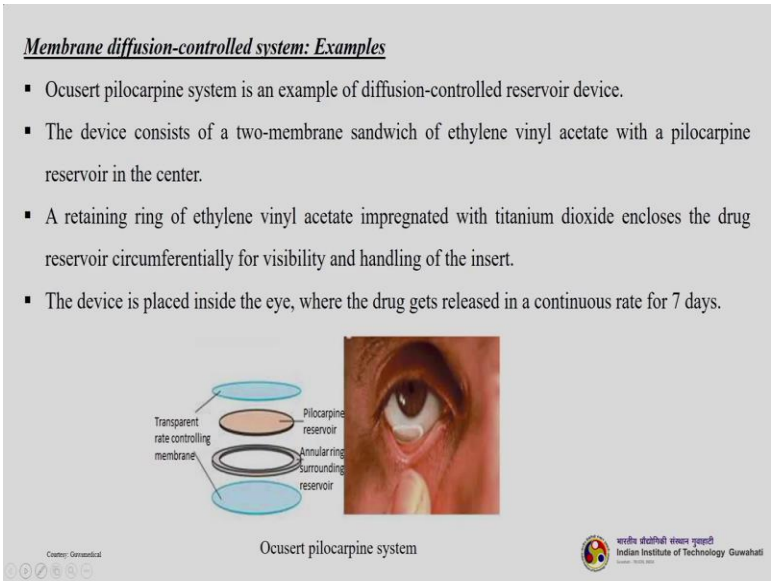

So, let us see one example of the membrane diffusion control system. So one classic example is the Ocusert pilocarpine system which are some sets of you can see here this is a small very small device ok transparent basically, which is being implanted inside the eyes. The device consists of two membrane sandwich of Ethylene Vinyl Acetate with pilocarpine, pilocarpine reservoir in the center. This is the reservoir ok this one and the two membrane. This is one member in this is one member and this is of course the annular ring which is holding this pilocarpine a reservoir.

So a retaining ring of Ethylene Vinyl Acetate impregnated with Titanium dioxide encloses the drug reservoir circumferential for visibility and handling of the insert. The device is placed inside the eye when the drug gets released in a continuous rate for 7 days.

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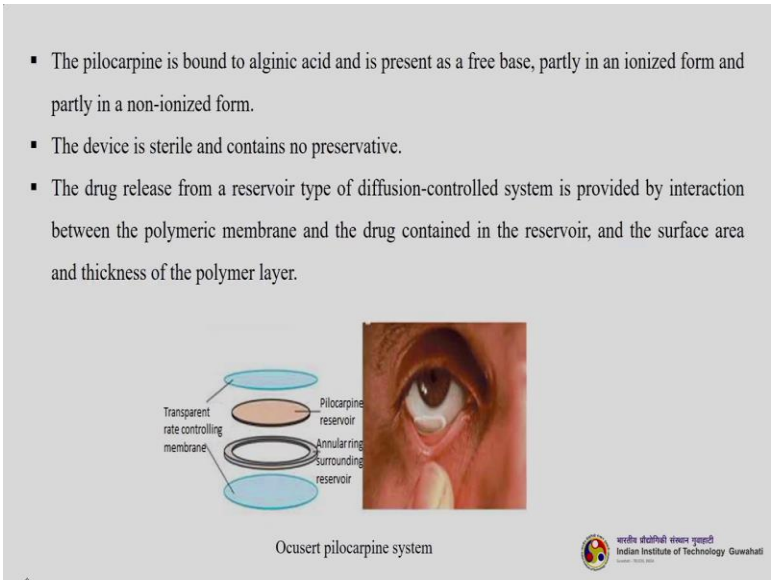

The pilocarpine is bound to alginic acid and his present as free base partly in an ionized form and partly non-ionized form. As the device sterile and contains no preservatives the drug release from a reservoir type of diffusion control system is provided by interaction between the polymeric membrane and the drug contain in the reservoir and the surface area and thickness of the polymer layer.

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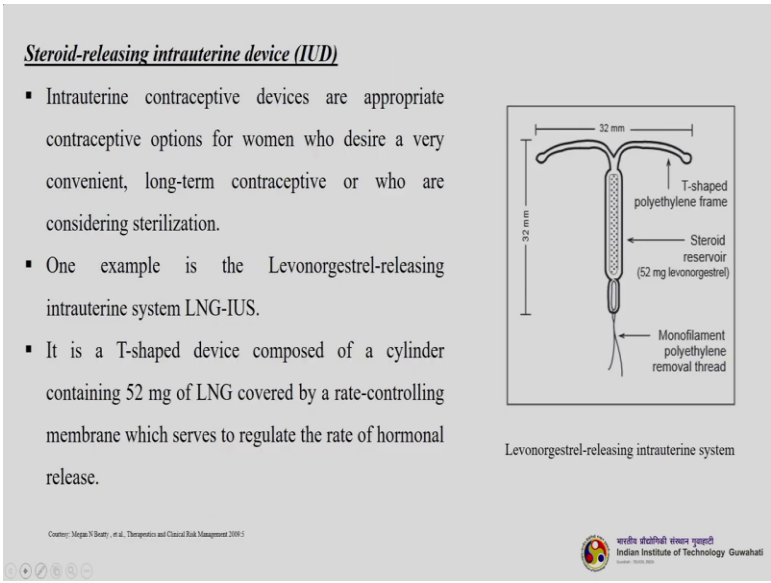

Another example is steroid releasing intrauterine device which is called IUD intrauterine contraceptive devices are appropriate contraceptive options for women who desire very convenient long term contraceptive for who are considering sterilization. So, one example is the Levonorgestrel releasing intrauterine system which is popularly known as LNG-IUS. It is T-

shaped device you can see how it looks like composed of a cylinder containing 52 grams of LNG this is a cylinder which contains 52 grams of LNG covered by a rate controlling membrane which serves to regulate the rate of hormonal release.

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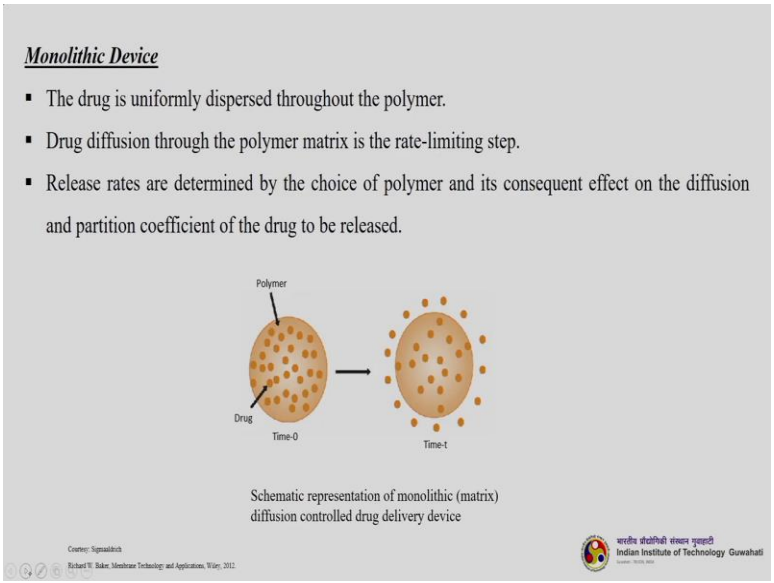

Another one is Monolithic device that drug is uniform be dispersed to the polymer drug diffusion through the polymer matrix is the rate limiting step. Release rates are determined by the choice of polymer and its constituent effect on the diffusion and partition coefficient of the drug to be released. So you can see here in the drugs are actually very uniform getting dispersion centre polymer matrix at time equals to zero at time equals to t the drugs are decreasing out of the matrix.

So the release profile depends on the loading of the dispersion the nature of the components in the geometry of the device. Problems associated with reservoir system such thin spots, pinholes or other similar defects do not substantially alter the release rate of the monolithic device.

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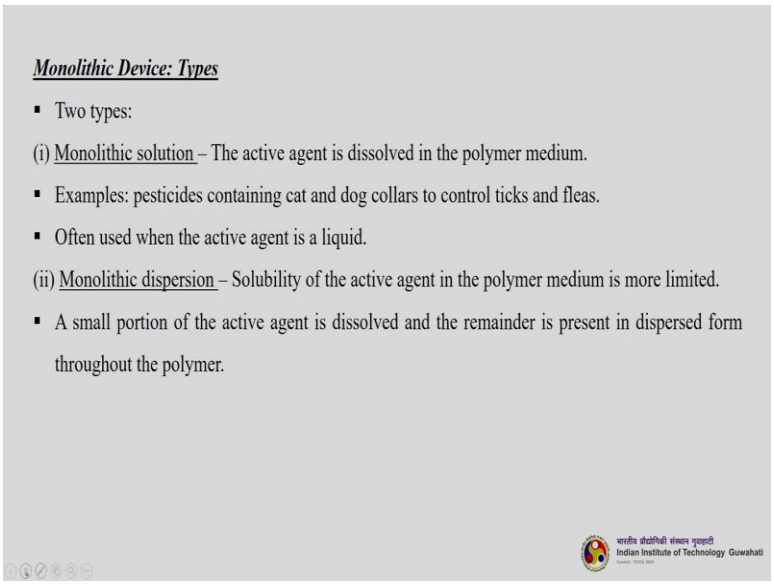

Two types of Monolithic devices are found one is Monolithic solution and other is monolithic dispersion. In Monolithic solution the active agent is dissolved in the polymer medium, so examples are pesticides containing cat and dog collars to control ticks and fleas often used when the active agent is a liquid. Monolithic dispersion is something in which the solubility of the active agent in the polymer medium is more limited small person of the active agent is dissolved in the remainder is present in disperse form throughout the polymer.

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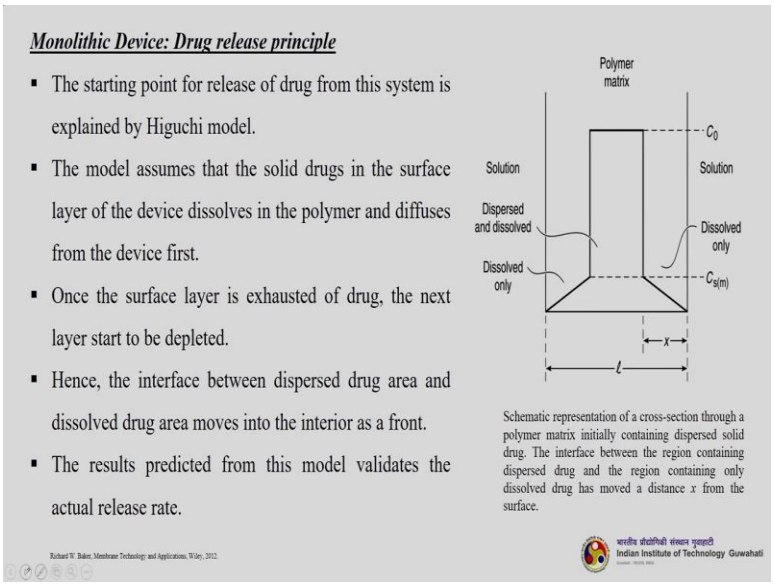

Let us understand the principle of Monolithic drug release the starting point for release of the drug from this system is explained by Higuchi model. The model assumes that the solid drugs in the surface layer of the device dissolves in the polymer and diffuses from the device first. Once

surface layer is adjusted for the of drug the next layer start to be depleted hence the interface between the dispersed drug area and the dissolved drug area moves into the interior as a front. The results predicted from this model validate the actual release rate.

You can see this is a schematic representation of a cross section through a polymer matrix initially containing dispersal drug. So the interface between the region containing discussed in the region containing only dissolved drug as moved a distance x from the surface.

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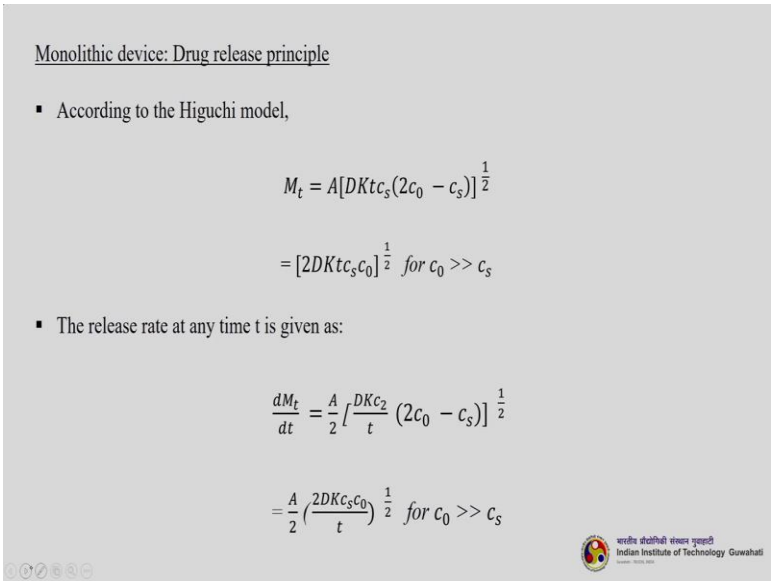

So according to the higuchi model, we can write the mass of drug that is released with at a time t is A into DK tc s 2c 0 – c s to the power of 1/2 so when c 0 get tendencies. So, M t is equals to 2 DK tcs c0 to the power of 1/2. The release rate at any time we can write dMt by dt is equals to A by 2 to DK c2 by t 2 c0 - cs to power 1/2 or when the c0 become greater than cs then we can write A by 2 into 2 basically 2 into DK cs c0 this is completely like this you should not get confused with equations.

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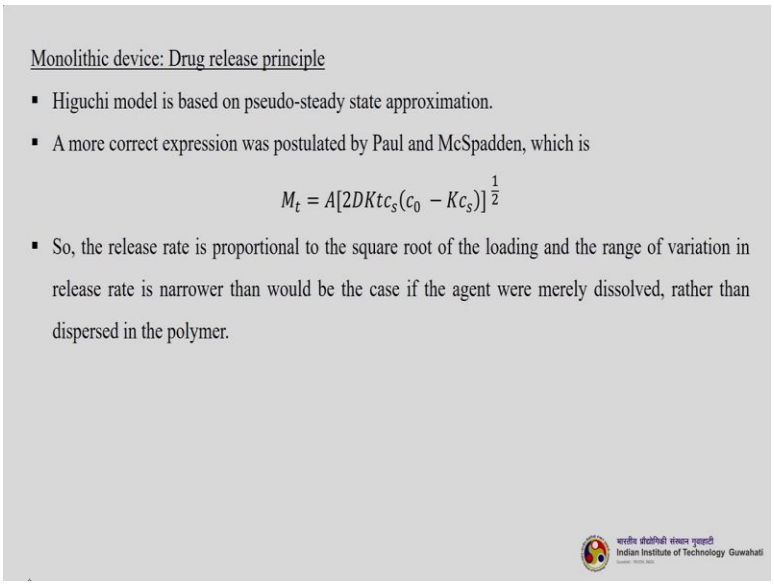

Higuchi model is based on pseudo-steady state approximation. A more correct expression was postulated by Paul and McSpadden, which is M t equals to A 2DK tcs c0 – Kc s to the power 1/2 so here the release rate is proportional to the square root of loading and the range of variation in release rate is narrower then would be the case in the agent were merely dissolved rather than dispersion polymer.

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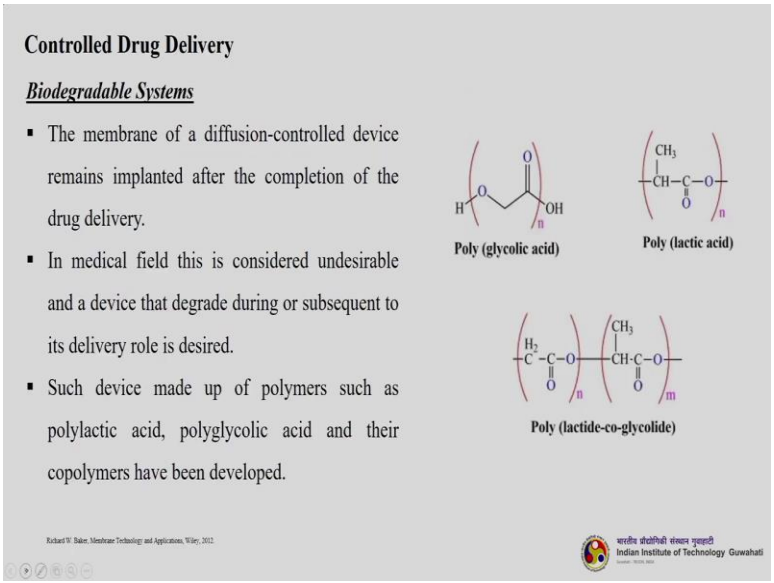

So, then another system biodegradable system under control drug delivery, the membrane of a diffusion controlled device is mainly elements implanted after the completion of the drug delivery. So that is what it is greatest disadvantage because you need to take the, take it out from the body in medical field, which is considered undesirable and a device that degrade during a

subsequent to its delivery is desired such device made up of polymer such as poly lactic acid polyglycolic acid copolymer have been developed. So, they will dissolve once the drug delivery is done.

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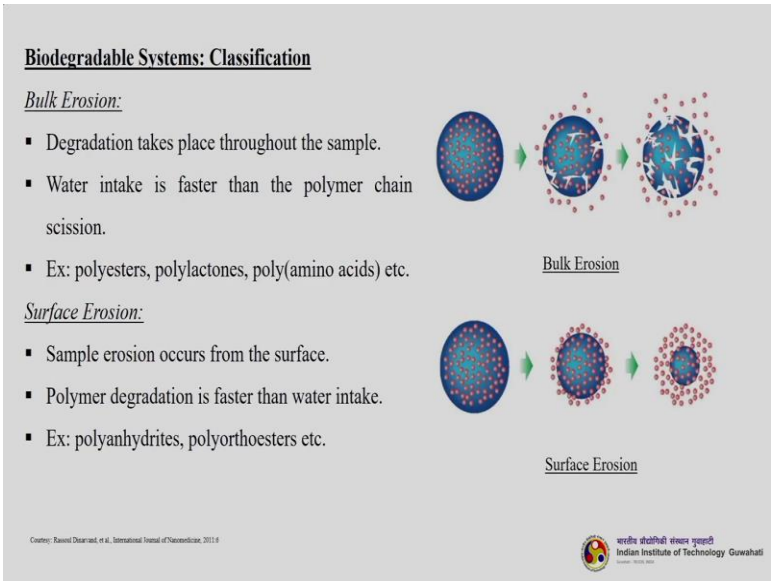

So two types of actually the classification of biodegradable system one is bulk erosion and another is surfaces erosion. So in bulk erosion the degradation takes place throughout the simple water intake is faster than the polymer chain system polyesters, polyolactones polyamino acids are the examples and in surface erosion simple erosion occurs from the surface. Nothing is getting inside basically polymer degradation is very faster than the water intake so polyanhydrite, polyorthoesters are the example surface erosion system.

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Few examples of biodegradable polymeric nanoparticle and their importance

Polymer	Method of synthesis	Cargo	Therapeutic improvement
Poly (lactic acid-co-glycolic acid)	Emulsion solvent evaporation	Finasteride	Improved drug loading efficiency and pharmacokinetic profile
	Double emulsion solvent evaporation	Exenatide	Improved cellular uptake and hypoglycemic effect on oral administration
Polylactic acid	Nanoprecipitation	Docetaxel	Improved cytotoxicity and apoptosis
Polyanhydrides	Anti-solvent nanoencapsulation	Mitochondria-targeted apocynin	Better protection from oxidative stress-induced mitochondrial dysfunction and neuronal damage
Chitosan	Electrostatic self-assembly process	Insulin	Improved controlled release, stability at various acidic and basic conditions and showed noncytotoxic response
Polyphosphoesters	Ionic gelation method	Sorafenib, paclitaxel and siRNA	Potential for the delivery of multiple drugs and diagnostic agents
Polyurethanes	Electrostatic interactions	Doxorubicin	Greater anti-tumor efficacy and cellular internalization
Poly(caprolactone)	Nanoprecipitation method	Aripiprazole	Pharmacokinetics exhibited improved brain targeting efficacy which will help to reduce dose related toxicities

Courtesy: Shiv KumarPrajapati, et al., European Polymer Journal, 120 (2011), 108191

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These are the examples of biodegradable polymer nanoparticles and their importance. You can go through it later on. I just tell the poly lactic acid is a polymer nanoprecipitation is the method of synthesis of docetaxel is the cargo and improved therapeutic improvement is improved cytotoxicity and practosis like there are many you can just go through it later on. I am just skping it.

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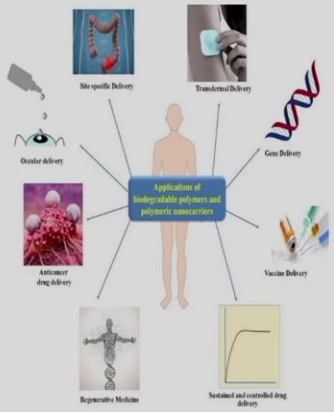
Biodegradable Systems: Applications

- The biodegradable polymeric biomaterials have improved the drug delivery applications and further refining applications in pharmaceutical and biomedical field.
- Recent breakthrough in controlled drug delivery system (CDDS), sustained release drug delivery system (SRDDS), vaccine, nucleic acid, protein, and anticancer drug delivery and tissue engineering, regenerative medicine, have paid attention toward biomaterial which are biodegradable.



Courtesy: Shiv KumarPrajapati, et al., European Polymer Journal, 120 (2011), 108191

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Indian Institute of Technology Guwahati

So, bio-degradable system application, biodegradable polymeric biomaterials have improved the drug delivery applications and for the refining applications in Pharmaceutical and biomedical field. So you can see the different types of applications regenerative medicine sustain and

controlled Drug Delivery, vaccine delivery, scissoring delivery, transdermal delivery, site-specific delivery, occular delivery and anticancer drug delivery.

Recent breakthrough in controlled Drug Delivery System sustained release Drug Delivery System vaccine nuclic acid protein and anticancer drug delivery in tissue engineering and regenerative medicine have paid attention towards biomaterial which are biodegradable.

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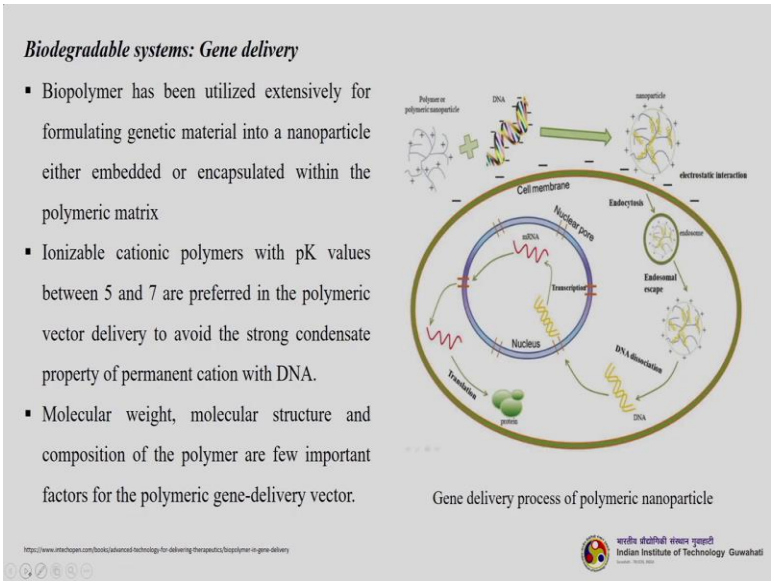

Another such application of biodegradable system in the gene delivery, biopolymer has been utilised extensively formulating genetic material into nanoparticle embedded or encapsulated within the polymer matrix. Do ionizable cationic polymers with pK values are between 5 and 7 are preferred in the polymeric vector delivery at to avoid the strong condenser property of the permanent cation with DNA.

So, molecular weight, molecular structure, composition of the polymer for few important factors for the polymer gene delivery factor, so this is how it is actually drug delivery process was using a polymeric nanoparticles.

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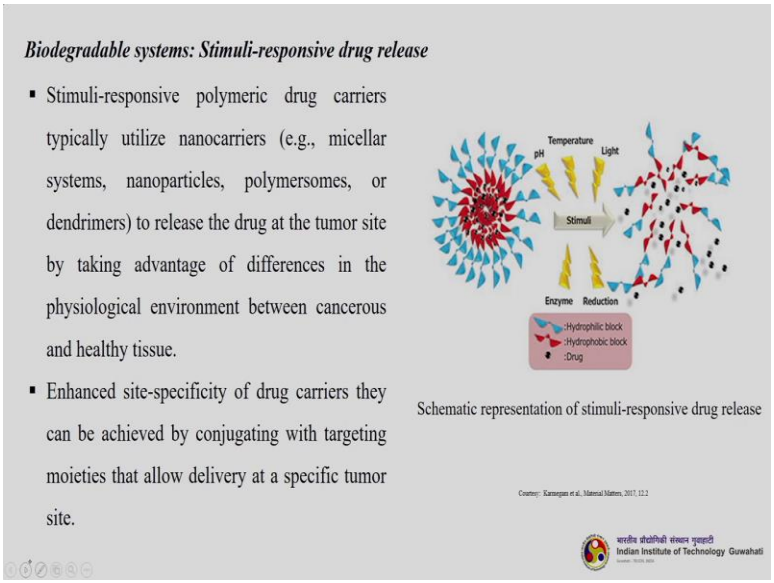

The next one is stimuli responsive drug release, so stimuli responsive polymeric drug careers typical utilize nano-careers micellar systems, nanoparticles, polymorphisms, or dendrimers to release the drug at the tumor side by taking advantage of differences in the physiological environment between the cancerous cell and the healthy cell. So there is physiological environment difference between the cancerous cell and healthy cell. So that is the basically the driving force.

So, enhanced site specificity of drug careers that can be achieved by conjugate in with targeting moieties that allows; drug delivery at a specific tumor site. So you can see this particular schematic diagram so you see the blue is actually the hydrophilic block that is the hydrophobic block and the blacks are the dots are the drugs which are embedded in the hydrophobic block here. Then which stimulates so that means pH temperature light enzyme reduction any of these are combination of this ok will result in degrading the entire structure that by releasing the drug from the hydrophobic block.

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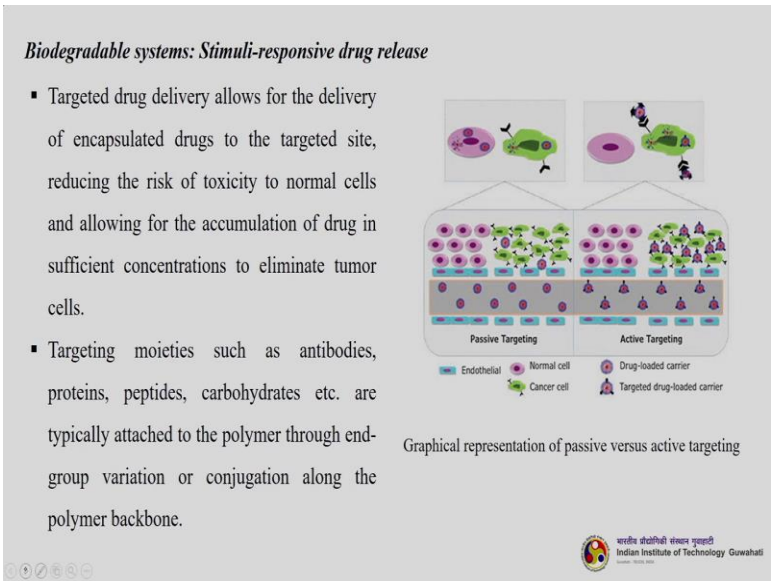

So, targeted Drug Delivery allows for the delivery of encapsulated drugs to the targeted site reducing the risk of toxicity to normal cells and applying for the accumulation of drugs in the sufficient concentrations to eliminate tumor cells. Targeting moieties like antibodies, proteins, peptides, carbohydrates etc are typically attached to the polymer through end group variation on conjugation along the polymer backbone.

This is the graphical representation of passive versus active targeting how 2 different types of targeting methods or mechanism and being adopted one is passive and other is active.

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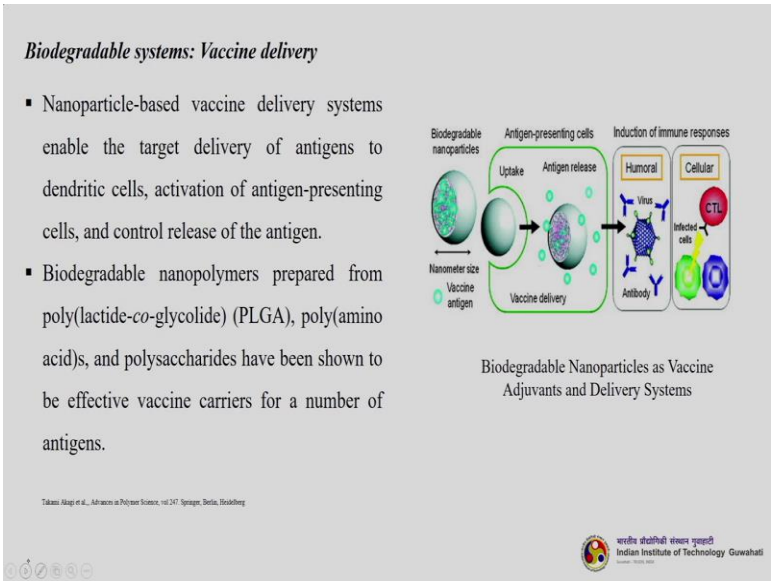

So another example is vaccine delivery so nanoparticle-based vaccine delivery system enable the target delivery of the antigens to dendritic cells. Activation of antigen representing cells and controlled release of the antigens you can see the biodegradable and particle is vaccine adjuvants and delivery system. so bio-degradable nanoparticles, ok nanomaterials vaccine is the antigen then how you can see how antigen representing the cell.

So once you get data and induction of human response will happen upon that the antibody will be detached ok and then of course there will be infected cells which can be taken out of being separated. So, biodegradable nano polymers prepared from poly lactide glycoside which is known as PLGA poly amino acids, polysaccharide shown to be effective vaccine careers for a number of antigens.

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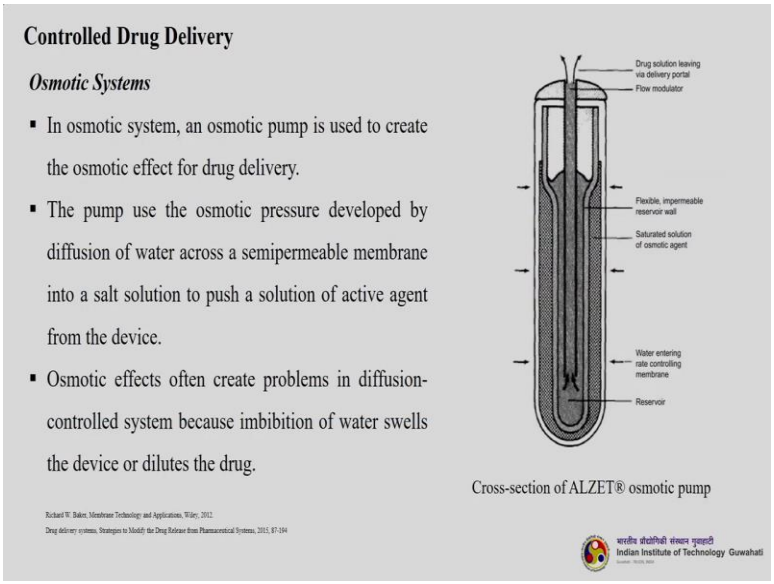

And another examples osmotic system design, very popular actually in osmotic system in osmotic pump is used to create the osmotic effect for drug delivery. What is happening here the pump use the osmotic pressure developed by the diffusion of water across a semipermeable the pump use the osmotic pressure developer diffusion of water across a semipermeable membrane into a salt solution to process solution for active agent from device.

The osmotic effect often create problems in diffusion control system because inhibition of water with the device or dilute the drug. This is the cross section of Aljet osmotic pump manufactured

by this particular company. You can see this is the drug solution leaving via delivery portal from here. The flow modulator will be here flexible impermeable reservoir valve a saturated solution osmotic or we can say osmotic solution water entering the rate controlling membrane here basically here, right? And then Osmosis will happen.

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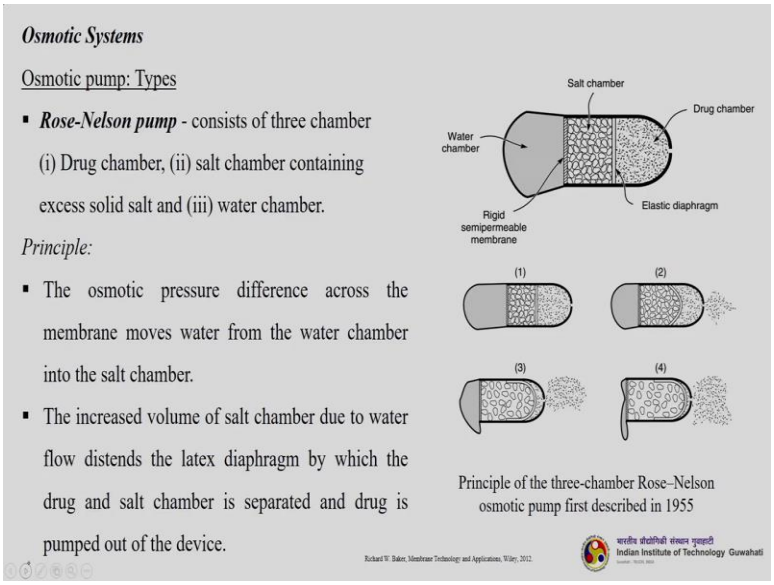

There are different types of osmotic pumps the first one will discuss is about Rose Nelson Pump It is very common. It consists of three chambers one is drug chamber and there is a salt chamber containing excess solution and another is water chamber. This is water chamber. This is salt number containing excess salt and this is a drug Chamber. Ok this is how a Rose Nelson pump looks like the principle is that the osmotic pressure difference across the membrane moves water from the water chamber into salt chamber.

So, when there is a osmotic pressure difference across the membrane here, this is your membrane then water will move from the salt; the water from the water chamber to the salt chamber the increase volume of solid chamber due to water flow distance the latex diaphragm by which the drug and salt number is separated. This is her. This is not a membrane this is a elastic diaphragm and salt chamber is separated and the drug is pumped out off the device here.

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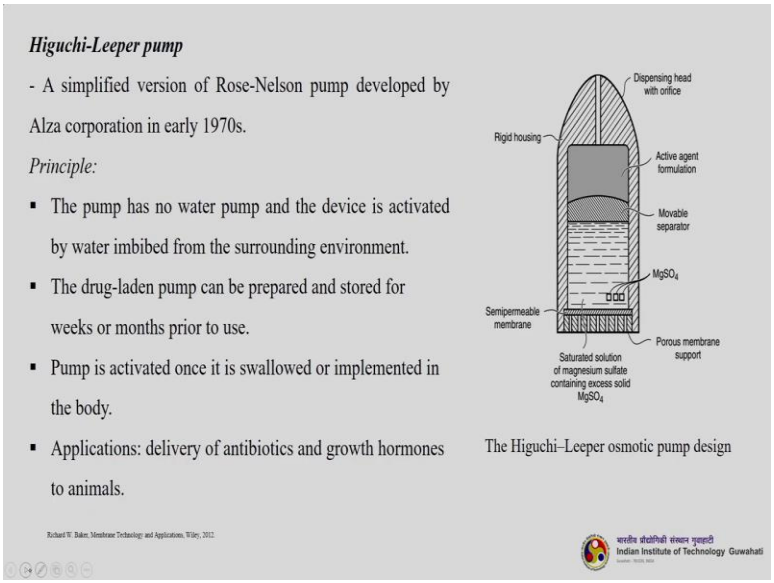

So a simplified version of the Rose Nelson pump developed by Alzak corporation is in the early 1970. So this is Higuchi Leeper pump. The principle is the pump is no water pump in the device is activated by water imported from the surrounding environment the drug pump can be prepared and store for week or months prior to use pump is activated once it is swallowed and implemented in the body.

Application is delivery of antibiotics and growth hormones to animals. This is the Higuchi Leeper pump design how it looks like ok you can just refer it later.

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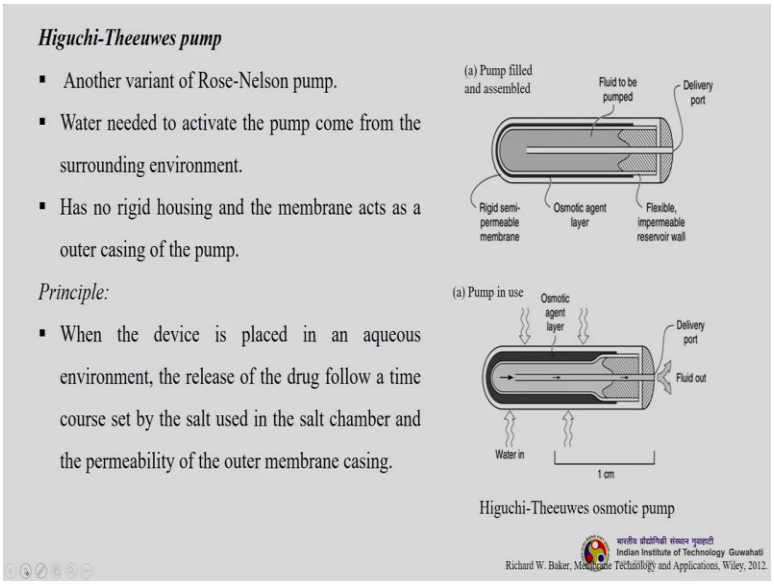

Another one is Higuchi Theenwes pump this is another variant of the Rose Nelson pump water needed to activate the pump that comes from the surrounding environment. So, has no rigit housing and the membrane acts as the outer casing of the pump. So the principle is that when the device is placed in a aqueous environment the release of the drug follows at time course set by the salt used in the salt chamber and the permeability of the outer membrane casing

So, you can see how that Higuchi Theeuwes osmotic pump looks like this is the rigid semipermeable membrane here. Ok this is osmotic layer this black one then the flexible impermeable reservoir are getting deposited here and then there is delivery port here. So whenever you will receive it here.

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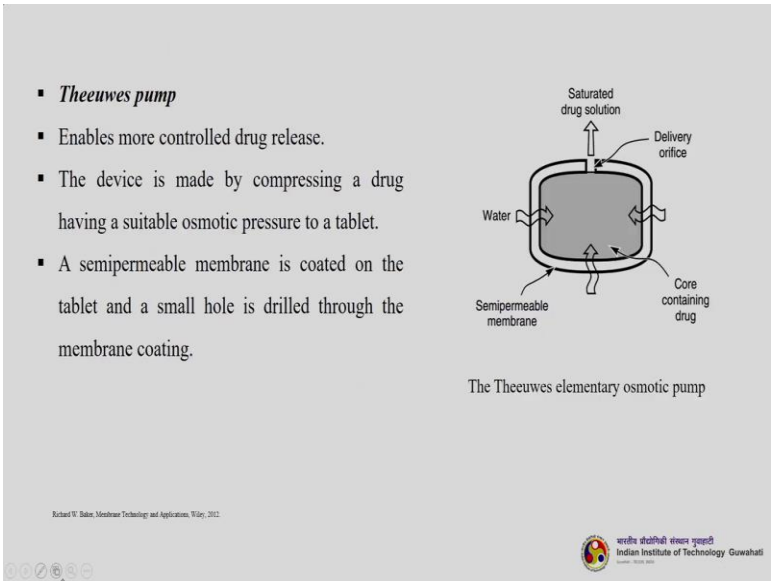

Another one is Theeuwes pump enables more control drug release, so you see how it is happening. So these are elementary osmotic pressure of the semipermeable membrane water is getting inside, so the core containing this is here the drug and then we get saturated solution here. The device is made by compressing a drug having a suitable osmotic pressure to a tablet. The semipermeable membrane is coated on the tablet and how small hole is drilled through the membrane coating.

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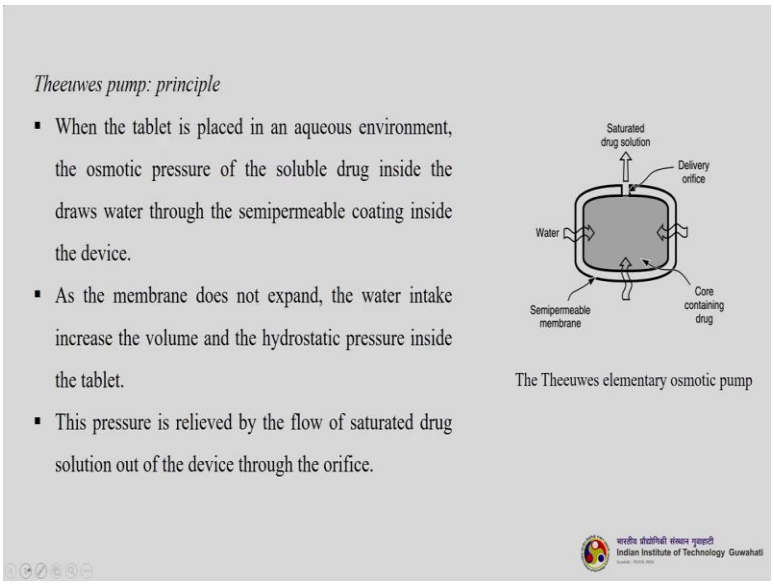

When the tablet is placed in a aqueous environment the Osmotic pressure of the solubility of drug inside the drugs water inside draws water through the semi permeable cutting inside the device is the membrane does not expland the water intake increase the volume in the hydrostatic pressure inside the tablet. This pressure is released by the floor saturated drug solution and out of the device through the orifice.

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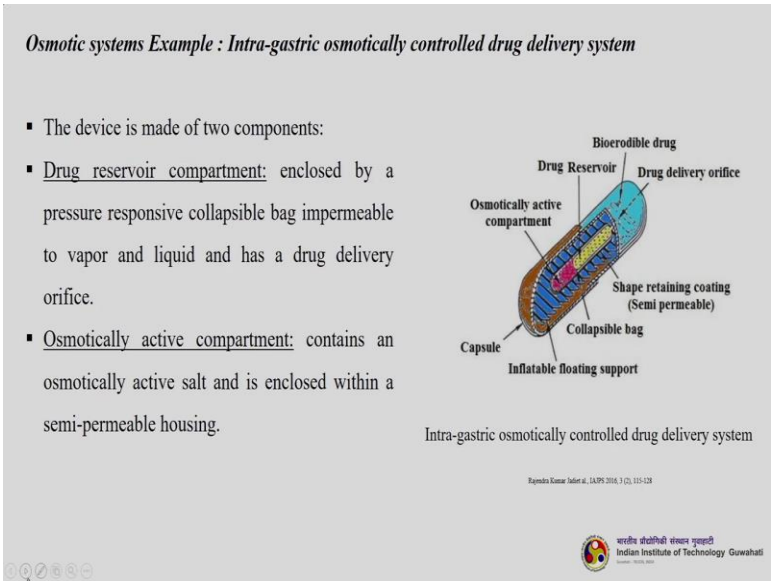

So, the next one is intra-gastric osmotically controlled drug delivery system. This device is made up of two compartments compound components. So the first one is Drug reservoir component another one is osmotically active compartment. The drug reservoir compartment is enclosed by pressure responsive collapsible bag impermeable to vapour and liquid and other Drug Delivery

office. You can see this is the drug reservoir the yellow one the osmotically active compartment contains an osmotically active salt and is enclosed within the semi permeable housing.

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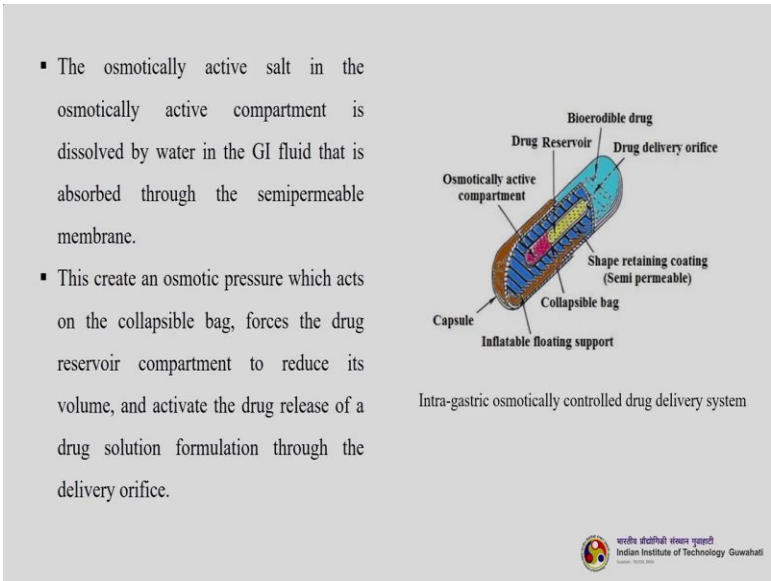

The osmotically active salt in the collective compartment is dissolved by water in the GI fluid that is observed through the semipermeable membrane this create an osmotic pressure which acts on the collapsible back forces, the drug reservoir compartment at reduce its volume and activate the drug release of the drug solution for the delivery orifice. So we can have a close look again. This is a drug reservoir, drug delivery orifice is located.

So, osmoticaly active component the pink one is the capsule which is the collapsible bag here. So these are the various parts of this intra-gastric osmotically controlled Drug Delivery System which is getting a lot of interest nowadays for its efficiency. So we come to the conclusion of this lecture as well as this course as I told you in the beginning that today is the last lecture of this membrane Technology course.

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You can refer these books today many material were taken from Richard and Baker and few references. So before I sign up the course, I would like to thank you and I hope that you have learnt something during the entire course and still you have any difficulty you can always ask me and you can always right to me at kmohanty@iitg.ac.in I am assuring you that I will definitely get back to your mail with my reply. So, thank you very much and I wish you all of you a bright career and future. Thank you very much.