Surface Engineering Nanomaterials
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Lecture – 32
Microencapsulation: Kinetics of release

Hello. Today we are going to discuss about the Microencapsulations: that is Kinetics of release. Means in these particular topics we are going to discuss that when we are taking any kind of microcapsules or maybe any kind of core materials which is surrounded by some kind of coating materials, like any kind of drugs, like tablets or maybe some kind of capsules then when we are taking it inside our body then how it is going to work inside our body. So, that actually depends upon this kinetics. There is some loss actually which we are going into details into the subsequent slides.

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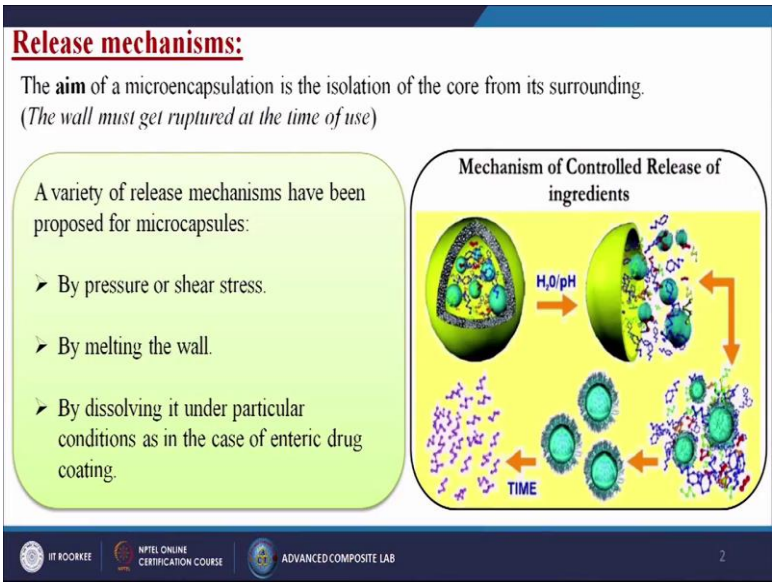

So, first one is called the release mechanisms. In this particular case we are going to discuss that when we are taking any kind of microencapsulations materials then when it is going inside our body how it is going to work actually. The aim of microencapsulations is the isolations of the core from it is surroundings. If we remember in our last lecture we have discussed about the microencapsulations; microencapsulations just for make it ready in our mind just once again I am going to tell you that we are having some kind of core materials which is may be some kind of medicine then we are

giving it some kind of coating like any kind of polymeric materials onto that which is known as the shell material and the whole material we are taking into our body so that it can work perfectly at that affected zone.

So, in these particular case when we are talking about the microencapsulations there are two things: first thing is that that medicines is encapsulated by some kind of polymeric material which should go inside our body which should melt or maybe dissolved in our body systems that is the number one criteria, and that also work depends upon the concentrations of that particular medicines and our body systems. So based on this; means based on the environment that medicines work perfectly.

So here, a variety of release mechanisms have been proposed for the microencapsules. First one is called the by pressure or shear stress by melting the wall by dissolving it under particular conditions as in the case of entering drug coating. So, as I told already, we are preparing that medicine into the environment so when it is going inside our body maybe it is going into some acidic medium or maybe some kind of basic medium. So, the outer material should react with that particular environment, it should be activated at that particular environment then only that medicine can release and it can work with our cell properly.

So, it depends upon that whatever the polymer we are going to use or maybe whatever the coating materials we are going to use whether it will melt or maybe dissolve inside our body properly or not and what conditions it should actually it needs. So that depends upon this kind of mechanisms.

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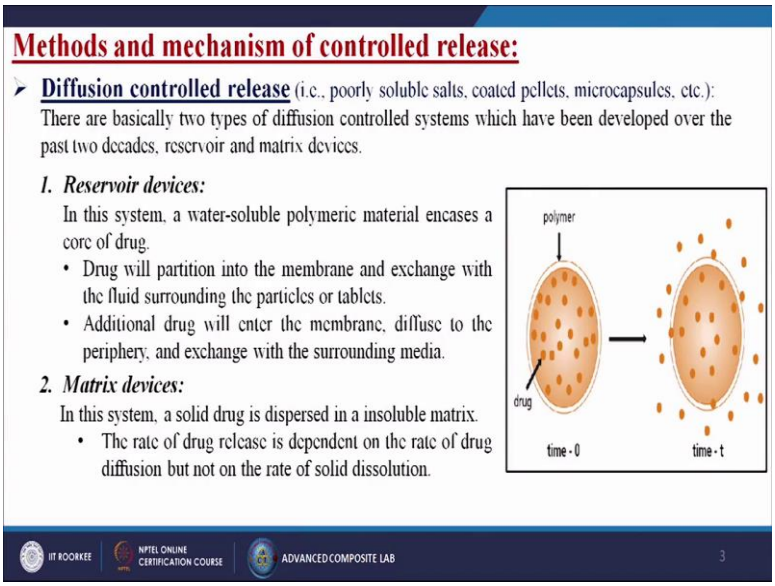

So, first is called the diffusion controlled release. So that is the one kind of controlled release. From the name itself controlled release you can understand that this totally it depends upon that time. So, you are having some medicines how fast it will dissolve in our body, so that can be controlled that what type of coatings we are going to use. Suppose we are putting some kind of materials which need longer time or maybe certain temperature to activate inside our body. That means, after that much time that medicine will work inside our body or maybe sometimes it can depends upon whatever the types of polymer actually I am going to use.

First is called the diffusion control release, which is nothing but the poorly soluble salts, coated pellets or maybe the microcapsules are the examples. There are basically two types of diffusion control systems which have been developed over the past two decades: one is called the reservoir and one is called the matrix devices. These are the two different types actually by which we can do the diffusion control release. Whatever that reservoir devices; first one is called the in these systems a water soluble polymeric materials encases a core or drug. So simple, the outside of the material it is made by the polymer which can be soluble in the water or maybe some low concentrations medium.

In that particular case the drug will partitions into the membrane and exchange with the fluid surrounding the particle or tablets, additional drug will enter the membrane diffuse to the periphery and exchange with the surrounding may media. So, these are the first

concepts for the reservoir devices. And what the matrix devices tells us, in these systems a solid drug is dispersed in insoluble matrix, the rate of drug release is dependent on the rate of drug diffusion but not on the rate of solid dissolutions.

So, the both the theory is totally independent; one is totally dependent upon the concentrations, one is another totally dependent upon the solid concentrations that how the polymer will bare.

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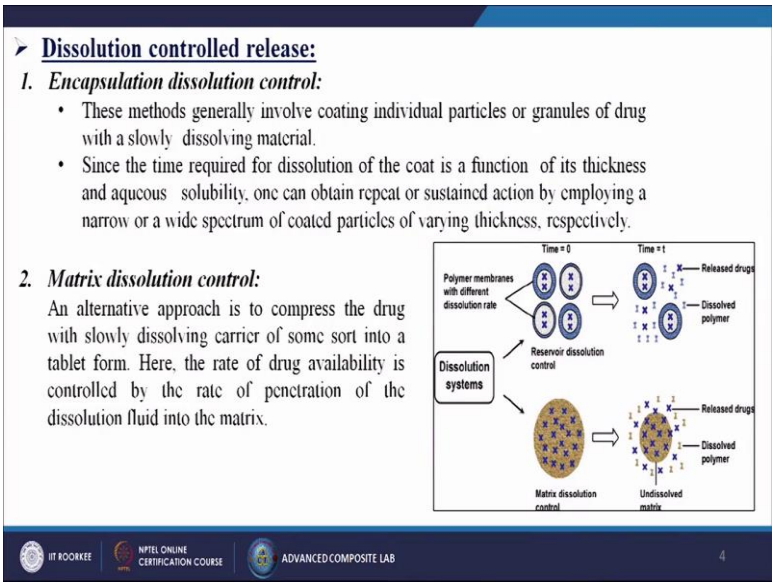

Next is called that dissolutions controlled release. In this particular case the encapsulations dissolution controls is generally tells us that these methods generally involve coating individual particles or granules of drug which is slowly dissolving materials. Since the time required for dissolution of the coat is a function of it is thickness and aqueous solubility one can obtain repeat or sustain action by employing a narrow or a wide spectrum of coated particles by varying thickness.

So here, the thing is that this method is totally the time dependent that when I am going to use my medicines should be activated based on that I can choose different kind of coating materials. Suppose, I can choose any kind of polymeric materials which needs the longer time to dissolve so that after certain time the medicine will be activated.

Next is called the matrix dissolution control. So, an alternative approach is to compress the drug with slowly dissolving carrier of some sort into a tablet form. Here, the rate of

drug availability is controlled by the rate of penetrations of the dissolution fluid into the matrix. So, here this is the concentrations based actually.

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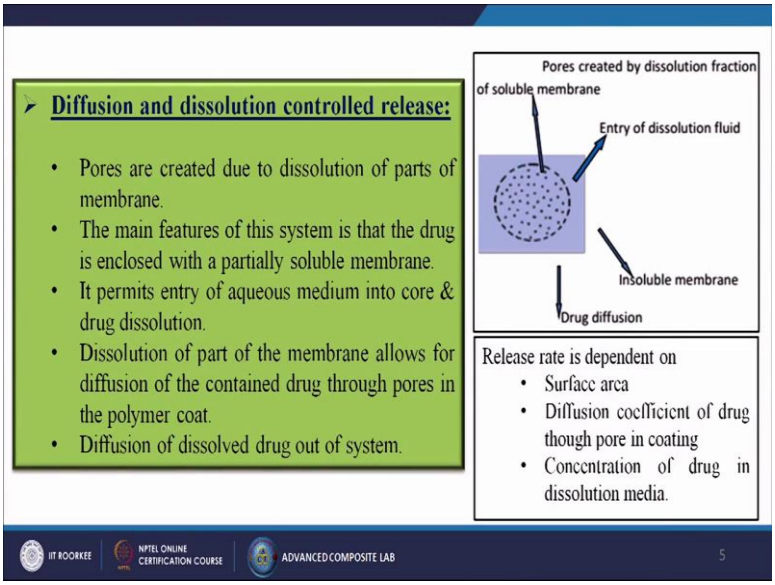

So now, it is the mixture of both diffusions and the dissolutions. So, pores are created due to the dissolutions of parts of the membrane. The main features of the system is that: the drug is enclosed with a partially soluble membrane, it permits entry of aqueous medium into core and drug dissolutions, dissolutions of part of the membrane allows for diffusion of the containing drug through pores in the polymer coat.

So here, first we are coating the drug into some materials that it depends upon what is the pore means permeability of that particular material so that that drug can go through this membrane or maybe that how that polymer is going to dissolve. So, here it is the mixture of two concentrations or maybe two logics which already I have discussed. Here the release rate is dependent on surface area of that particular material, diffusion coefficient of drug through pore in coating concentration of drug in dissolution media.

Next we are going to discuss about the release controlled by the ion exchange. So, here the simple thing is that when we are taking the medicines not only we are taking that particular medicines means particular group maybe with some kind medicines we are taking some kind of acids based or may be some kind of base based or may be some kind of other materials when these drugs and that materials directly go inside our body and

then it will create some kind of resins or maybe some kind of ions by which that particular drug may be activated. So, this is the basic logic for this particular release.

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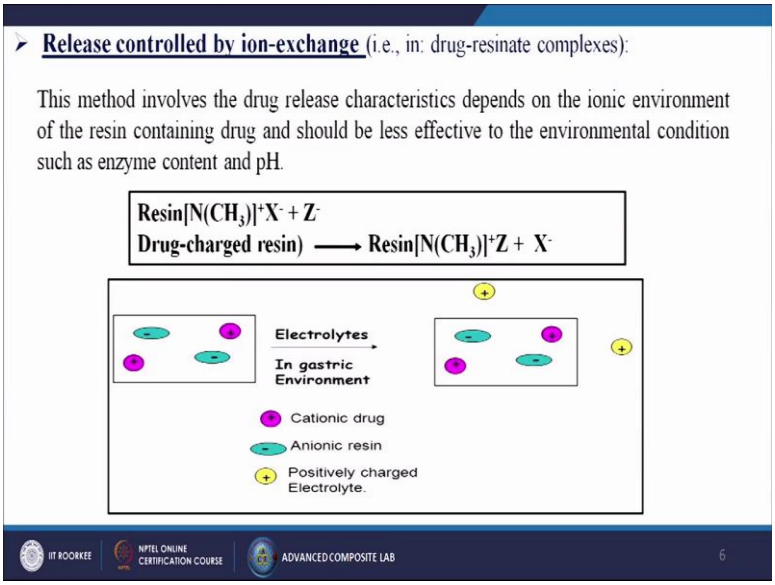

So, this method in involves the drug release characteristics depends on the ionic environment of the resin containing drug and should be less effective to the environmental conditions such as enzyme content and pH. So, sometimes we are creating some kind of drugs when it needs maybe the acidic medium to activate. So, what we are doing? Certainly with that drug we are putting some kind of sodium chloride, NaCl and then the whole thing we are solving so that first initial is dissolving inside our stomach so that it is creating some kind of particular condition then that drug will be activated at that particular medium.

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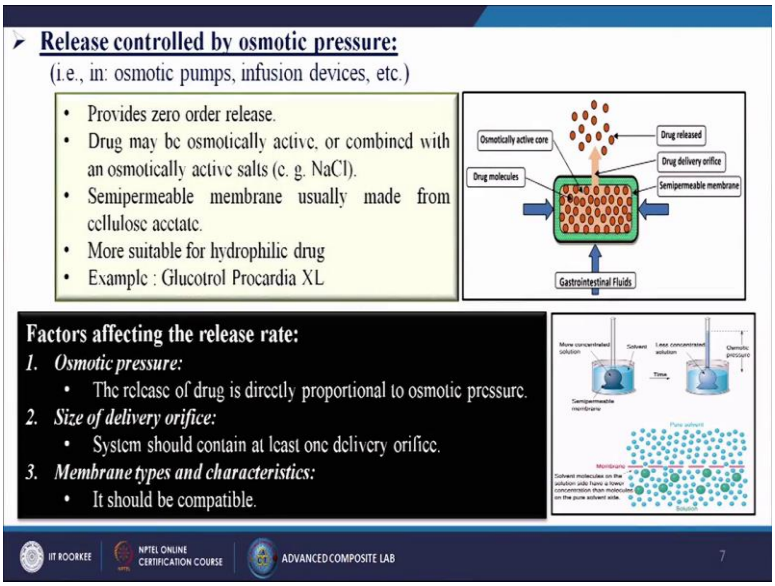

Next is called the release control by the osmotic pressure. From this particular figure you can understand that the inside is the medicines drug molecules outside is some kind of coated materials which is some kind of polymeric materials. So here, due to that osmotic pressures there is a some hole is creating at the particular wall from which the drug molecule is directly coming and it is going inside our body. The logics tells us that provides zero order release, drug may be osmatically active and combined with an osmotically active salts, semi permeable membrane usually made from cellulose acetate, more suitable for hydrophilic drug; example glucotrol procadia XL.

Now what are the factors that affecting these kind of techniques? First one is called the osmotic pressures, because from the name itself this is the release controlled by the osmotic pressures. So, the release of drag is directly proportional to osmotic pressures, size of delivery orifice that what is the size because if the drug molecule size will be bigger than the orifice size then automatically the drug will not be released. So, the drug particle size should be smaller than the orifice size then only easily that the drug can come out through these pores.

Next one is called the membrane types and characteristics it should be compatible. Means, what kind of membrane? Whether it will be activated inside that particular medium or not? So these all are the logic behind this osmotic pressure.

Next, we are going to discuss is the most fundamental things of this particular lecture what is called the release mechanisms of the loss. Here, before going to start I am telling you that we are having some kind of materials or maybe that core materials or maybe the drug materials or maybe our substitute materials whatever may be, now we are going to do some kind of coatings on top of that which is known as the sale materials. So that is why it is called a core cell structure. So now, when you are taking some kind of materials suppose this concentration is C 1, so our main drug material the concentration will be C 1 then we are coating with another materials which concentration is called the C 2.

Then the overall material concentrations maybe we can call it as a C d. That means the concentration of that donor; donor means we are taking that medicine inside our body so that is why we are taking that material as donor materials. Now our body concentration is called the receptor, so that is known as the C r; means concentration of the C r. So, the medicines when it is going inside our body how it is going to dissolve it totally depends upon the C d and C r; means concentration of the donor and concentration of the receptor.

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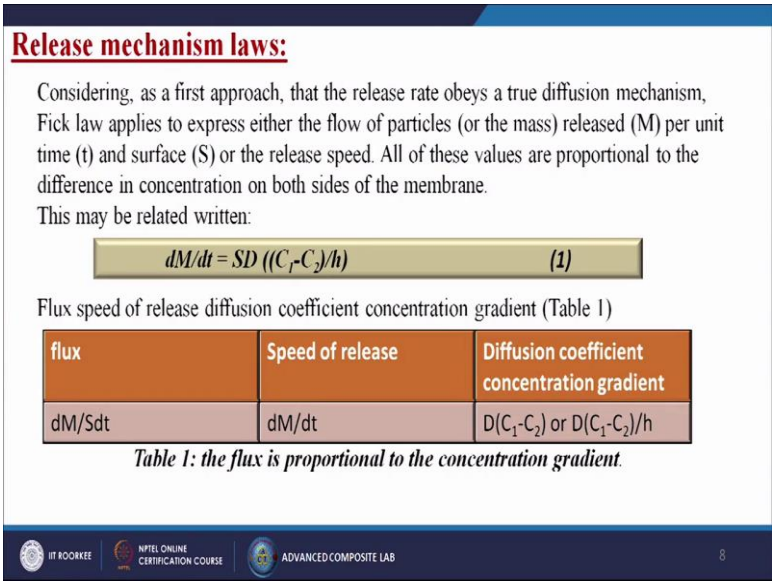

So here, this loss is actually the name of that scientist which is called the Fick law. So, this is the standard law by which generally we are following this kind of release mechanisms. So, considering as a first approach that the release rate obeys the true diffusion mechanisms; Fick law applies to express either the flow of particles released

per unit time and surface of the release speed. All of these values are proportional to the direct difference in concentration on both sides of the membrane; these may be related written dM by dt is equal to s D into C 1 minus C 2 by h.

So, here this is the famous equations for the Ficks law. In this particular case what it is telling that it depends upon the concentrations it depends upon the speed. Suppose the drug is coated by some kind of polymeric materials, so it depends upon the concentration in between the body and in between the drug so that the drug how fast it will go towards the body and it can work.

So here, the flux speed of release diffusion coefficient concentration gradient which we have shown in this particular table is known as the flux is called the dM by s dt speed of release is equal to dM by dt diffusion coefficient concentration of gradient D into C 1 minus C 2 or maybe D C 1 minus C 2 by h; h is nothing but the thickness of that particular core materials and particular coating materials or maybe the core materials and C 1 C 2 is the concentrations of that substrate or maybe that core materials and the coating materials.

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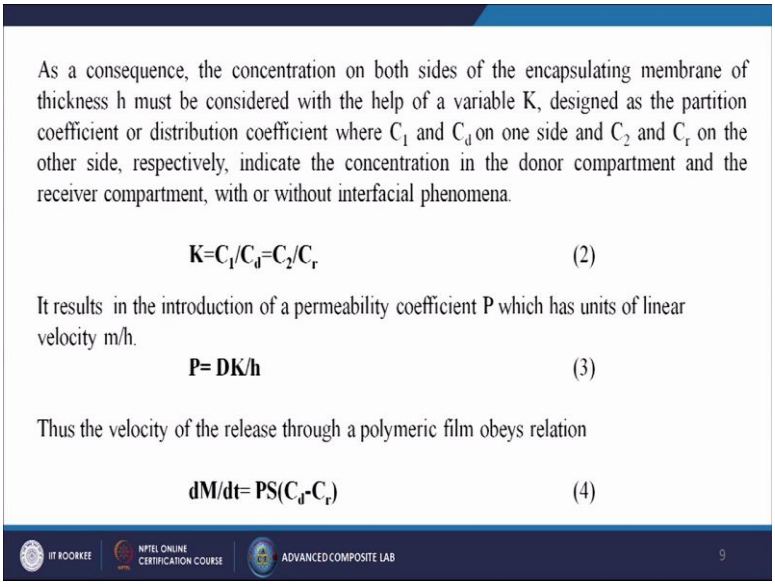

So, here when you are going through these equations it will tell us that what is the kinetics actually is behind these particular mechanisms. It will depend upon the permeability also of that particular polymer. So, whatever the polymer pores are there if it is bigger or maybe if it is smaller whether how much time the polymer needs to

dissolve inside our body. So, it totally depends upon how the medicine will act with our body so easily.

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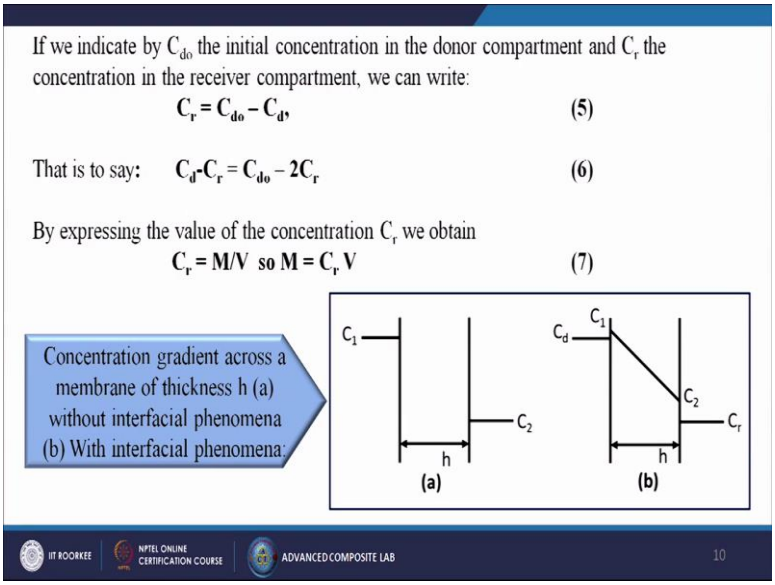

In this particular case from this graph actually we can easily understand that how the medicine is working inside our body. C 1 is nothing but our core materials, C 2 is nothing but the concentration of coating material, and h is the thickness of that particular shell onto the core materials itself. So, it totally time dependent as I have already told, so these total systems C 1 plus C 2 is known as the C d that is the concentration of the donor that means the whole medicines and C r is the concentration of our body. So, when we are taking some kind of medicines it totally depend upon the concentrations.

So, first the concentration will be higher at that particular core material then with time or maybe with thickness slowly slowly the concentration will be going down at the wall of that C 2 means core shell materials. And then these C 2 is total depend upon the C r. So, there should be some kind of concentration difference in between the C 2 and C r then only that medicine will directly go and it can work with our body itself.

So, concentration gradient across a membrane of thickness h without interfacial phenomena with interfacial phenomena so this is called the without interfacial phenomena and this is called with interfacial phenomena. So, these all are the logics behind the mechanisms and kinetics.

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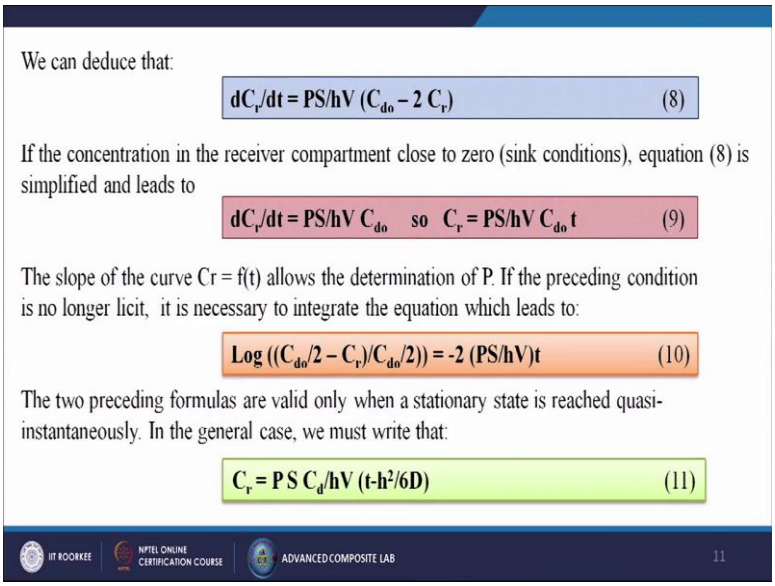

So, if we go further up to that equation here also it depends upon the slope of that particular ingredient. And not only that this is the actually the summarizations of the whole law where it can tells that the close to the zero means sink conditions that was almost the concentration will be in to the same level, then only the medicine will act properly inside our body.

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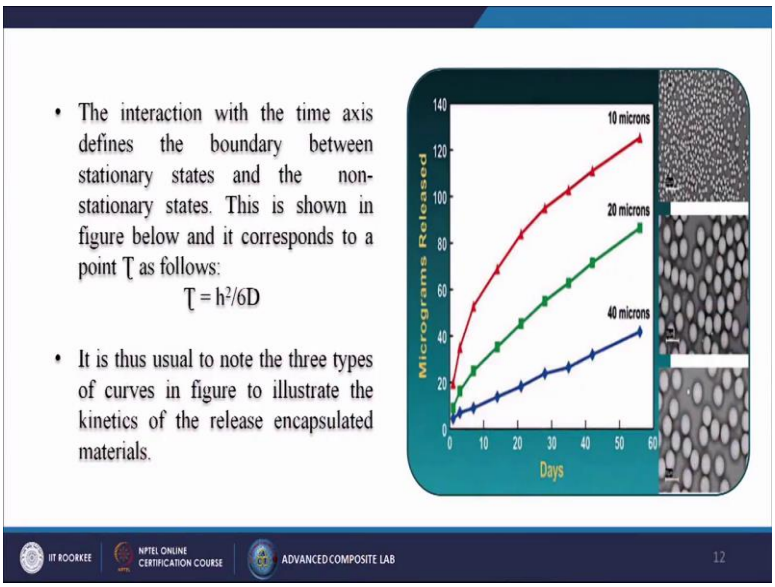

So here, this is a one literature review results or maybe one kind of results what we are getting from some literature or maybe it has been developed by some scientist. So, the

interaction with the time axis defines the boundary between stationary states and the non stationary states. This is shown in figure below and it correspondence to a point tau as follows is equal to h square by 6D. So here, the y axis is giving you the micrograms released means how much medicine is releasing with time and the x axis is giving the days; means what is the time period of that particular medicines.

It is a simple method, so if the drug molecules will be bigger or maybe the quantity will be bigger it needs more time to dissolve inside our body, and if the particle or maybe quantity will be lesser so that time it needs the lesser time to dissolve in our body. So, where we can see that when we are talking at taking the 40 microns means gram released over there it needs around 50 to 60 days, but when we are taking about the 10 microns size and then it micrograms released is almost 140 it needs 50. That means, the particle size is less, but the quantity is more but it needs the same time for dissolving.

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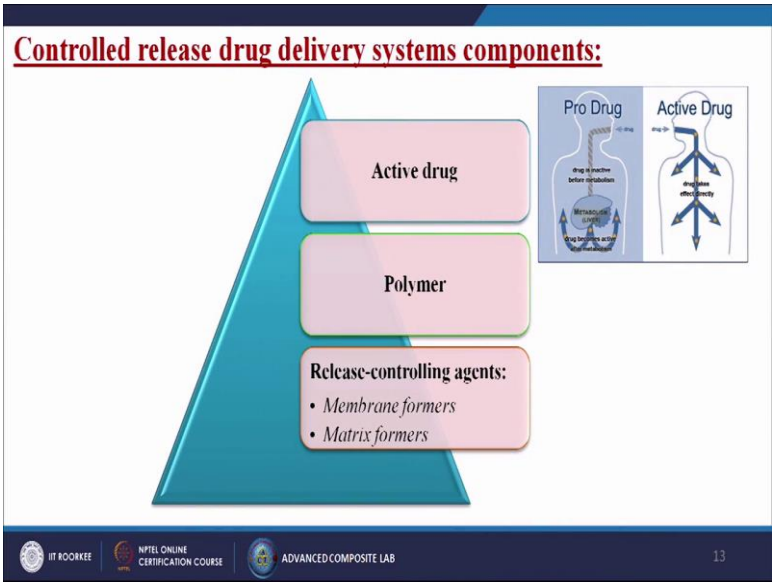

Next we are going to discuss about the control released drug delivery system components. From this particular figure you can understand that we have given two mechanisms over there one is called the pro drug another one is called the active drug; I am coming later. So, first if we follow this check one is called the active drug, one is called the polymer, and another one is called the release controlling agents like membrane formers or may be the matrix former. As I already discussed inside the

medicines covered by some kind of polymers then our body fluid, so whatever how it will work it totally depends upon the characteristics of these materials.

So, in these pro drug concept we are going to tell you that we are taking some medicines, but that medicines needs some environment specific environments whether some acidic environment or maybe some basic environment, some neutral environment, some particular pH concentrations then only that medicines can be activated. So that is why it is known as the pro drug concentrations. And another one is called the active drug that does not needs any kind of environment; in any environment the drug can be automatically activated.

Next, till now we are discussing about the how we are making the microcapsules, how we are taking that medicines, how it is working inside our body. So now, this is some kind of techniques by which we can see or maybe characterized our microcapsules.

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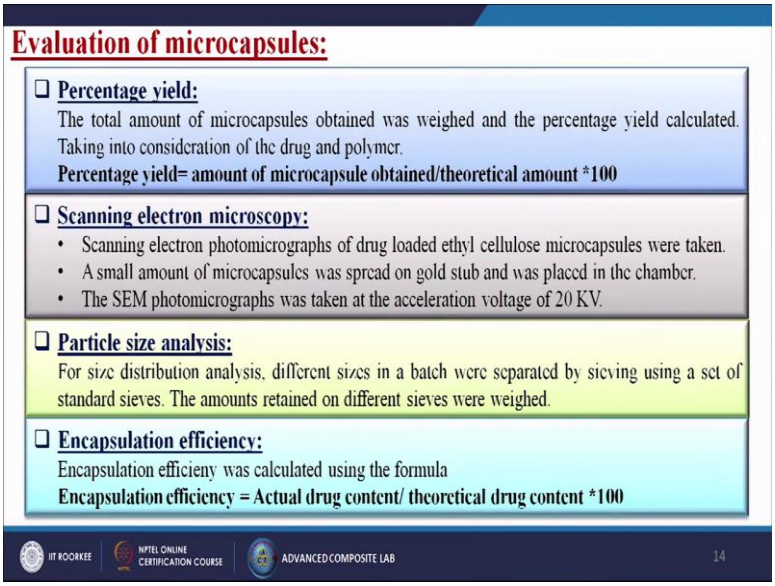

So, fist one is called the percentage yield: the total amount of microcapsules obtained was weighed and the percentage yield calculated, taking into considerations of the drug and the polymer. Percentage yield amount of microcapsules obtained oblique theoretical amount in 200. So, that will give you the percentage yield of that particular drug.

Then we are having that scanning electron microscopy, so by which we can characterize this kind of drug. So, scanning electron micro photomicrographs of drug loaded ethyl

cellulose microcapsules were taken, a small amount of microcapsules were sprayed on gold stub and was placed in the chamber, the SEM photomicrographs was taken at the exhalation voltage of 20 KV.

For size distribution analysis different size in a batch were separated by sieving using a set of standard sieves and then encapsulation efficiency, which is nothing but the actual drug content by the theoretical drug content into the 100 percent. So here, just we are going to characterize what is the polymeric conditions, how we are going to characterize those polymers by the efficient methods, how we are calculating the number of pores or maybe the permeability of that particular polymer so that drug can easily be go through with that pores and react with our body fluids.

So now, we are going to discuss some in-vitro methods for studying the releasing characteristics. So, in-vitro method, means generally we are going to do this is all kind of preliminary research generally we can call it, these kind of research generally or maybe normally we are doing in our lab itself. So, simple by doing some kind of chemical treatment or maybe that by simply using the chemistry we are doing this kind of experiments by petridis or maybe some test tubes.

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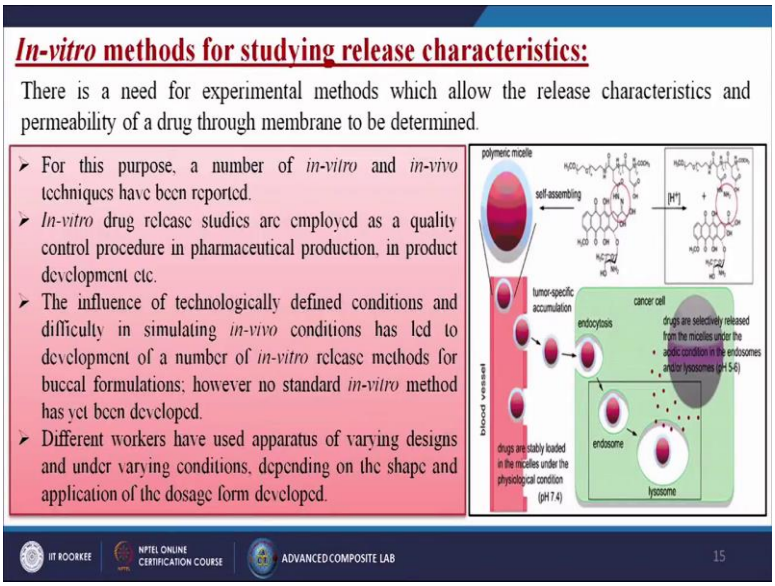

There is a need for experimental methods which allow the release characteristics and permeability of a drug through membrane to be determined. Here, this is the first step by which we are going to use that whether our mechanisms is working or not, our polymer

is dissolving or not, our drug is perfectly working on not. Then based on these results we are going for the in-vivo. That means, after that we are going to pull insert that medicines into the body or maybe into the mice so that it can properly work inside the body or not whether our body is accepting that particular medicines or not; so these all at the later stage by which we can do this kind of techniques.

So, for this purpose a number of in-vitro and in-vitro techniques have been reported. In-vitro drug release studies are employed as a quality control procedure in pharmaceutical productions in product development. The influence of technology defined conditions and difficulty in simulating in-vivo conditions has led to development and number of in-vitro release methods for buccal formulations; however no standard in-vitro method has yet been developed. So, from these particular case you can see that we are having the medicines which is quoted by some kind of polymeric missile then when it is going inside the blood vessels it totally depends upon the pH concentrations of that particular blood; whether that pH concentration of that particular blood sweeps with the pH conditions what is need to activate for this polymeric messily will be the same then only the drug can be work finely, otherwise we have to keep that blood pH concentrations we have to change then only the drug will be activated and it will work perfectly.

So here, we are talking about some kind of the cancer cells, so by which it can work in two different medium actually. So, drugs are selectively released from the missiles under the acidic conditions in the endosomes and all lissomes pH means 5 to 6. So, only for this particular environment that drug can work otherwise if we take that drug it will not work inside our body unless and until it will get the perfect conditions for each.

So, now we are going to discuss the controlled drug delivery systems. So here, how we are going to do it or maybe how we are going to follow this path.

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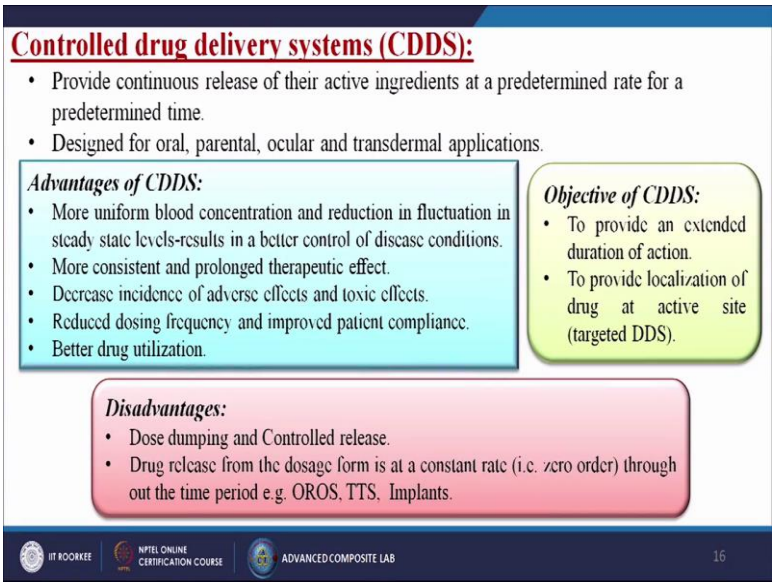

So, first one is called provide continuous release of their active ingredients at a predetermined rate for a predetermined time. So, we are taking the medicines, but the thing is that how fast that medicine will work with our body that depends upon the concentrations or maybe the quantity or maybe the release rate. And another one is called the how much time that medicines will work for our body. So, based on that generally doctors prescribe us medicines for a twice a day or maybe single a day on may be thrice a day. So, how our body can react with that medicine or maybe how our body can accept that medicine so quickly, it depends upon the time, it depends upon the conditions and so on.

So here, what are the advantages of these particular techniques? First is called a more uniform blood concentrations and reductions in fluctuation in steady state level results in a better control of disease conditions, more consistent and prolonged therapeutic effect, decreased incidence of adverse effect and toxic effects, reduced dosing frequency and improve patient compliances and better drug utilization. So, these all are the advantages for these particular techniques. Of course, there are some objectives why we are going to do actually. So, to provide an extended duration of actions to provide localization of drug at active site; that means, targeted drug delivery systems.

So, when we are talking about disadvantages of course there is certain disadvantages also otherwise no improvement will be done. So, those dumping and control release drug

release from the dosages from it is at a constant rate; that means zero order throughout of time period; OROS, TTS, implants, these all are the examples for these particular techniques.

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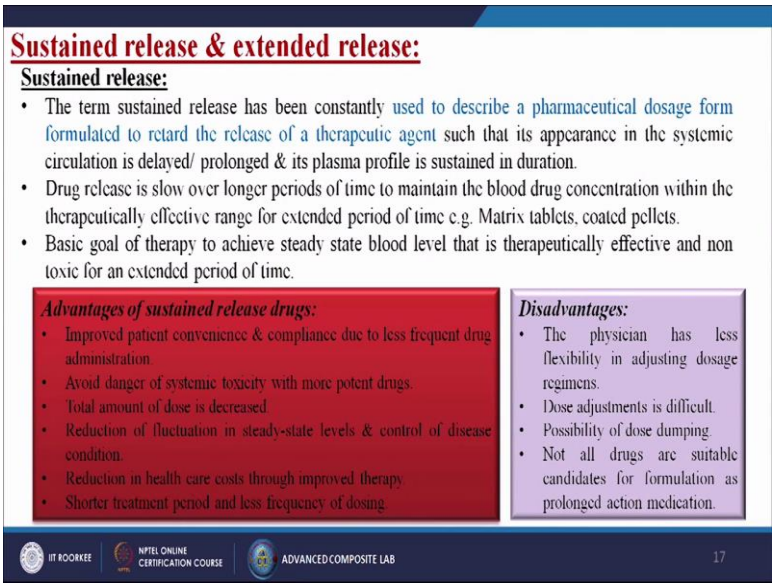

Next we are going to discuss about the sustained release and the extended release. So, when we are talking about the sustained release is totally the time dependent one. So, here the term sustained release has been constantly used to describe a pharmaceutical dosage from formulated to return the release of a theoretic agent such that it is appearance in the systemic circulation is delayed prolonged or it is plasma profile is sustained in durations. The drug release is slow over longer periods of time to maintain the blood drug concentration within the theoretically effective range of extended period of time means metric tablets, coated pellets.

So, already I have discussed a little bit about these sustained release and the extended release. So here, what are the advantages of sustained release drugs? Improve patient convenience compliance due to less frequent drug administration's, avoid danger of systemic toxicity with more potent drugs, total amount of dose is decreased, reduction in healthcare cost during improved therapy, short a treatment period and less frequency of dosing.

There are certain disadvantages: the physician has less feasibility in adjusting doses regiments, dose adjustments is difficult possibility of dose dumping because it is very

difficult because it depends upon person to person that how the conditions is there inside our body. So, whether that medicines is needs for maybe 1 hour to activate or maybe 2 hour to activate or 3 hour to activate. So, that is why there is some kind of difficulties may come for the doctor to prescribe these medicines.

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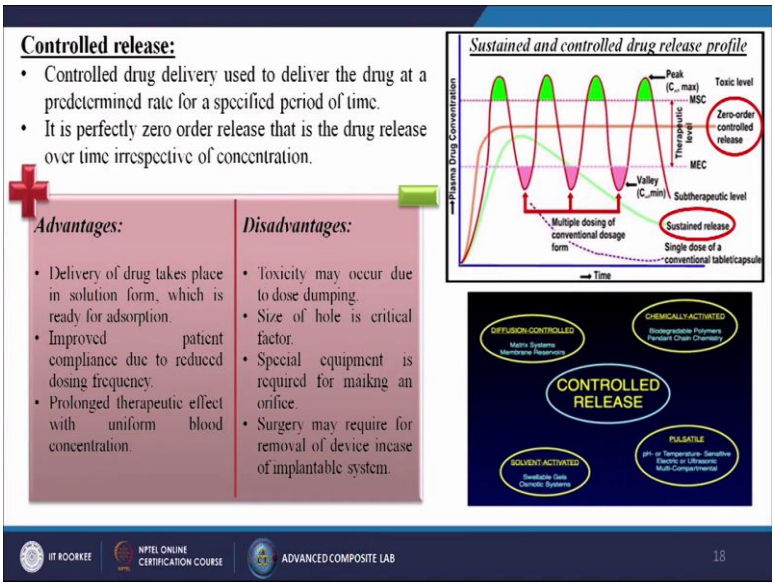

But when we are talking about the controlled release, so controlled drug delivery used to deliver the drug at a predetermined rate for a specified period of time. So, everything is known to me that how, what should be the controlled atmosphere, what should be the controlled conditions by which we can activate these medicines.

So, it is perfectly zero other release that is the drug will is over time irrespective of the concentrations. So, here the advantages are: delivery of drug takes place in solution form which is ready for adsorptions, improve patient compliance due to reduced dosing frequency, prolonged therapeutic effect with uniform blood concentrations. So, these all are the advantages. And of course there is certain kind of disadvantages also: toxicity may occur due to dose dumping size of hole is critical factor, special equipment is required for making an orifice, surgery may require for removal of device increases in case of implantable systems. So control level means, it can be controlled by us and the previous one it cannot controlled by us,

So, when you are talking about the controlled release it depends upon the diffusions control, chemically activated, pulsatile and the solvent activated. So, when you are

talking about the diffusion control it depends upon the matrix systems membrane, reservoirs. When you are talking about the chemically activated it depends upon the biodegradable, polymers, pendent, and chain chemistry. So, it totally depends upon certain theory that how that polymer, how the drug will react with our body and how it can work with our body systems. So, from this particular figure also we can see that if we take the multiple dosing of conventional dosage. So, there is some kind of valley where the plasma drug concentration will be the lesser one, but when we are going for some high value then maybe the toxic level can be increased. So, it totally gives you some kind of therapeutic level and some kind of sub therapeutic level of that particular medicine.

So, already we have reached the last slide of this particular lecture. In this particular slide we can summarize that what we have discussed till now that we have discussed about the controlled drug layer systems depending upon so many mechanisms.

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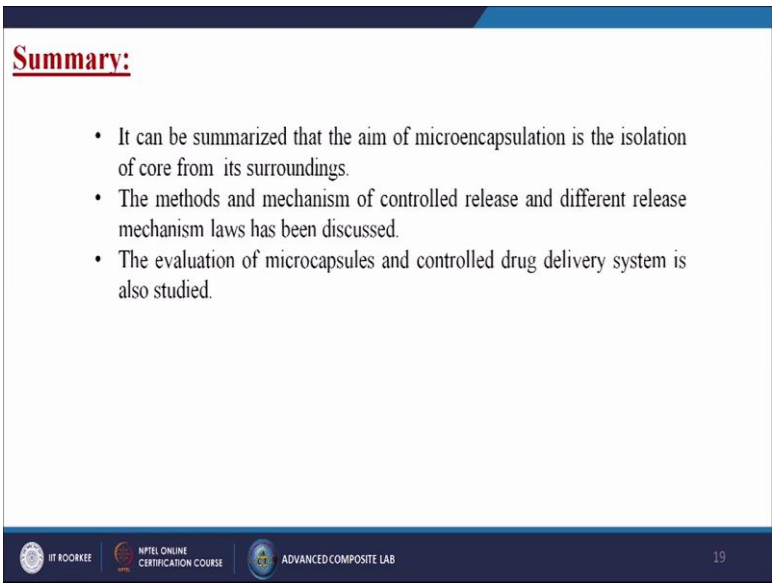

We have given the Fick's law by which the drug release kinetics actually working or maybe the based on. And also the evolutions of the microcapsules and controlled drug delivery systems are also studied from this particular lecture.

Thank you.