INDIAN INSTITUTE OF TECHNOLYGY ROORKEE

NPTEL

NPTEL ONLINE CERTIFICATION COURSE

Biomedical Nanotechnology

Lec-08
Lipid Nanotechnology

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Hello everyone I welcome you to this eighth lecture of this course that is on lipid nanotechnology.

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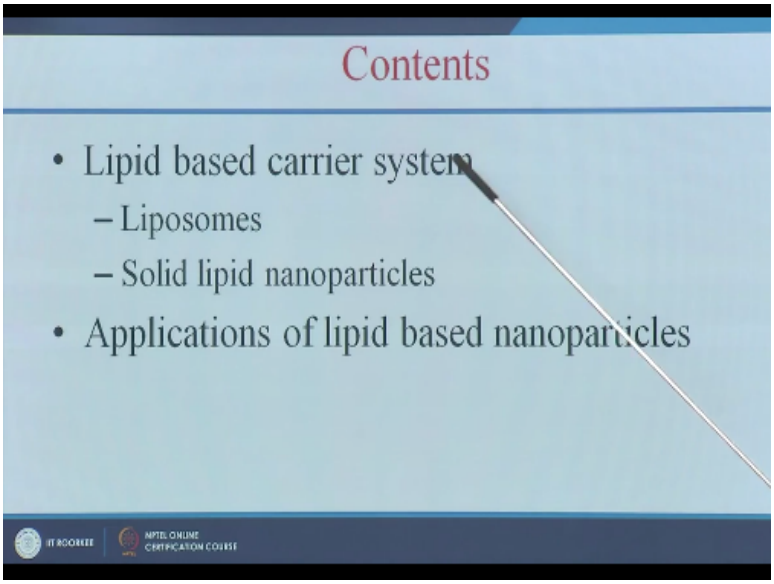

So in this lecture we are region to know the lipid based carrier system. And mainly Liposomes and solid lipid nanoparticles. And also we are going to see various applications of lipid based nanoparticles.
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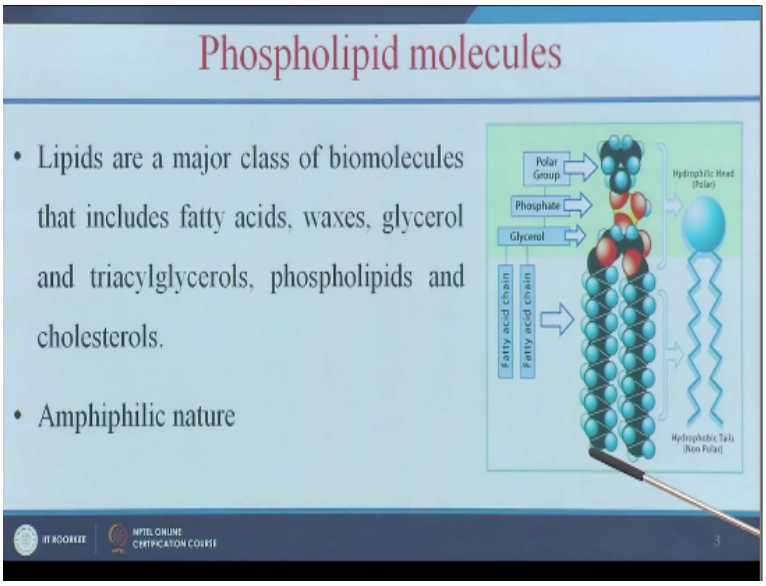

So first we are se what is phospholipids. So lipids are the major class of bimolecular that includes fatty acids, waxy glycerol and triacylgycerols. Phospholipids and cholesterols. And fatty acids okay. So lipids are amphiphilic nature that means it is having hydrophilic head that is non polar.

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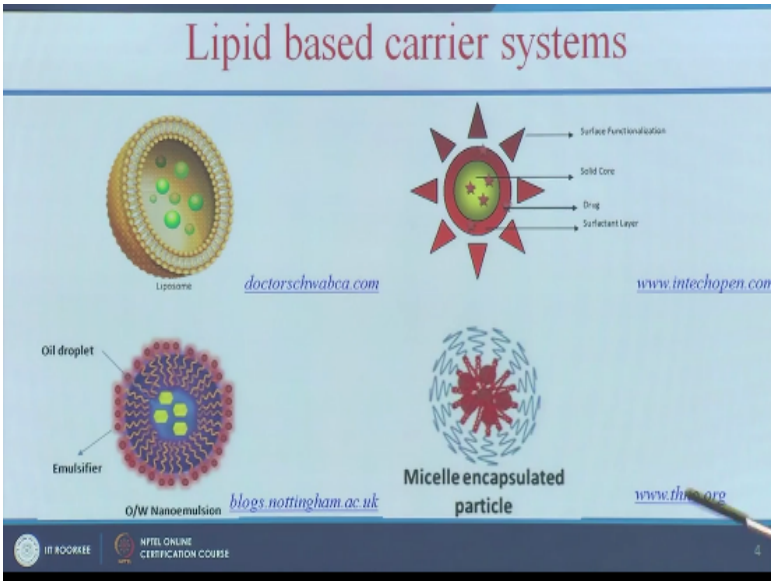

So these are the various lipid based carrier system. And this one liposome and this solid lipid nano particles and this is nanoemultion and this is mycellence okay. So in this lecture we are going to learn all these entire lipid based carrier system.

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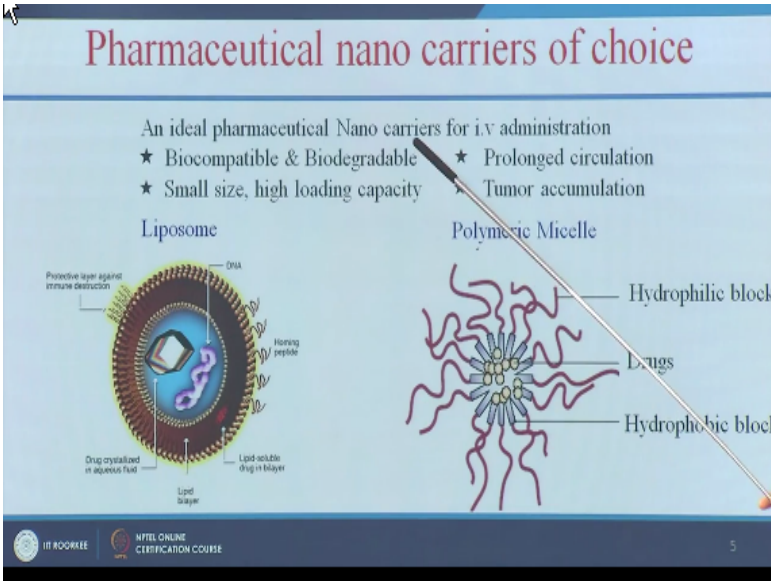

So why we are using this lipids and nano carries for drug liar application because it is biocompatible and biodegradable and it is having a high loading capacity and it is also having prolonged circulation and tumor accumulation.

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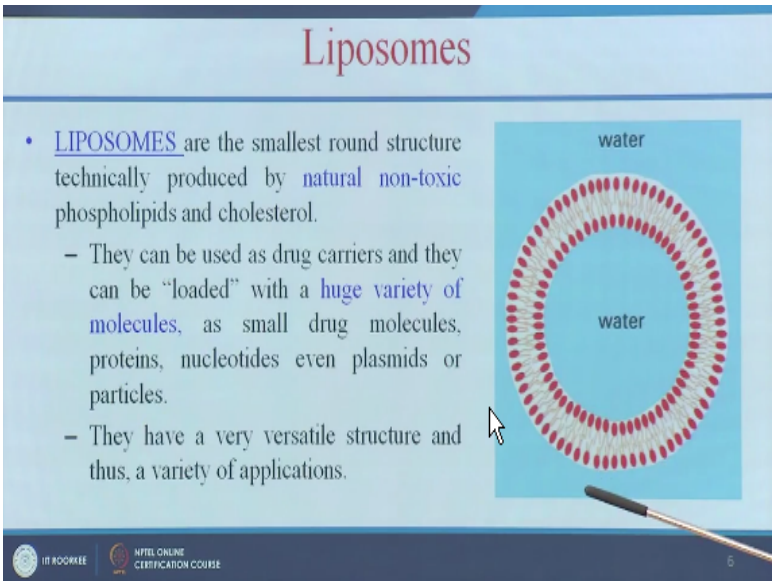

Let us see what is liposome? Liposomes are the smallest round structure okay. and it is made by non toxic phospholipids and cholesterol. And again it can act like very good drug carrier and also it can carry even plasmids lipid acid and anything. So that is why it has a wide application in drug delivery.

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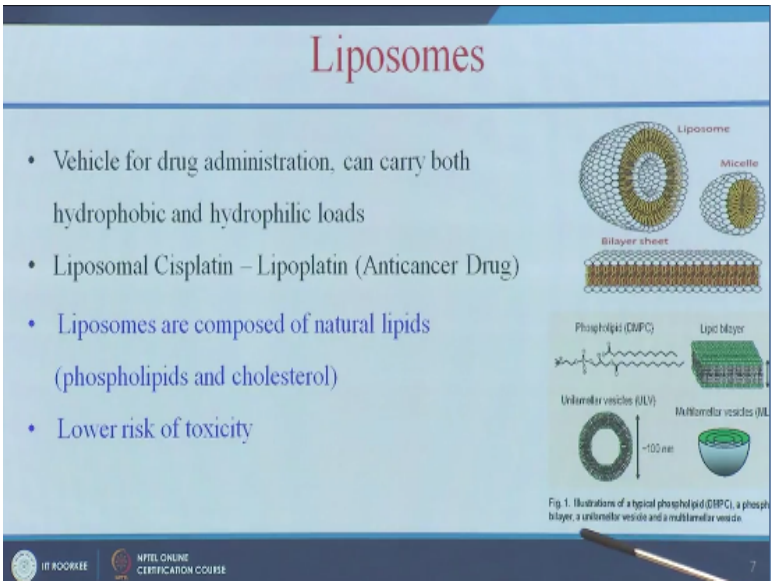

And the liposomes are made up of natural lipids. So it is lower risk of toxicity. And it can carry even hydrophilic drugs.

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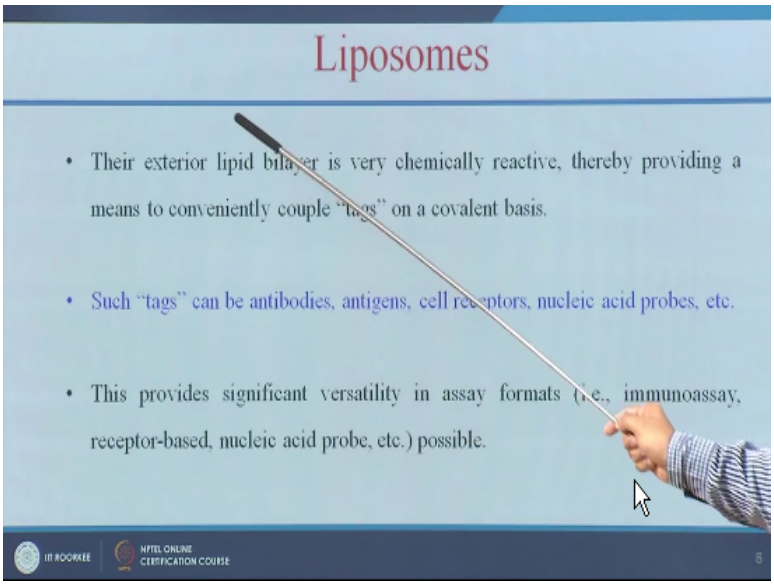

So another important property of their exterior lipid bilayer which is chemically reactive, and using this property we can tag antibodies, and we can target is liposomes to the cancer cells so physically.

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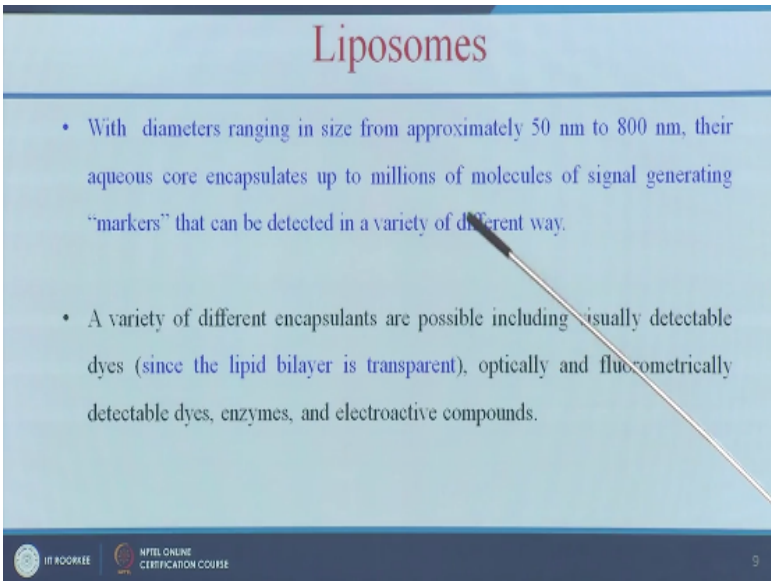

Another important point to this liposomes size can be varying from 50 nanometer to 800 nanometer. So we can ornament drugs anti cancer drugs and or anydiabetical molecules. And another important property is this lipid bilayer is transparent, so we can use clorocent nanoparticles or closen martial. And we can it also for various imaging and diagnostic applications.

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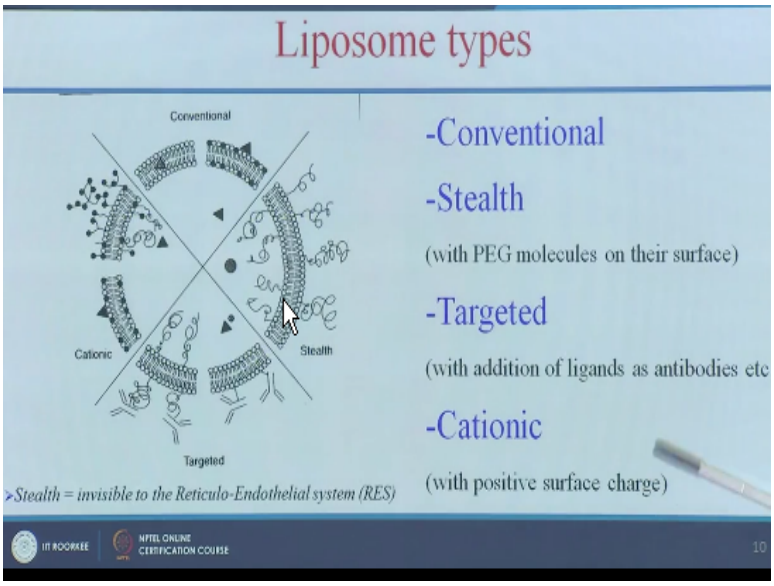

So let us see the type of liposomes. And the first one is conventional liposomes and next one stealth okay. The stealth liposome is like at his liposomes with poly ethylene glycol. So the surface of the liposomes will be covered with polyethylene glycol molecules. That is called as stealth technology and it can escape from the reticular endothelial systems.

And third one is targeted so here we can add antibodies or tepid ligands so target to target your liposomes to the specific cell okay. That is called as targetable liposomes. And fourth one is cationic liposomes so here it will have a positive surface charge so and will know the DNA as well as your cells are negatively charge. So these cationic liposomes can easily bind and it can useful for various drug elemental drugs applications.

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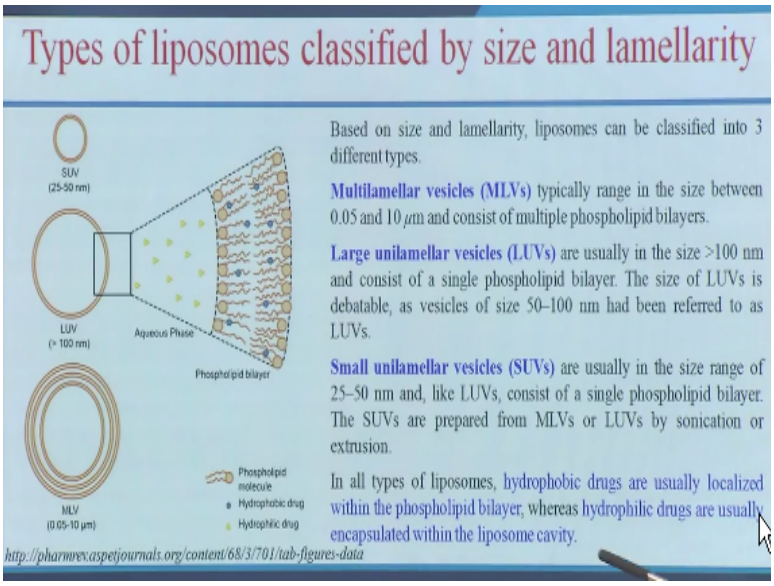

And the types of liposomes can be classified based on the size as well as lamellarity okay. so the first one is multilamellar vesicles so these typically range in the size between 0.05 to 10 micrometer. And it is consist of multiple phospholipids bilayers. And the next one is LUV large unilamellar vesicles so here the size is between 100 nanometer 50 to 100 nanometer okay. And it is also made up of single phosphor bilayer and the third one is small unilamellar vesicles and here the sizes between 25 to 50 nanometer and here of made up of single phospholipids bilayer.

And this SUV are prepared from MLVs or LUVs okay by sonication extrusion method. And in all types of liposomes hydrophobic drugs are usually localized within the phospholipids bilayer and the hydrophilic drugs are usually encapsulated within the liposome cavity okay. so in this liposome cavity were can load the hydrophilic drugs and in the phospholipids bilayer we can load the hydrophilic drugs.

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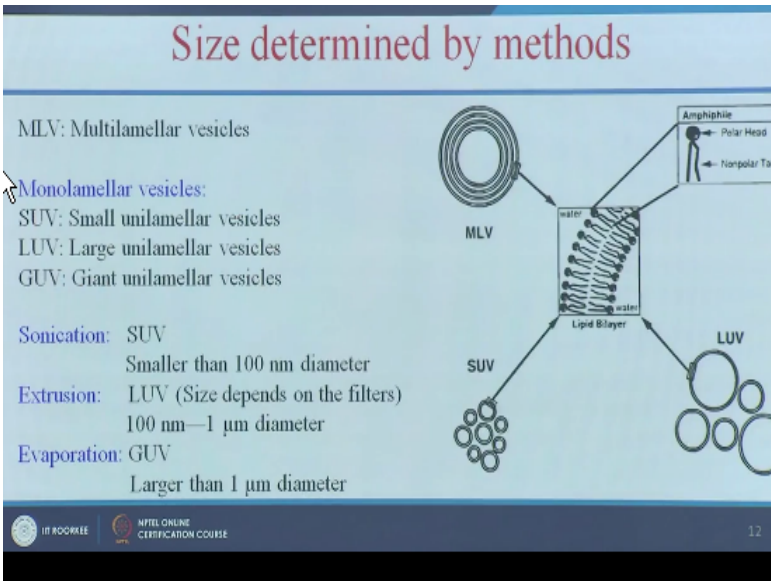

And the sizes of the liposomes are determined by the preparation methods. For example if you are preparing a by sonication method you will get SUV that is smaller the 100 nm diameter liposome. And we can using this method to the extrusion will get LUV and if you using this evaporation method you will get GUV that is giant unimellar vesicles. That is larger than one micrometer diameter. So depends on the preparation method the size varies.

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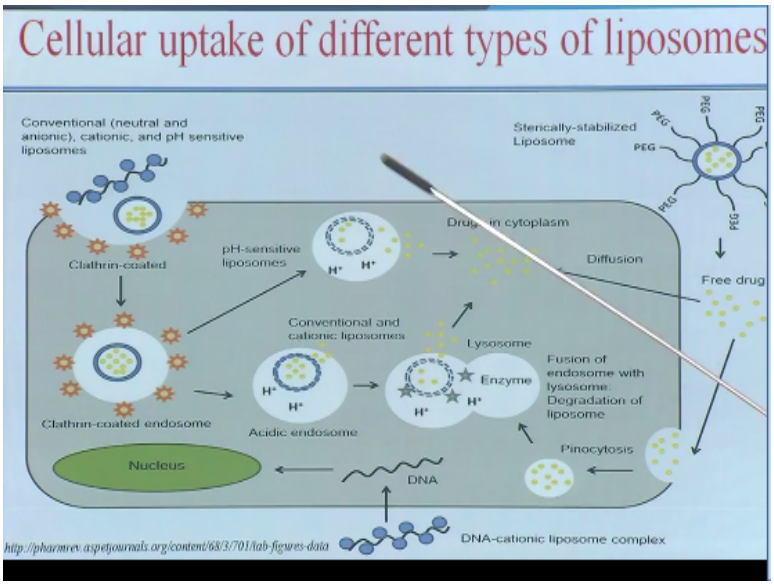

So let us see cellular uptake of different types of liposomes how the cell attack on the liposomes into the cells. So these are the conventional and cationic liposomes so that will be taken by the clathrin coated particles. And will go a endocytosis process so this will be uptake by this endosome. And this clathrin coated endosome will reach the liposome and it will form the endolysosome so there it will get degraded and it will leave the drugs to the cytoplasm.

In case of PH sensitive liposomes so due to asitication of this endosomes so it will relive the drug to the cytoplasm and if you are using the DNA cationic liposome complex so it will bind to this cell membering based on the elctrostic attraction than the DNA will be differentiate to the nucleus. And if your using this sterically stabilizer liposome so where your adding this PEG for sterically stability. And here it will release the free drug. And this free drug can enter the cells by diffusion or it can enter the cells by pinocytocis. That is called as cell drinking process and that will go to the cytoplasm and it can deliver the drugs to the cytoplasm.

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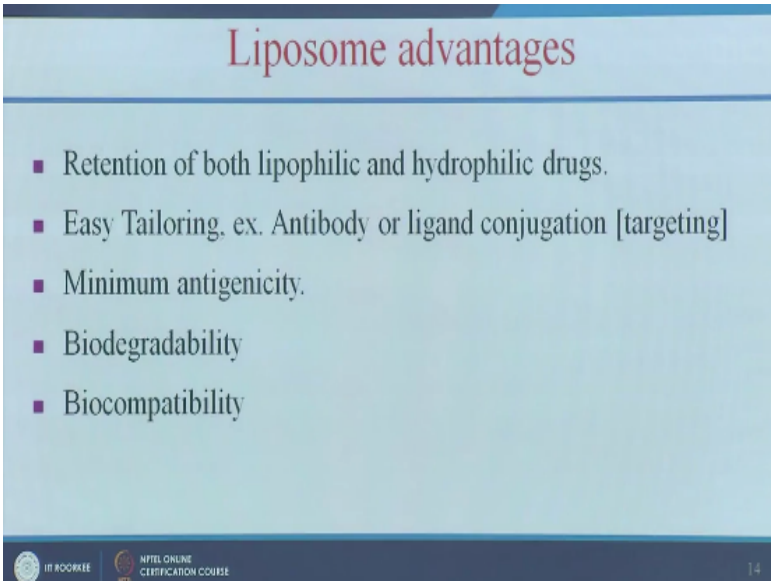

So let us see the advantages of liposomes so it can load hydrophilic as the hydrophilic drugs. And we can easily modify the surface by antibody or some other ligands so we can target this liposome and it is having low antigencity. That means highly biocompatibility and biodegradable.

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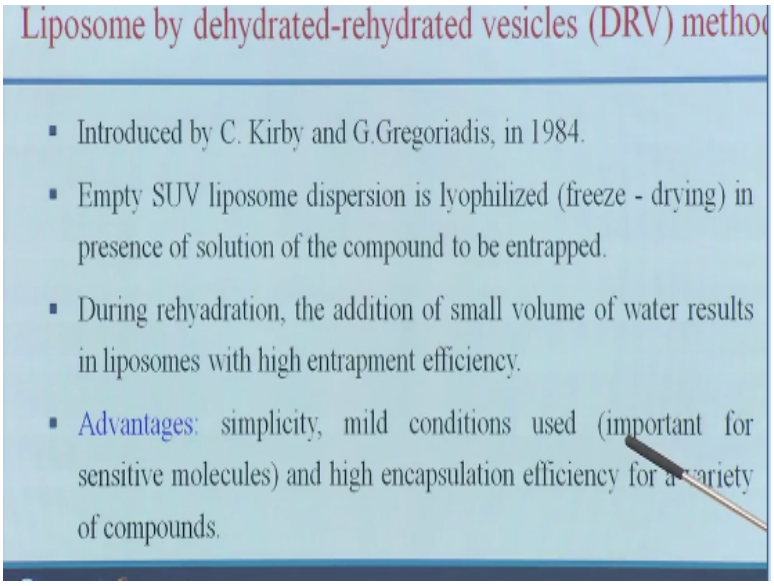

This liposomes can be prepared by seven methods so here I will be explaining some methods here I will be expiring some simple methods that is DRV method. Dehydrated and rehydrated vesicles so how to make this here empty SUV liposomes will be lyophilized. In presence of solutions of the compound to be entrapped. If you want to entropy your drug or if you want to entrapped the florescent particles.

So that should be lyofelence in presence of SUV liposomes. So during rehydration the addition of small volume of water results in liposome with hyentrappment efficiency. Here the advantages are it is the simple methods here will using mild condition so we can achieve high encapsulation efficiency for variety of components.

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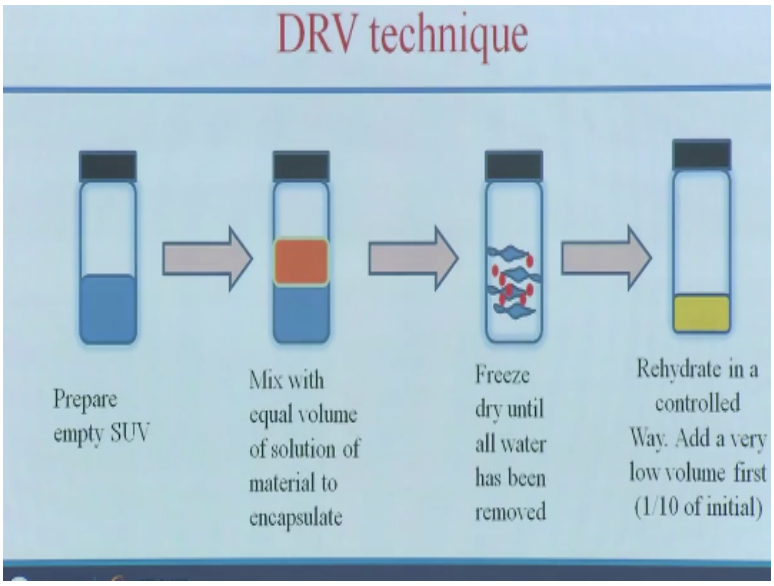

So here we can see the DRV technique so we can prepare the empty SUV and we can mix with the equal volume of solution of material to encapsulate with the SUV. And freeze dry that is lyophilizes when you freeze dry until all the water has removed then you do the rehydrate in a controlled way. When you add a very low volume like 1:10 of volume. And it will get very food small size SUV particles with drug loaded nano particle.

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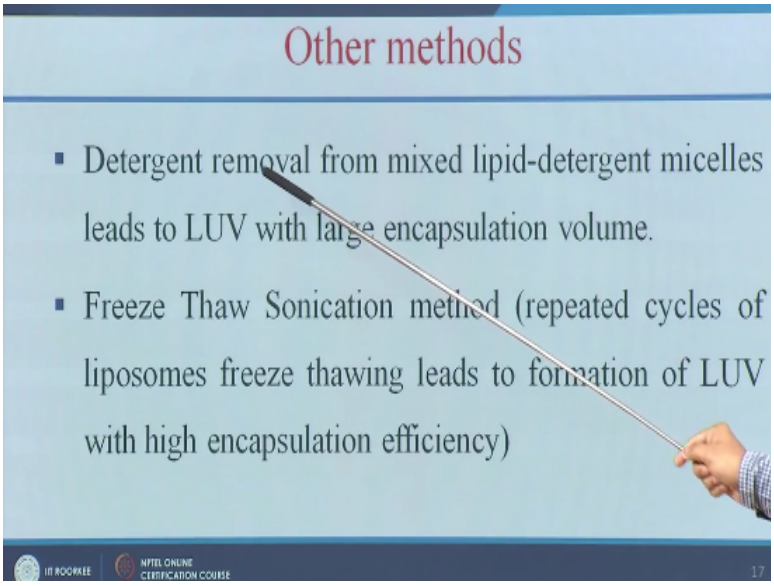

So other methods are it will use like a detergent removal from mixed lipid detergent micelles which leads to LUV with large encapsulation volume. And the next method is freeze thaw sonication method. So in this method will be having repeated the cycles of liposomes freeze thawing leads to formation load LUV with high encapsulation efficiency. So once you load the liposomes drugs than to purify. So how to purify that we can follow certificate and technique and we can follow dialyses and gel filtration.

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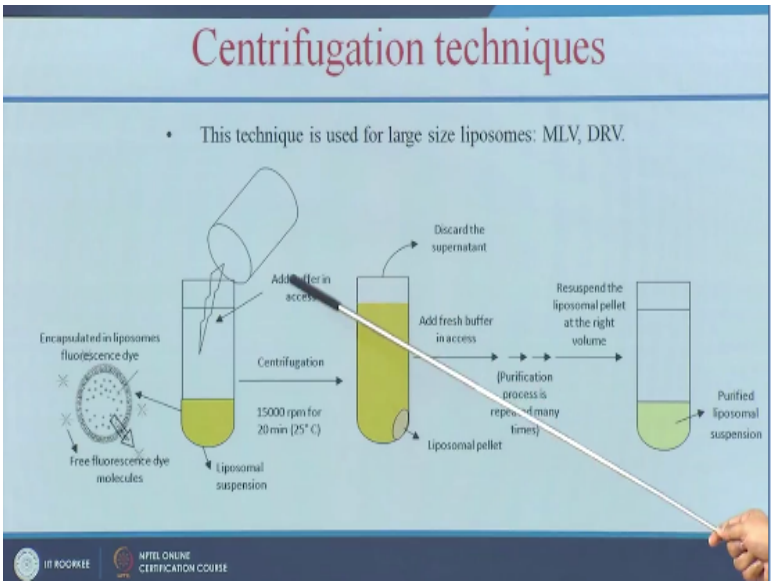

So in this lecture centrifugation technique when you centrifuge your liposomes which is loaded with the fluorescence dry molecules and it can remove the supernatant and your liposomal pellet and you are to add fresh buffer and again you can repeat the centrifugation process. By this process we can get the purify liposome suspension with your fluorescent nano particles or fluorescent dry molecules.

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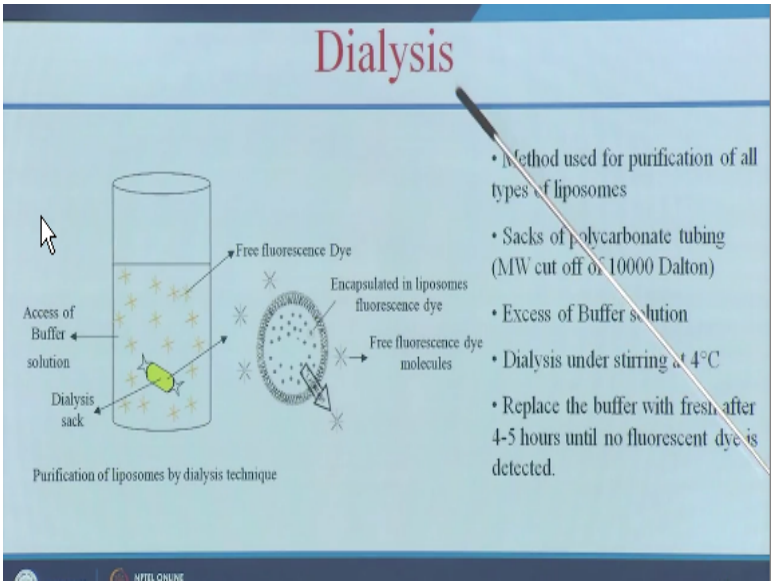

And next method is dialysis so here we are used for purification of all types of liposomes. And here will be using of dialysis back with the cut of molecular cut of 10000 Dalton. And we have excess of buffer solution and will dialyzing under stirring condition at 4º. And we have to replace the buffer a every 4-5 hours until no fluorescent dye is detected. So when i do the dialysis then you will get the particle loaded with fluorescent dye or fluorescent nanomolecules okay.

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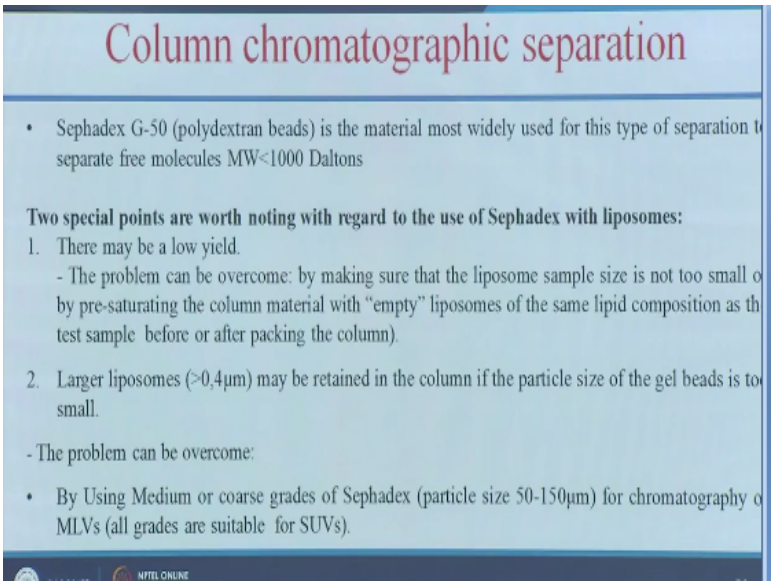

So the third method is column chromatographic separation. So here will be using sephadex G-50 that is polydexton beads and this molecular weight cut of is 10000 Daltons. When we using this spatters column you have to consider two important points. That is the may be a lower yield okay. So this problem can be cover come by making show that the liposome sample sizes not too small or the column can be please accurate with the empty liposome okay.

The second thing is larger liposome of more than 0.4 micrometer may be written in the column. So these are the problems with these sephadex methods. And these problems can be overcome by medium or coarse grades sephadex beats okay. So before we learn what is a solid sephadex nano particle let us see some other particles of lipid based nano particles. That is so noisome, so noisome are non ionic surfactant vesicles, oaky. And these are the widely studied as an alternative to liposomes.

So here the noisome overcome the disadvantages associated with the liposomes. For example chemical invisibility and variable purity of phospholipids and high cost. So these are the drawback of liposomes. This can be overcome by the noisome. So the preparation method can everything are the same for noisome or liposomes. So the only thing is it will be having non ionic surfactant. And this noisome are enhanced the penetration of drugs. And also we can have the controlled and targeted drug delivery using this noisome.

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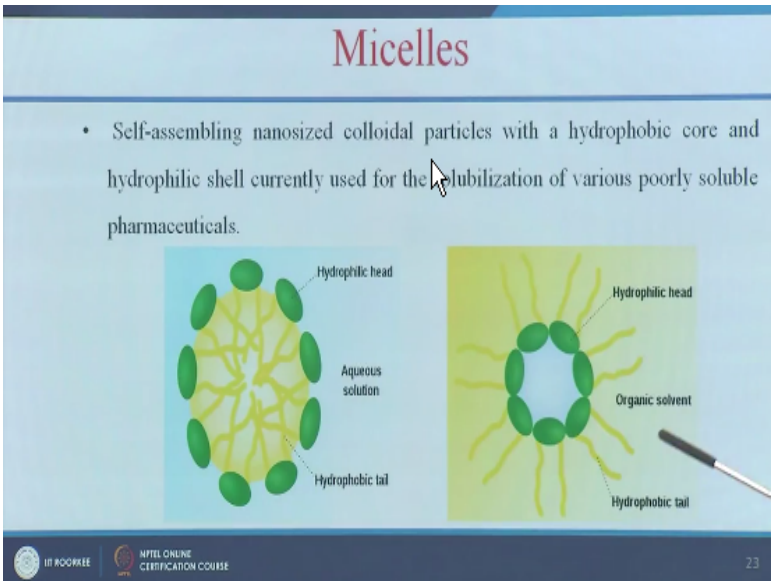

The next carrier is micelles, so here we can have the self assembling nano size colloidal particles with hydrophobic care and hydrophilic shell and it is mainly used for stabilizing of various poorly soluble pharmaceuticals. So here we can see is this hydrophilic head is facing two as water and a hydrophobic tail is towards inside. So it is in presence of water and the presence of organic solvent. So it is form the reverse micelles where the hydrophilic head will move toward inside and the hydrophobic head will move toward the outside toward the organic solvent.

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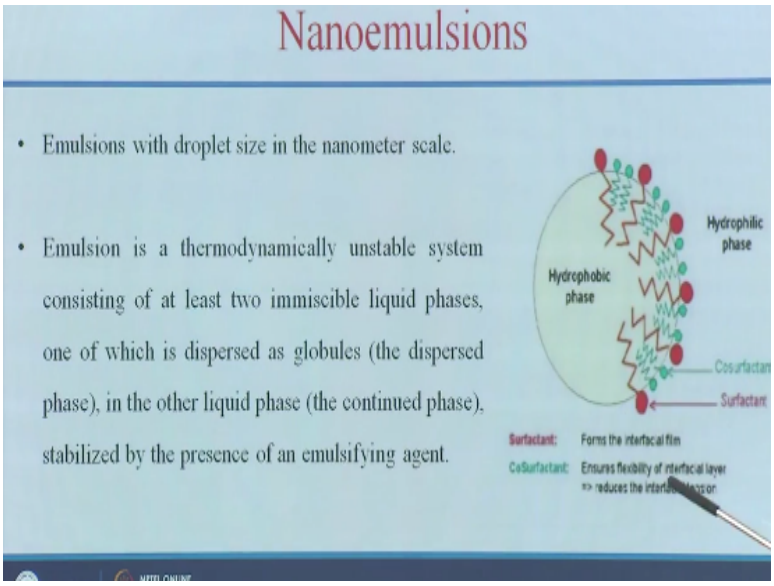

And another type of lipid based nanoemulsion so here the we can achieve emulsion in nano meter escape scale so emulsion means it is thermodynamically unstable system consist of two least immiscible liquid phases. So one of which is dispersed a globules okay. And the other one in the liquid phase. So these are stabilized by the presence of an emulsifying agent.

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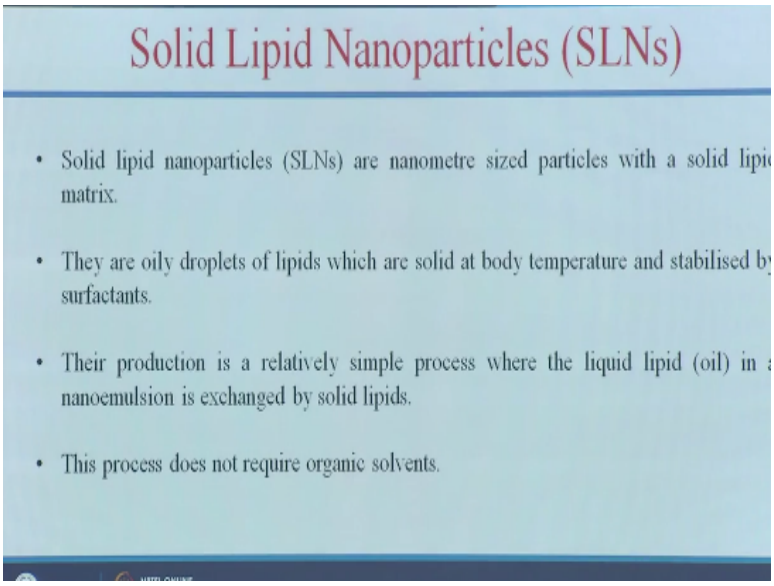

So that is called as nano emulsion. So let us see what solid lipid nano particles so solid lipid nano particles are nanometer size particles with solid lipid matrix okay. So these are oily droplets of which are body temperature and stabilized by surfactant. And there production is lately simple process where the liquid lipid oil in a nano emulsion is exchanged in by solid lipid okay. And this process is not required in a organic solvent.

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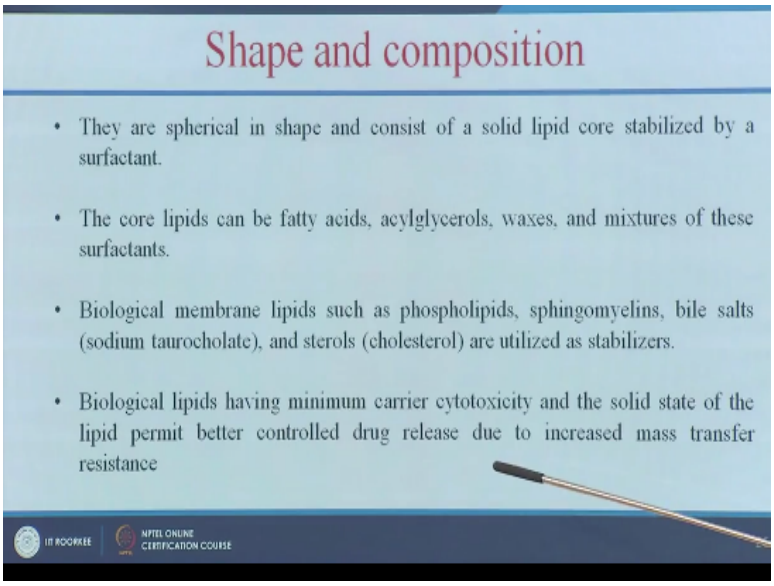

And here we can get the excellent that is solid lipid nano particles spherical in shape okay. and we will have the solid lipid core and this core lipid can be made up of fatty acids or vexes and the biologic membranes lipid such as phospholipids can be utilize as a stabilizer okay.

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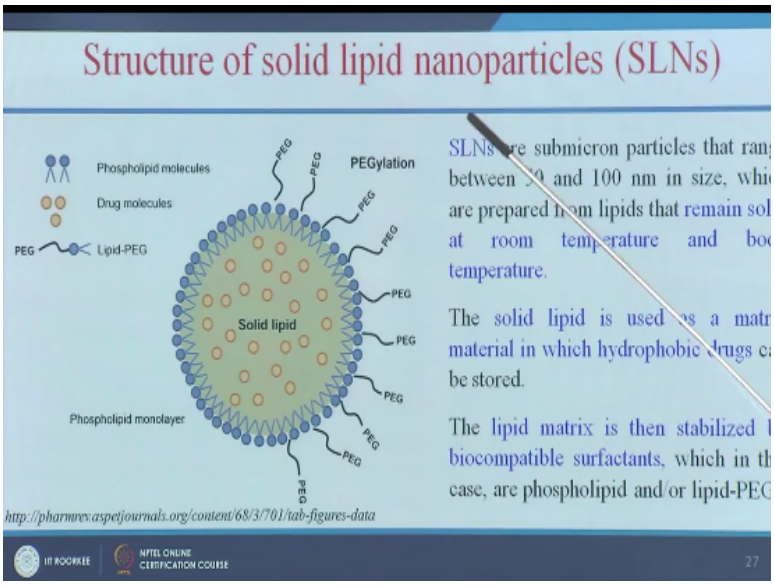

And this solid lipid nano particle will be in the size of between 50 to 100 nanometer. And it will be remain solid and room temperature and body temperature. And this solid lipid matrix is useful for your hydrophilic drugs okay. And this lipid matrix is stabilized to the biocompatible surfactant and in this case we can use phospholipids or we can use lipid PEG that is poly ethylene glycol for stabilizing your solid lipid nano particles.

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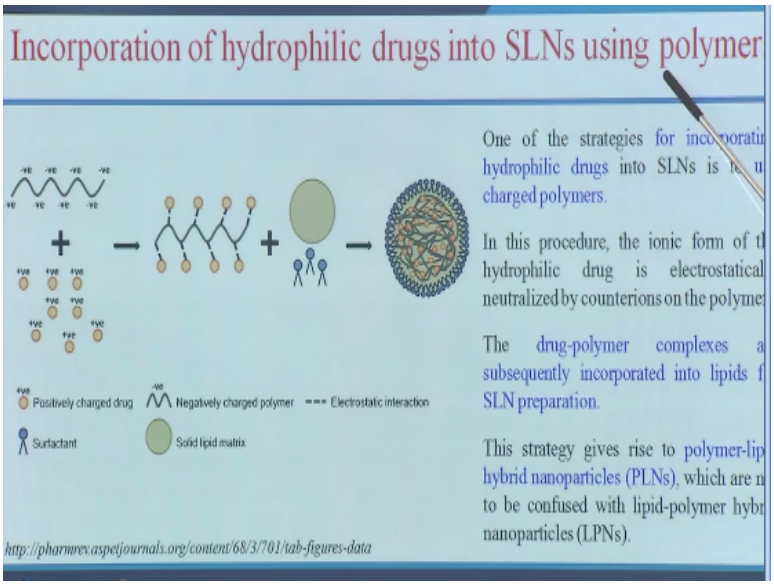

And we can incorporate hydrophilic drugs into this SLN using polymers. So here you can use that negative charge polymer and positively charge drug. So it will combine a form this kind of complex. And when you mix with the solid lipid matrix surfactant so it will form this kind of structure. So in this process the drug polymer complex are incorporated into the lipids for SLN preparation and this strategy gives rise to polymer lipid hybrid nanoparticle that is PLN. So there is another type of material that is LPN so that we will see what is LPN.

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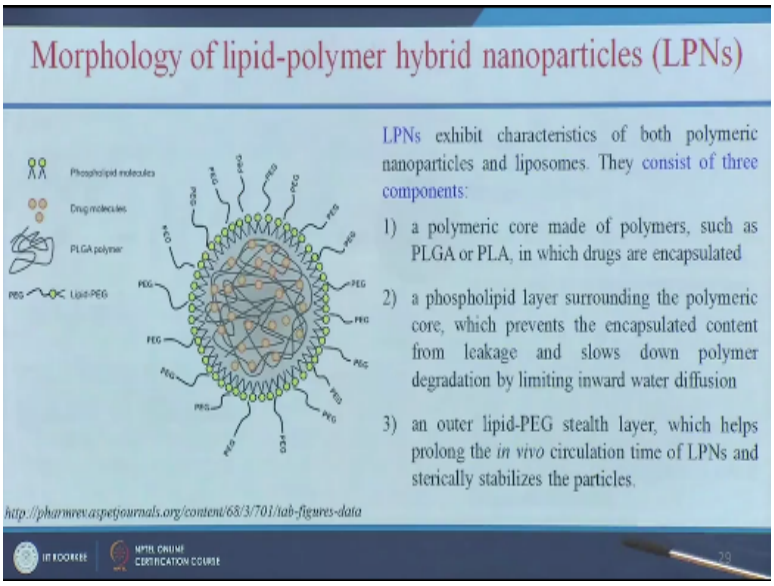

So LPN is lipid polymer hybrid nanoparticles, so here this LPN exhibit the characters of both polymeric nanoparticles as well as liposomes okay. So it mainly consists three components, the first one is polymeric core okay, the polymeric core is made up of your polymers like PLGA or PLA where your drug will be encapsulated followed by you will be having a phospholipids layer okay.

So that is surrounding your polymeric core, and which will prevent your encapsulated drug from leakage okay. And you will be having another outer lipid PEG so that is your stealth layer, so if you are having PEG outer layer, so that will make your nanoparticle to escape from the vertical system and that will increase your in vivo circulation time.

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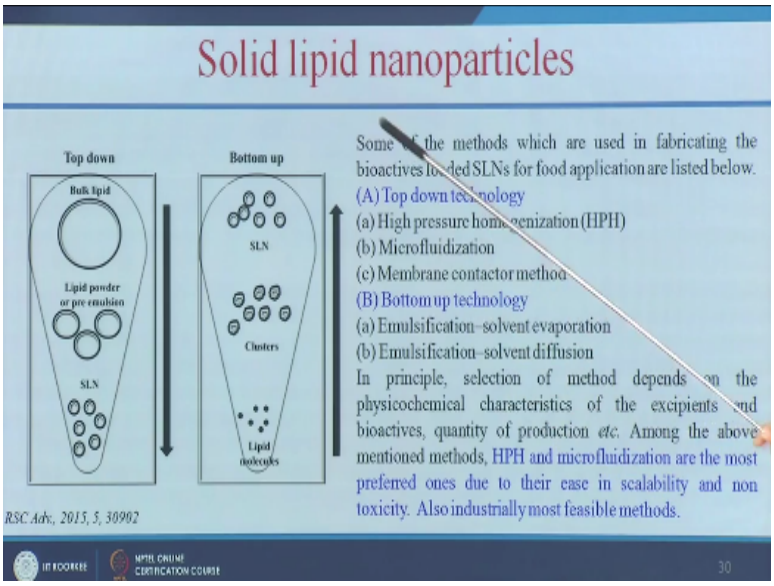

So how to make this solid vapor nanoparticles, again we can use the top down approach and bottom up approach. So top down approach is we can make from a bulk lipid, we can get the solid lipid nanoparticles, and bottom is from the lipid molecules we can get the solid lipid nanoparticles. Under the top down technology these are the methods, high pressure homogenization, micro fluidization, and membrane contractor method.

And under the bottom of you will be having emulsification, solvent evaporation and emulsification solvent diffusion. So out of these techniques this high pressure homogenization and micro fluidization are the most preferred ones, because it is easy to make at the same time it is also industrially most feasible method.

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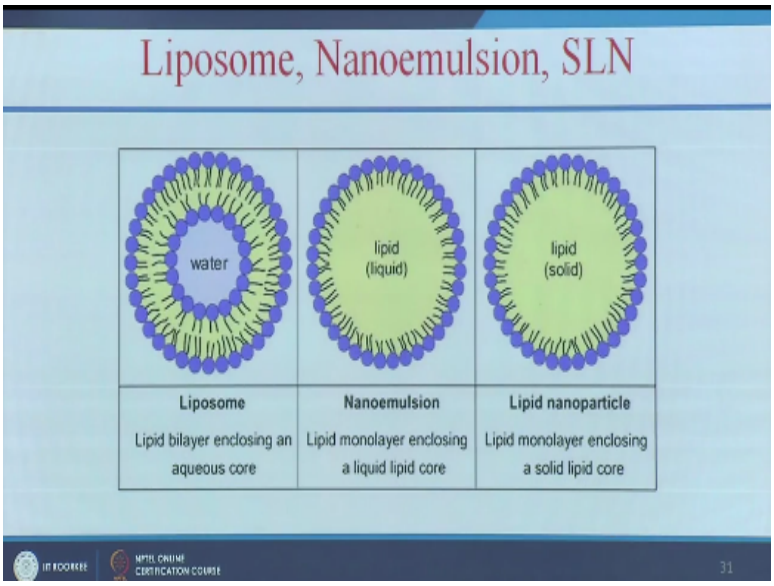

So let us see the difference between the liposome and nanoemulsion and lipid nanoparticle. So here in liposome the lipid bilayer enclosing an aqueous core okay, here it is water in nanoemulsion the lipid monolayer enclosing a liquid lipid core, and in case of lipid nanoparticle and solid lipid nanoparticle, so lipid monolayer enclosing a solid lipid core okay.

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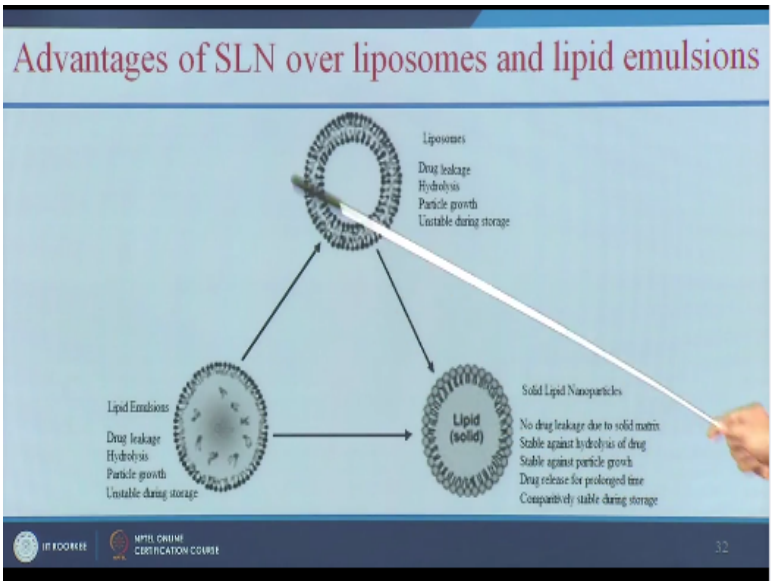

So what are the advantages of solid lipid nanoparticles when compared to the liposomes and lipid emulsions. So here in drawback of liposomes are drug leakage, hydrolysis and particle growth and unstable during storage. And in case of liquid emulsions same like drug leakage, hydrolysis and particle growth and unstabled during storage in the lipid emulsions. But these drawbacks will be overcome using solid lipid nanoparticle.

Here there is no drug leakage due to solid matrix, because we are having solid matrix in the core, so it will give the drug very slowly and it is stable like an hydrolysis of drug and this stable against the particle growth. And also it is having a solid core so it will release the drug very slowly for a long time, and it is comparative in the stable during storage.

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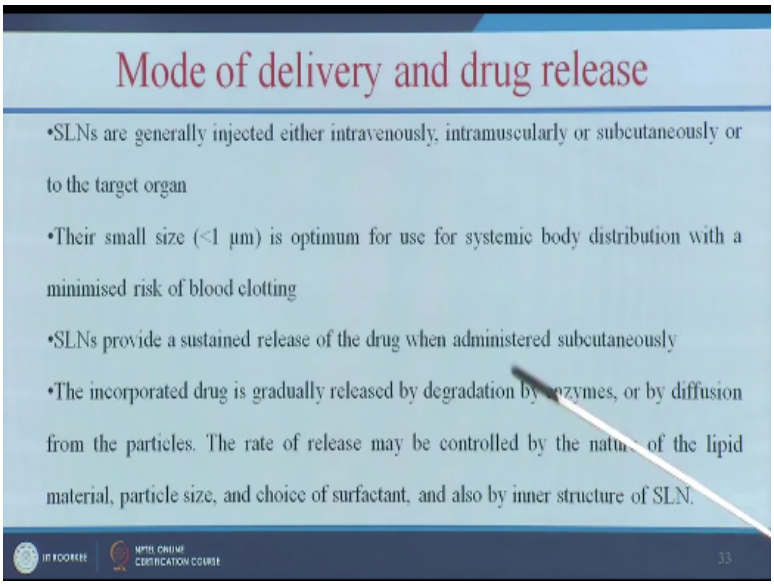

So let us see the mode of delivery and drug release of SLN, so here SLNs generally injected either intravenously or intramuscularly to target the organ. So due to the small size it can be useful for the systemic body distribution with the minimized risk of blood clotting okay. And SLN provide a sustained release of drug when administered subcutaneously.

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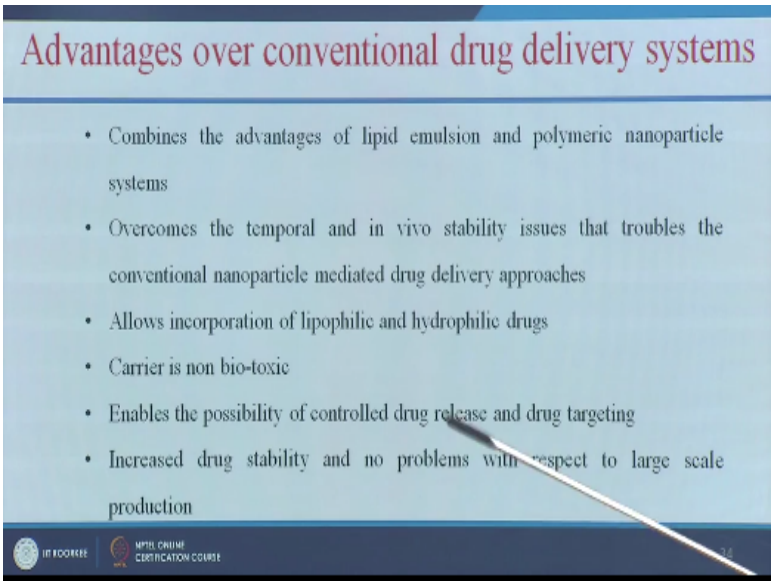

So let us see the advantages over the conventional drug delivery systems. So it combines the advantages of lipid emulsion as well as polymeric nanoparticle and it also overcomes the temporal and n v o stability which is very important for the nanoparticle of the drug delivery and the approaches and again here the we can load any hydrophilic and carrier is not toxic and again we can have the control of the drug and we have the anti body to target the carrier .

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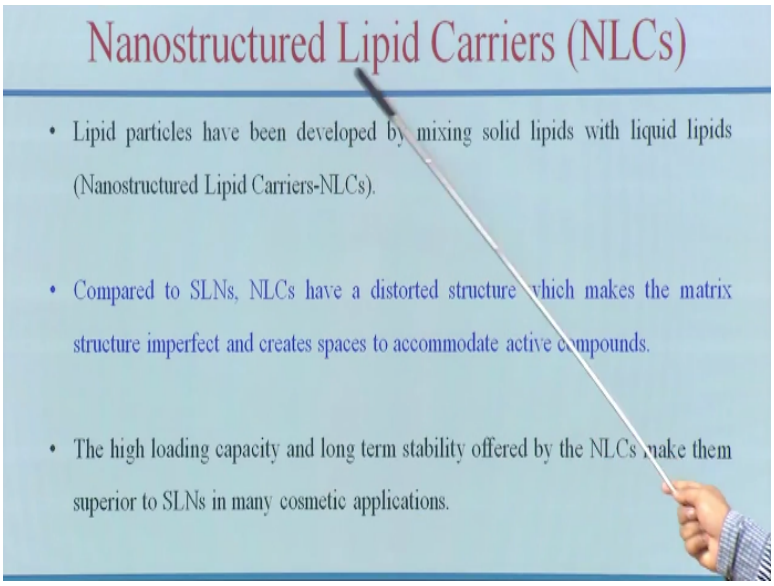

And the nano structure liquid career NILCS and it is similar to the nano particles but here the nano particles have been developed in the liquid lipids so when compare as in no have the deported structure, so which makes the matrix structure and in the create space to the actives compound so we have like a high loading capacity again in the long terms of the debility when comported to the assailment.

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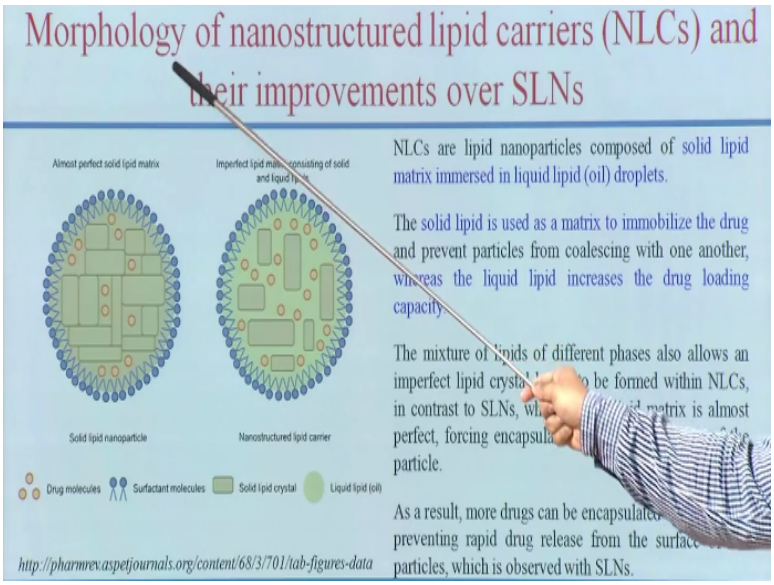

The morphology of the nano structure liquid carriers and the improvement over the lens , so the carriers are the liquid and the nano particle of the solid liquid and the matrix emerged in the liquid ,droplets this is the solid used in the matrix to the immobilize the drag and it Weill prevent the particle from the collapsing with and also the liquid and in the drug and in the capacity see the structure and the solid liquid nano particle and it is all the profile matrix and in the nano particles we check the carrier it is having in the liquid matrix and it is consisting and the solid and so due to this imperfect we can have the more drug and in the drug loading story and in the nice and also to prevent in the rapid from the surface which is the drawback of the SLNs .

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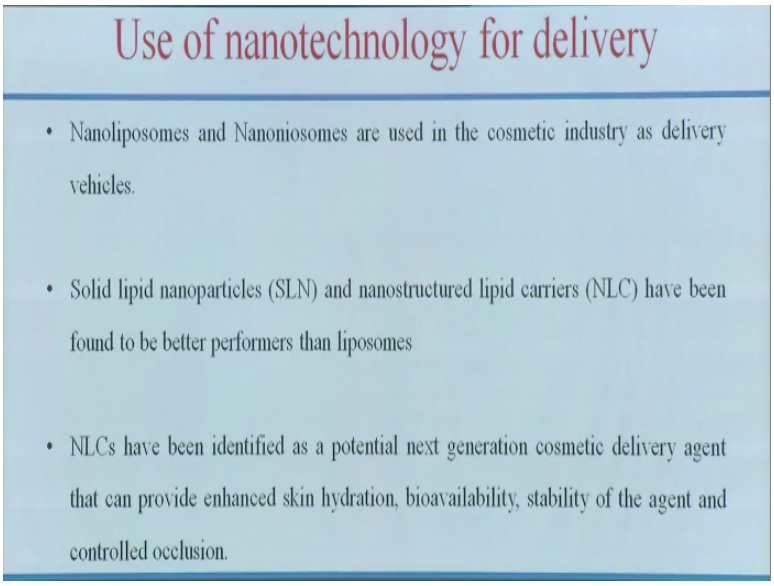

And this how we can use this nano technology for the various and the nanoniosomes carries' so the nano liposome Carrie and the nano new liposozone are mainly used in the osmotic and in the industry delivery vehicle and this (SLN)it is also a very good drug agent when compare to the lip zones and the nls have been in the depends on the potential net generation cosmetic delivery agent ,which can provide enhanced skin hydration bioavailability and the stability of the agent .

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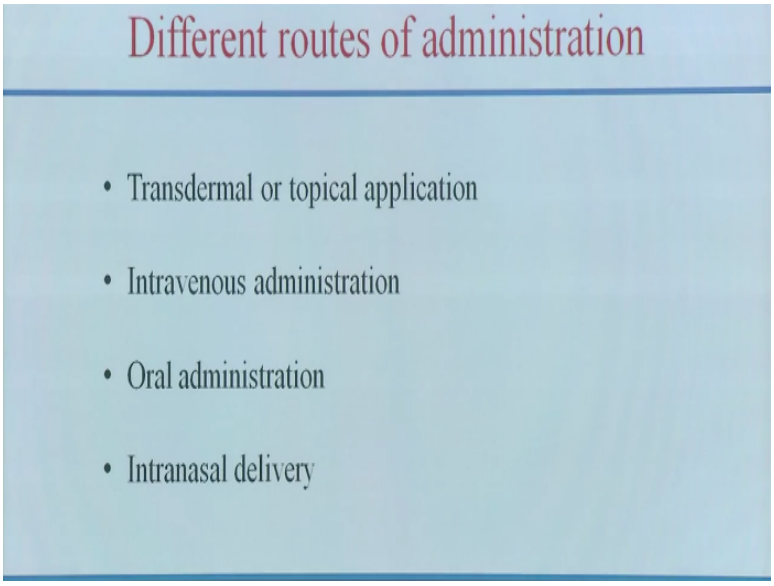

And the different roots of the administrative is possible using this liquid based career so this can be trans thermal and the intravenous or oral or it can be intranasal delivery

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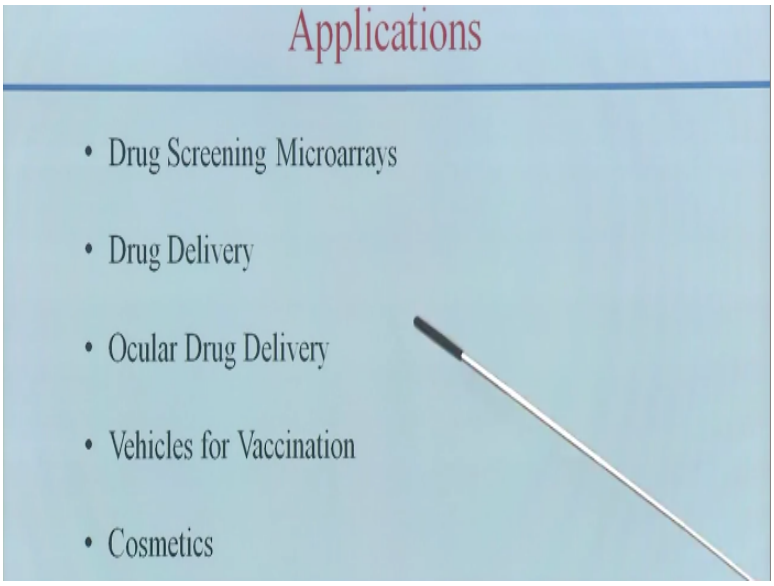

These are the various application liquid based particle let us see one by one.

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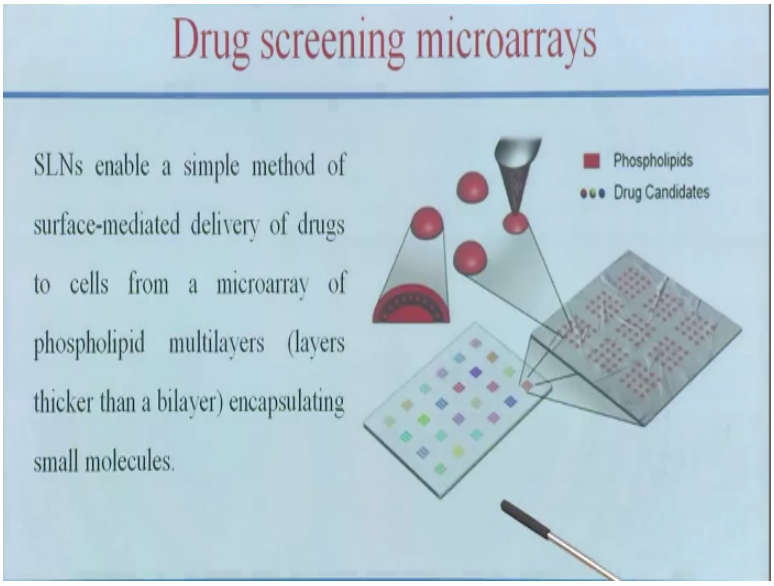

First one is drug screening micro waves and the solid liquid nano particles enable a simple method of the surface mediated delivery of drug to cells from a micro ray of the phosphoric multi layer and which is encapsulating small molecules. So this SLN will be useful for identifying the suitable drug candidate in a shorter duration of time. And next one is for drug delivery application.

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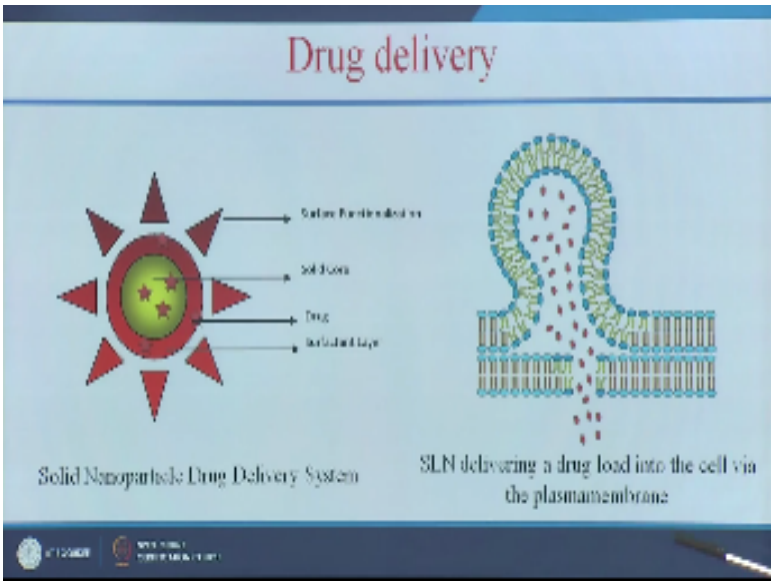

So this solid liquid nano particle based drug delivery system will be having a prolonged and control release of drug and it can release the drug through diffusion or by membrane fusion that we already explain in the mechanism part.

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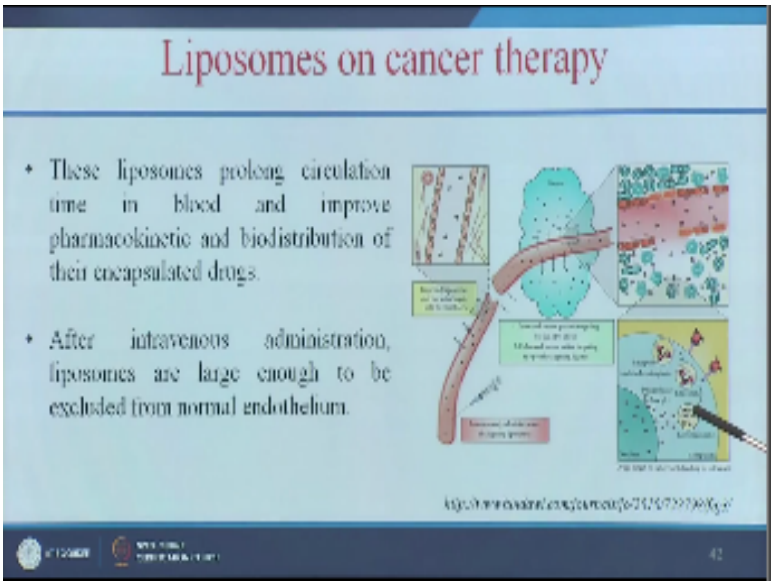

And this liposome can be useful for cancer therapy so usually in the tumor location it will have leaky blood vessels so if your liposome of size between 200 or more so it can accumulate in the tumor location and it can deliver the drug and which could be useful for cancer therapy.

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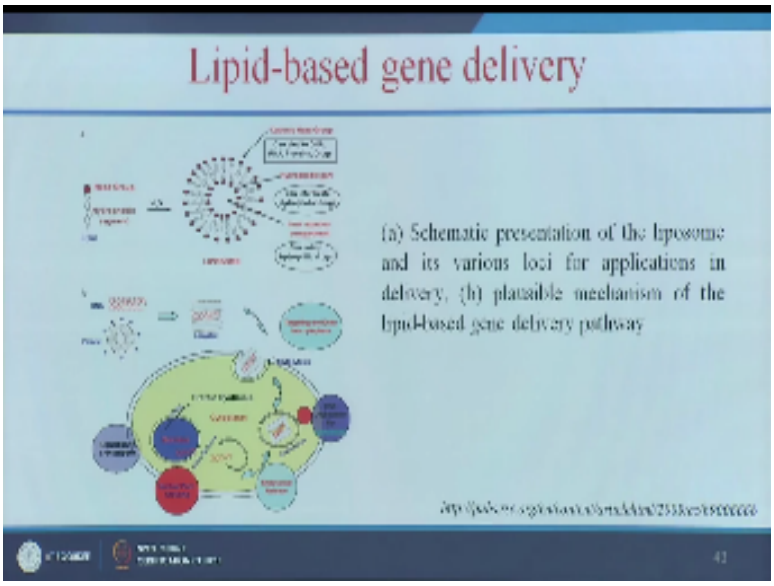

Next one is we can also use lipid based gene delivery agent so when you use that cationic lipid that is with positively charged lipid and you will have the DNA which is having negatively charge, so it will combine and form a lipoblast and this can attach to the cell and through endocytosis process it can deliver the gene. So we can use the lipid based nano carriers for gene therapy or gene delivery applications.

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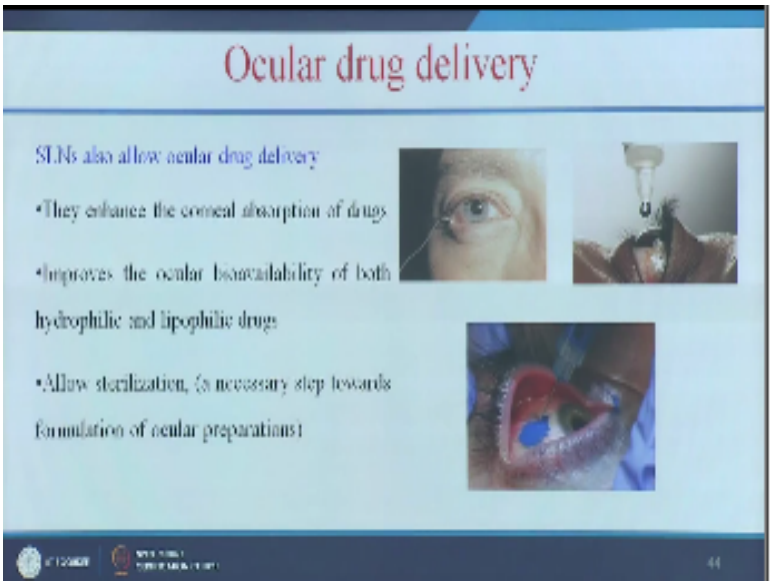

And we can also use solid liquid nano particles for ocular drug delivery okay, so this SLN will enhance the corneal absorption of drugs and improves the ocular bio availability of both hydrophilic and lipophilic drugs. And another important advantage of this SLN is it will allow the sterilization process so which is a very necessary step towards formulation of any ocular preparations.

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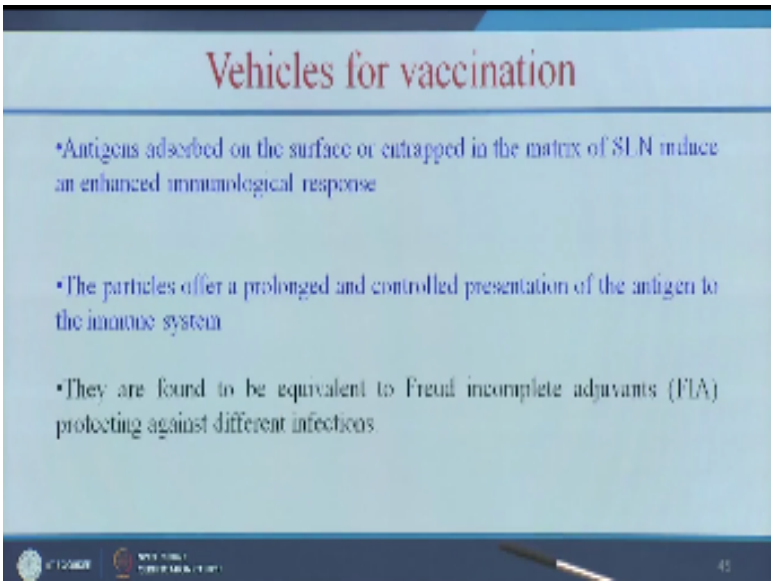

And it can also act like a vehicles for your vaccination so usually the antigens are absorbed on the surface or entrapped in the matrix of solid liquid nano particle so which will induce the enhance the immunological response okay, and her the particles offer a prolonged and controlled presentation of the antigen to the immune system so this SLN based vaccine will have a very good protecting effect against the different kind of infections.

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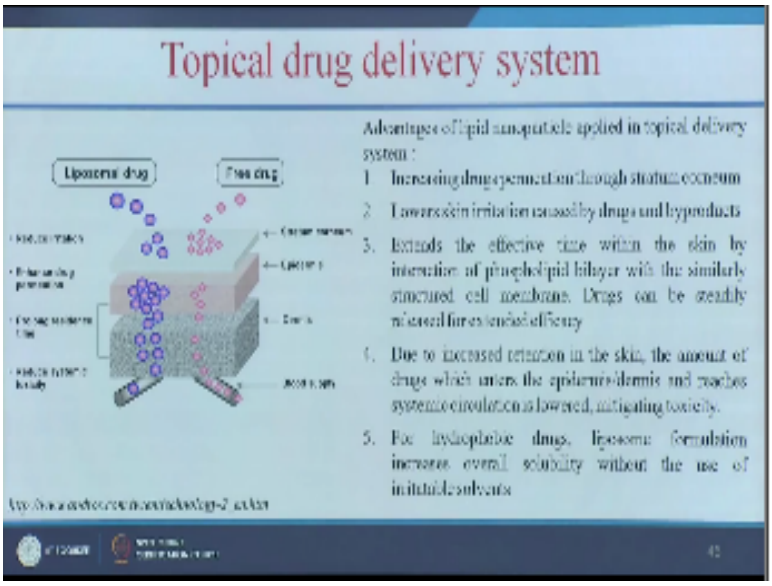

So the next application is topical drug delivery system so we can see the different between the free drug as well as liposomal drug and the free drug it is entering through the screen and it is reaching the blood supply which will induce the systemic toxicity incase of liposomal drug it will reduce the irritation and it will enhance the drug permeation and also it will show prolong residence time and it will reduce the systemic toxicity so we can see the difference in free drug there are more amount of drug molecules are going to the blood and here you can see that liposomal based drug delivery that is control and slow release of your drug molecules.

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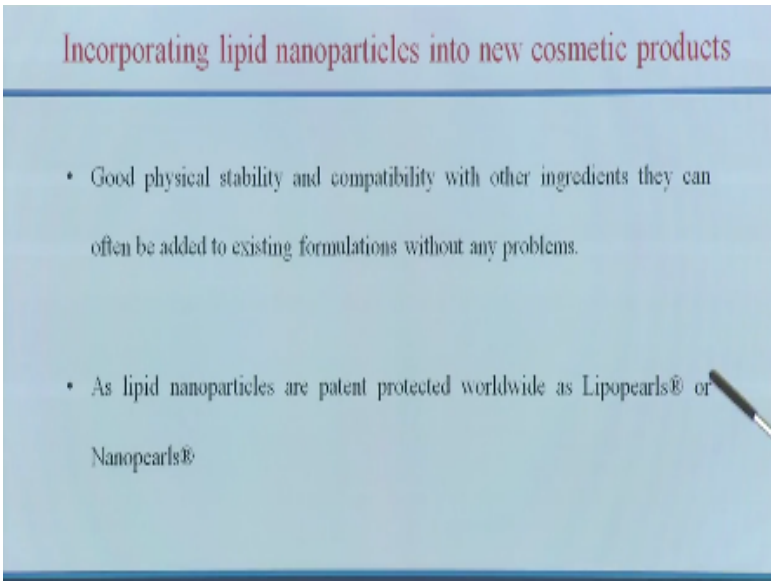

And we can also incorporate lipid nano particles into new cosmetic products because it has very good physical stability and compatibility with other ingredients and this lipid nano particles also patent provided worldwide as lippopearls or nanoperals or various cosmetics applications.

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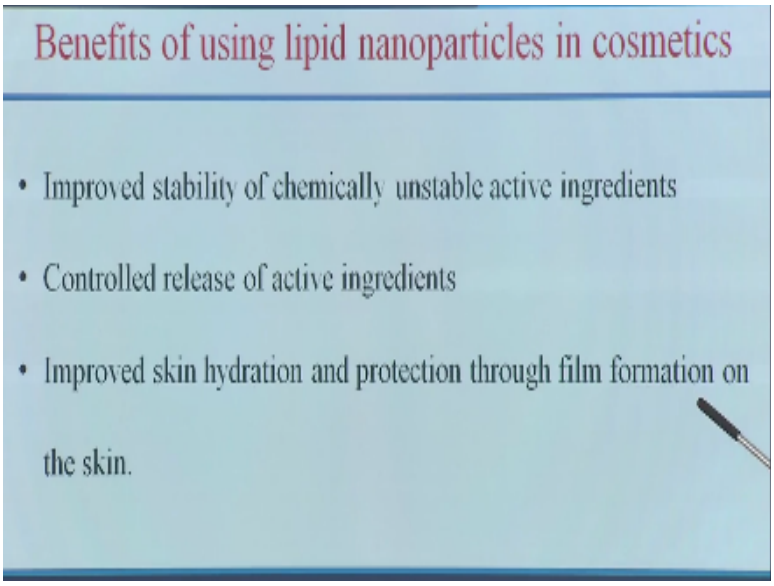

So in cosmetics it will have improved stability of chemically unstable ingredients and also it will have controlled release of active ingredients and it will improve the skin hydration and protection through the film formation on the skin.

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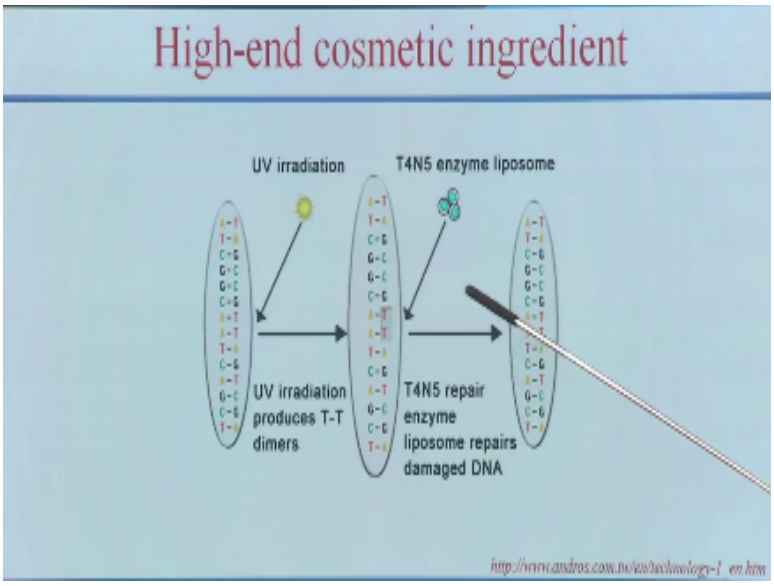

So another application is high end cosmetic ingredient okay, so usually the uv rays in the sun light it will create time in timer formation in your DNA, so you can see here this TT form that is time and timer it is the ultra bond and it will leads to damage the cell and also it can cause skin cancer. So when you have the T4N5 enzyme liposome so that will repairs this time and time dimer repair in the DNA.

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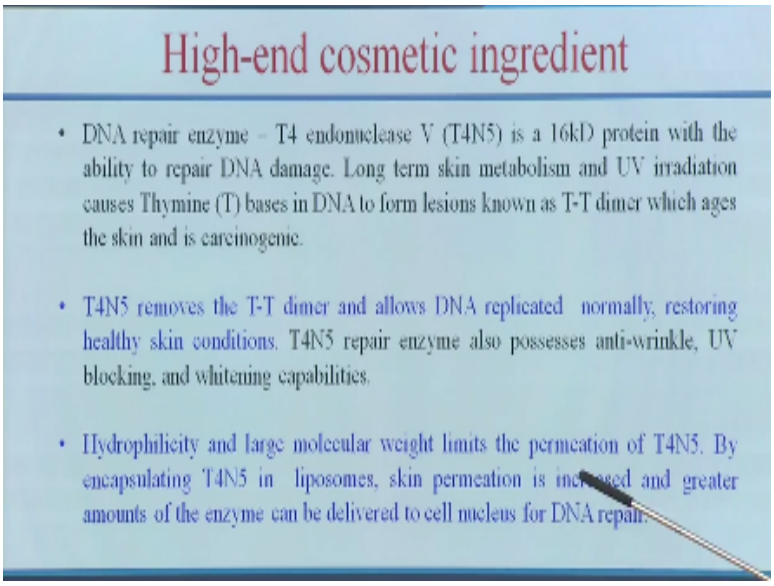

And this T4N5 removes the T for T dimer will allows and DNA replicated normally, restoring healthy skin conditions, so the hydrophilicity and large molecular weight limit the permeation of T4N5. By encapsulating T4N5 in liposome it will enhance the skin condition and greater amounts of enzyme can be delivered to cell nucleus for DNA repair.

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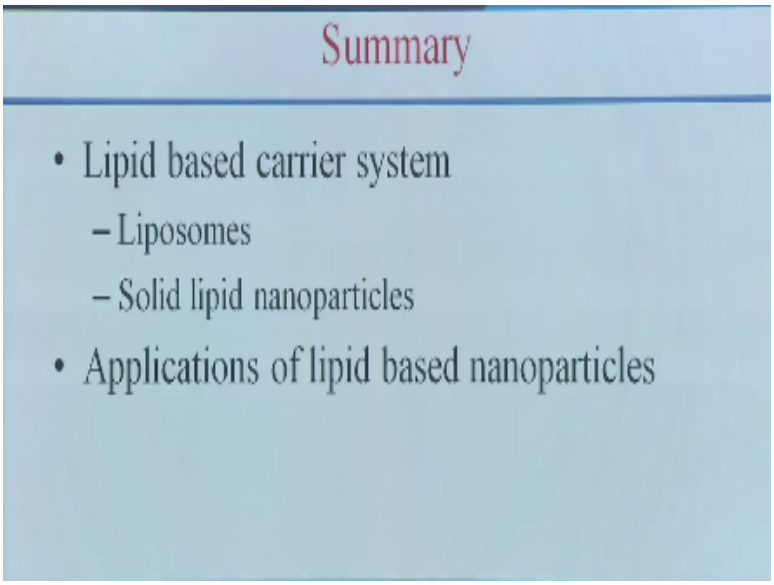

So as a summary in this lecture we have learnt various lipid based carrier system and especially liposome and solid lipid nanoparticles and also we have learned various applications of lipid based nanoparticles. So I end my lecture here and I thank you all for listening I will see you in another lecture.

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