

INDIAN INSTITUTE OF TECHNOLOGY ROORKEE

NPTEL

NPTEL ONLINE CERTIFICATION COURSE

Biomedical Nanotechnology

Lec-08

Lipid Nanotechnology

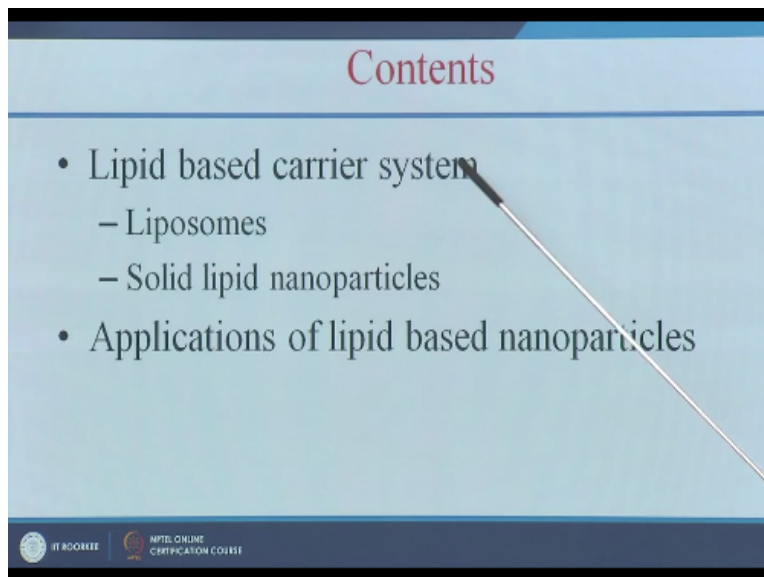
Dr. P. Gopinath

Department of Biotechnology

Indian Institute of Technology Roorkee

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

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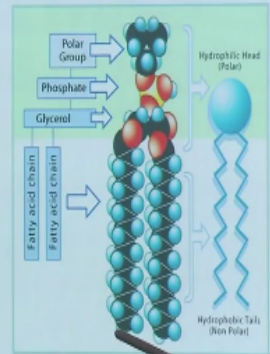


So in this lecture we are going to know the lipid based carrier system. And mainly Liposomes and solid lipid nanoparticles. And also we are going to see various applications of lipid based nanoparticles.

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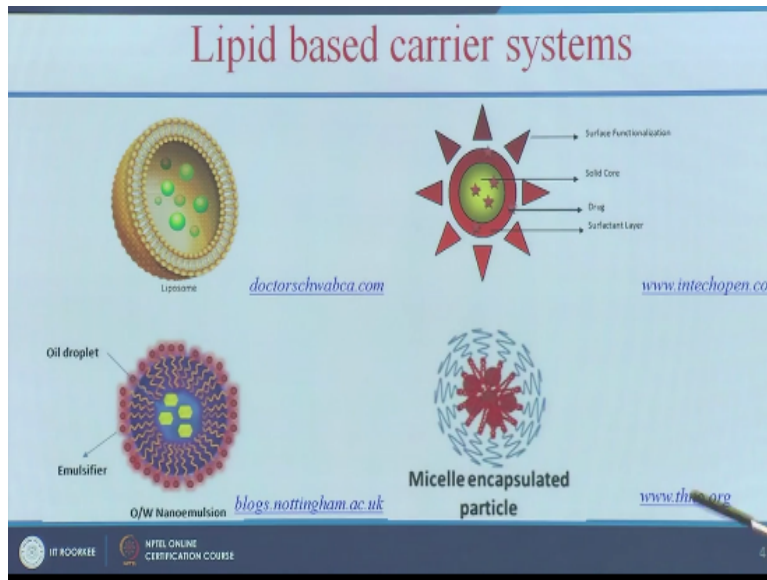
Phospholipid molecules

- Lipids are a major class of biomolecules that includes fatty acids, waxes, glycerol and triacylglycerols, phospholipids and cholesterol.
- Amphiphilic nature



So first we are see what is phospholipids. So lipids are the major class of bimolecular that includes fatty acids, waxy glycerol and triacylglycerols. Phospholipids and cholesterol. 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 nanoemulsion and this is micelle okay. So in this lecture we are going to learn all these entire lipid based carrier system.

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Pharmaceutical nano carriers of choice

An ideal pharmaceutical Nano carriers for i.v administration

- ★ Biocompatible & Biodegradable
- ★ Small size, high loading capacity
- ★ Prolonged circulation
- ★ Tumor accumulation

Liposome

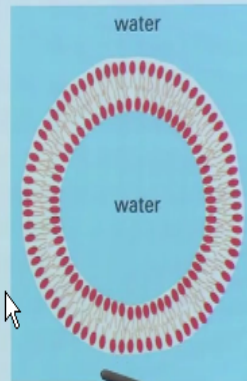
Polymeric Micelle

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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Liposomes

- **LIPOSOMES** are the smallest round structure technically produced by natural non-toxic phospholipids and cholesterol.
 - They can be used as drug carriers and they can be “loaded” with a huge variety of molecules, as small drug molecules, proteins, nucleotides even plasmids or particles.
 - They have a very versatile structure and thus, a variety of applications.



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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Liposomes

- Vehicle for drug administration, can carry both hydrophobic and hydrophilic loads
- Liposomal Cisplatin – Lipoplatin (Anticancer Drug)
- Liposomes are composed of natural lipids (phospholipids and cholesterol)
- Lower risk of toxicity

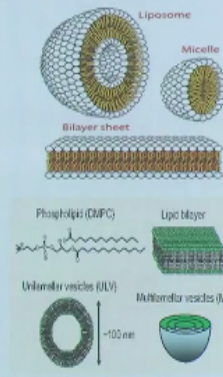


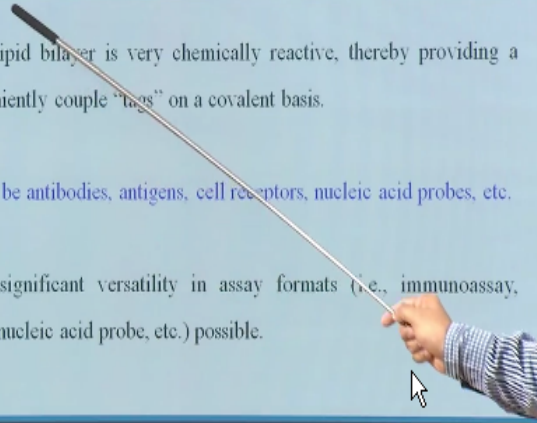
Fig. 1. Illustration of a typical phospholipid (DMPC), a phospholipid bilayer, a unilamellar vesicle and a multilamellar vesicle.

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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Liposomes

- Their exterior lipid bilayer is very chemically reactive, thereby providing a means to conveniently couple “tags” on a covalent basis.
- Such “tags” can be antibodies, antigens, cell receptors, nucleic acid probes, etc.
- This provides significant versatility in assay formats (i.e., immunoassay, receptor-based, nucleic acid probe, etc.) possible.



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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 liposomes to the cancer cells so physically.

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Liposomes

- With diameters ranging in size from approximately 50 nm to 800 nm, their aqueous core encapsulates up to millions of molecules of signal generating "markers" that can be detected in a variety of different way.
- A variety of different encapsulants are possible including visually detectable dyes (since the lipid bilayer is transparent), optically and fluorometrically detectable dyes, enzymes, and electroactive compounds.



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 cloro-cent nanoparticles or closed martial. And we can it also for various imaging and diagnostic applications.

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Liposome types

Conventional

Cationic

Stealth

Targeted

>Stealth = invisible to the Reticulo-Endothelial system (RES)

-Conventional

-Stealth
(with PEG molecules on their surface)

-Targeted
(with addition of ligands as antibodies etc)

-Cationic
(with positive surface charge)

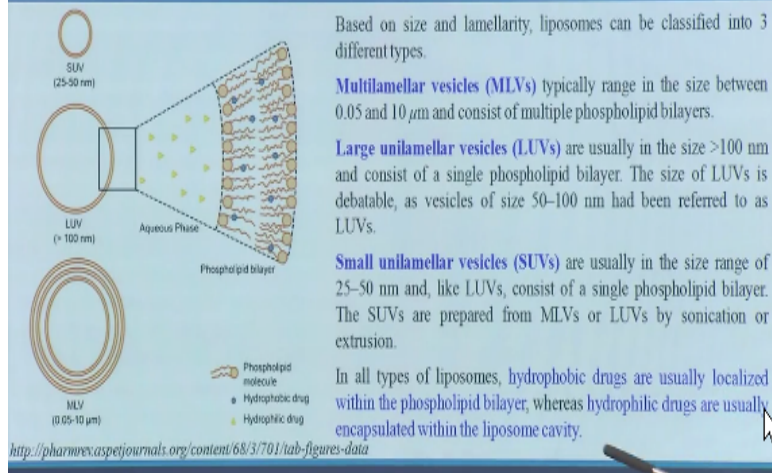
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So let us see the type of liposomes. And the first one is conventional liposomes and next one stealth okay. The stealth liposome is like at his liposomes with poly ethylene glycol. So the surface of the liposomes will be covered with polyethylene glycol 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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Types of liposomes classified by size and lamellarity



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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Size determined by methods

MLV: Multilamellar vesicles

Monolamellar vesicles:
 SUV: Small unilamellar vesicles
 LUV: Large unilamellar vesicles
 GUV: Giant unilamellar vesicles

Sonication: SUV
 Smaller than 100 nm diameter

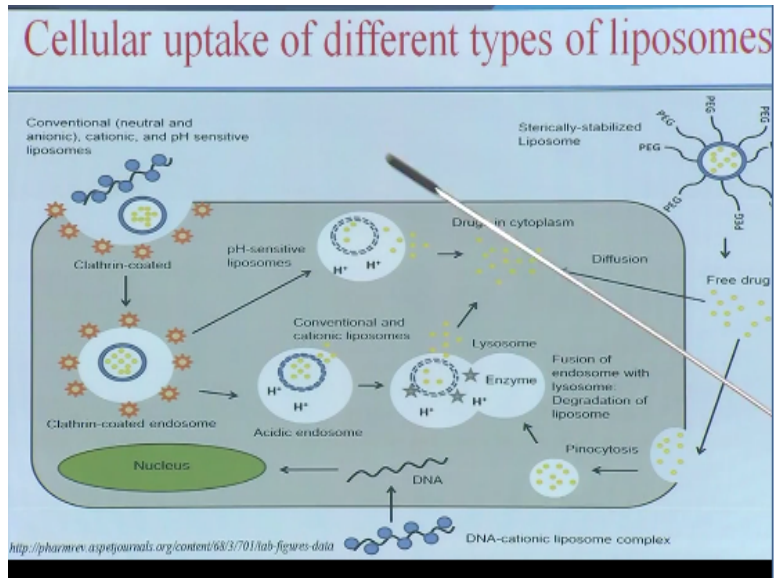
Extrusion: LUV (Size depends on the filters)
 100 nm—1 μ m diameter

Evaporation: GUV
 Larger than 1 μ m diameter

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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 elctrostatic 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 pinocytosis. 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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Liposome advantages

- Retention of both lipophilic and hydrophilic drugs.
- Easy Tailoring, ex. Antibody or ligand conjugation [targeting]
- Minimum antigenicity.
- Biodegradability
- Biocompatibility



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 antigenicity. That means highly biocompatibility and biodegradable.

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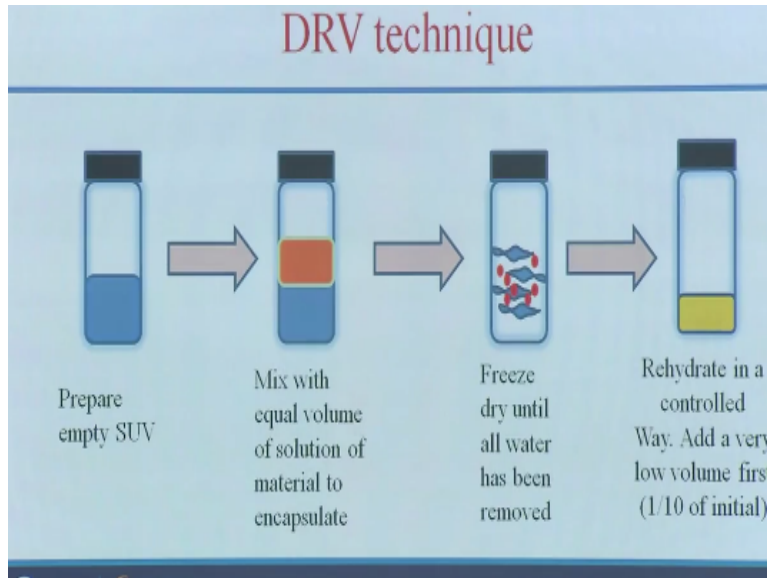
Liposome by dehydrated-rehydrated vesicles (DRV) method

- Introduced by C. Kirby and G. Gregoriadis, in 1984.
- Empty SUV liposome dispersion is lyophilized (freeze - drying) in presence of solution of the compound to be entrapped.
- During rehydration, the addition of small volume of water results in liposomes with high entrapment efficiency.
- **Advantages:** simplicity, mild conditions used (important for sensitive molecules) and high encapsulation efficiency for a variety of compounds.

This liposomes can be prepared by seven methods so here I will be explaining some methods here I will be explaining 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 entrap your drug or if you want to entrap the fluorescent particles.

So that should be lyophilized in presence of SUV liposomes. So during rehydration the addition of small volume of water results in liposome with high entrapment 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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Other methods

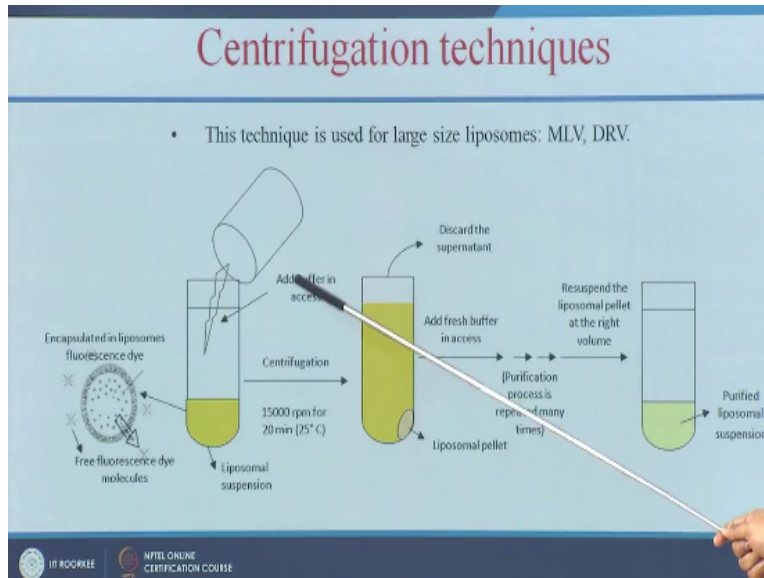
- Detergent removal from mixed lipid-detergent micelles leads to LUV with large encapsulation volume.
- Freeze Thaw Sonication method (repeated cycles of liposomes freeze thawing leads to formation of LUV with high encapsulation efficiency)



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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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Dialysis

Purification of liposomes by dialysis technique

- Method used for purification of all types of liposomes
- Sacks of polycarbonate tubing (MW cut off of 10000 Dalton)
- Excess of Buffer solution
- Dialysis under stirring at 4°C
- Replace the buffer with fresh after 4-5 hours until no fluorescent dye is detected.

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 4°. 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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Column chromatographic separation

- Sephadex G-50 (polydextran beads) is the material most widely used for this type of separation to separate free molecules MW<1000 Daltons

Two special points are worth noting with regard to the use of Sephadex with liposomes:

1. There may be a low yield.
 - The problem can be overcome: by making sure that the liposome sample size is not too small or by pre-saturating the column material with "empty" liposomes of the same lipid composition as the test sample before or after packing the column).
2. Larger liposomes (>0.4µm) may be retained in the column if the particle size of the gel beads is too small.
 - The problem can be overcome:

- By Using Medium or coarse grades of Sephadex (particle size 50-150µm) for chromatography of MLVs (all grades are suitable for SUVs).

So the third method is column chromatographic separation. So here will be using sephadex G-50 that is polydextran beads and this molecular weight cut off is 10000 Daltons. When we use this slotted column you have to consider two important points. That is there may be a lower yield okay. So this problem can be overcome by making sure that the liposome sample size is not too small or the column can be pre-saturated with the empty liposome okay.

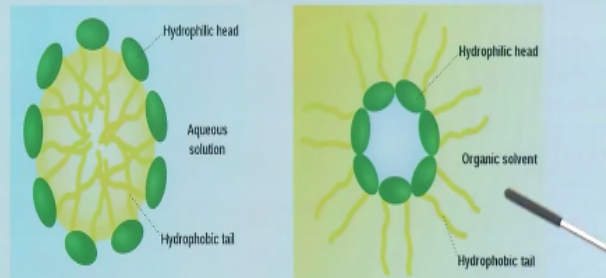
The second thing is larger liposome of more than 0.4 micrometer may be retained in the column. So these are the problems with these sephadex methods. And these problems can be overcome by using medium or coarse grades sephadex beads okay. So before we learn what is a solid sephadex nanoparticle let us see some other particles of lipid based nanoparticles. That is so noisome, so noisome are non ionic surfactant vesicles, okay. And these are 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 drawbacks of liposomes. This can be overcome by the noisome. So the preparation method can be the same for noisome or liposomes. So the only thing is it will be having non ionic surfactant. And this noisome enhances the penetration of drugs. And also we can have the controlled and targeted drug delivery using this noisome.

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Micelles

- Self-assembling nanosized colloidal particles with a hydrophobic core and hydrophilic shell currently used for the solubilization of various poorly soluble pharmaceuticals.

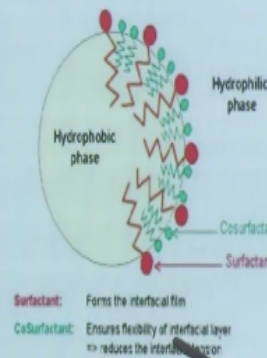


The next carrier is micelles, so here we can have the self assembling nano size colloidal particles with hydrophobic care and hydrophilic shell and it is mainly used for stabilizing of various poorly soluble pharmaceuticals. So here we can see is this hydrophilic head is facing two as water and a hydrophobic 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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Nanoemulsions

- Emulsions with droplet size in the nanometer scale.
- Emulsion is a thermodynamically unstable system consisting of at least two immiscible liquid phases, one of which is dispersed as globules (the dispersed phase), in the other liquid phase (the continued phase), stabilized by the presence of an emulsifying agent.



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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Solid Lipid Nanoparticles (SLNs)


- Solid lipid nanoparticles (SLNs) are nanometre sized particles with a solid lipid matrix.
- They are oily droplets of lipids which are solid at body temperature and stabilised by surfactants.
- Their production is a relatively simple process where the liquid lipid (oil) in a nanoemulsion is exchanged by solid lipids.
- This process does not require organic solvents.



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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Shape and composition

- They are spherical in shape and consist of a solid lipid core stabilized by a surfactant.
- The core lipids can be fatty acids, acylglycerols, waxes, and mixtures of these surfactants.
- Biological membrane lipids such as phospholipids, sphingomyelins, bile salts (sodium taurocholate), and sterols (cholesterol) are utilized as stabilizers.
- Biological lipids having minimum carrier cytotoxicity and the solid state of the lipid permit better controlled drug release due to increased mass transfer resistance



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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 waxes and the biologic membranes lipid such as phospholipids can be utilize as a stabilizer okay.

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Structure of solid lipid nanoparticles (SLNs)

SLNs are submicron particles that range between 50 and 100 nm in size, which are prepared from lipids that remain solid at room temperature and body temperature.

The solid lipid is used as a matrix material in which hydrophobic drugs can be stored.

The lipid matrix is then stabilized by biocompatible surfactants, which in this case, are phospholipid and/or lipid-PEG.

<http://pharmrev.aspetjournals.org/content/68/3/701/tab-figures-data>

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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 at 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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Incorporation of hydrophilic drugs into SLNs using polymer

One of the strategies for incorporating hydrophilic drugs into SLNs is to use charged polymers.

In this procedure, the ionic form of the hydrophilic drug is electrostatically neutralized by counterions on the polymer.

The drug-polymer complexes are subsequently incorporated into lipids for SLN preparation.

This strategy gives rise to polymer-lipid hybrid nanoparticles (PLNs), which are not to be confused with lipid-polymer hybrid nanoparticles (LPNs).

<http://pharmrev.aspetjournals.org/content/68/3/701/tab-figures-data>

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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Solid lipid nanoparticles

Top down

Bulk lipid

Lipid powder or pre-emulsion

SLN

Bottom up

SLN

Clusters

Lipid molecules

Some of the methods which are used in fabricating the bioactives loaded SLNs for food application are listed below.

(A) Top down technology

- (a) High pressure homogenization (HPH)
- (b) Microfluidization
- (c) Membrane contactor method

(B) Bottom up technology

- (a) Emulsification-solvent evaporation
- (b) Emulsification-solvent diffusion

In principle, selection of method depends on the physicochemical characteristics of the excipients and bioactives, quantity of production etc. Among the above mentioned methods, HPH and microfluidization are the most preferred ones due to their ease in scalability and non-toxicity. Also industrially most feasible methods.

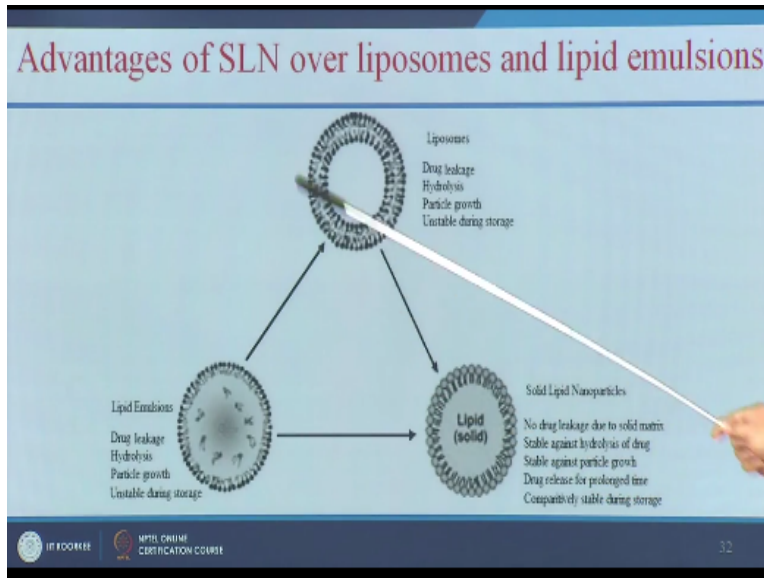
RSC Adv., 2015, 5, 30902

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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 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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Mode of delivery and drug release

- SLNs are generally injected either intravenously, intramuscularly or subcutaneously or to the target organ
- Their small size (<1 μm) is optimum for use for systemic body distribution with a minimised risk of blood clotting
- SLNs provide a sustained release of the drug when administered subcutaneously
- The incorporated drug is gradually released by degradation by enzymes, or by diffusion from the particles. The rate of release may be controlled by the nature of the lipid material, particle size, and choice of surfactant, and also by inner structure of SLN.

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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Advantages over conventional drug delivery systems

- Combines the advantages of lipid emulsion and polymeric nanoparticle systems
- Overcomes the temporal and in vivo stability issues that troubles the conventional nanoparticle mediated drug delivery approaches
- Allows incorporation of lipophilic and hydrophilic drugs
- Carrier is non bio-toxic
- Enables the possibility of controlled drug release and drug targeting
- Increased drug stability and no problems with respect to large scale production

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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 in vivo 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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Nanostructured Lipid Carriers (NLCs)

- Lipid particles have been developed by mixing solid lipids with liquid lipids (Nanostructured Lipid Carriers-NLCs).
- Compared to SLNs, NLCs have a distorted structure which makes the matrix structure imperfect and creates spaces to accommodate active compounds.
- The high loading capacity and long term stability offered by the NLCs make them superior to SLNs in many cosmetic applications.

And the nano structure liquid carrier NLCs 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 distorted structure, so which makes the matrix structure and in the create space to the active compound so we have like a high loading capacity again in the long terms of the stability when compared to the emulsion.

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Morphology of nanostructured lipid carriers (NLCs) and their improvements over SLNs

NLCs are lipid nanoparticles composed of solid lipid matrix immersed in liquid lipid (oil) droplets.

The solid lipid is used as a matrix to immobilize the drug and prevent particles from coalescing with one another, whereas the liquid lipid increases the drug loading capacity.

The mixture of lipids of different phases also allows an imperfect lipid crystal to be formed within NLCs, in contrast to SLNs, where the lipid matrix is almost perfect, forcing encapsulation into a solid lipid particle.

As a result, more drugs can be encapsulated, preventing rapid drug release from the surface of the particles, which is observed with SLNs.

<http://pharmrev.aspetjournals.org/content/68/3/701/tab-figures-data>

The morphology of the nano structure liquid carriers and the improvement over the SLNs, 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 drug and it will 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 perfect 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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Use of nanotechnology for delivery

- Nanoliposomes and Nanoniosomes are used in the cosmetic industry as delivery vehicles.
- Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) have been found to be better performers than liposomes
- NLCs have been identified as a potential next generation cosmetic delivery agent that can provide enhanced skin hydration, bioavailability, stability of the agent and controlled occlusion.

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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Different routes of administration

- Transdermal or topical application
- Intravenous administration
- Oral administration
- Intranasal delivery

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

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Applications

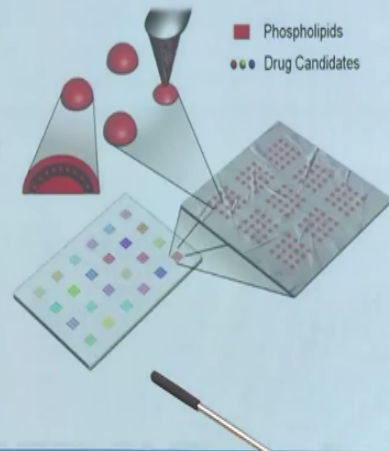
- Drug Screening Microarrays
- Drug Delivery
- Ocular Drug Delivery
- Vehicles for Vaccination
- Cosmetics

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

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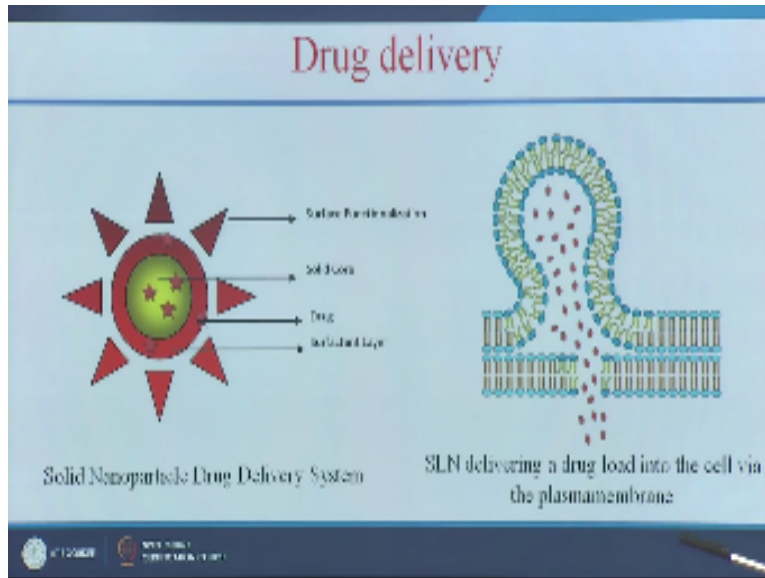
Drug screening microarrays

SLNs enable a simple method of surface-mediated delivery of drugs to cells from a microarray of phospholipid multilayers (layers thicker than a bilayer) encapsulating small molecules.



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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Liposomes on cancer therapy

- These liposomes prolong circulation time in blood and improve pharmacokinetic and biodistribution of their encapsulated drugs.
- After intravenous administration, liposomes are large enough to be excluded from normal endothelium.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1711077/figure/fig1/>

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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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Ocular drug delivery

SLNs also allow ocular drug delivery

- They enhance the corneal absorption of drugs
- Improves the ocular bioavailability of both hydrophilic and lipophilic drugs
- Allow sterilization, (a necessary step towards formulation of ocular preparations)



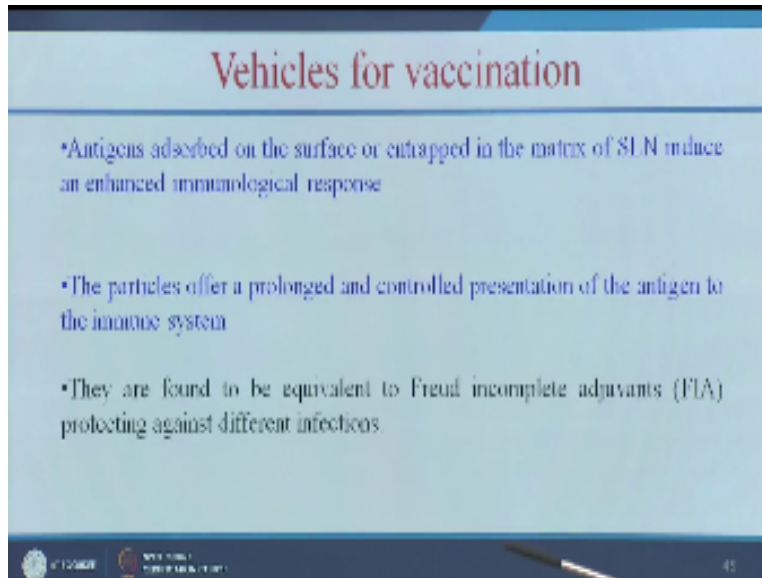
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And we can also use solid liquid nano particles for ocular drug delivery okay, so this SLN will enhance the corneal absorption of drugs and improves the ocular bio availability of both hydrophilic and lipophilic drugs. And another important advantage 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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Vehicles for vaccination

- Antigens adsorbed on the surface or entrapped in the matrix of SLN induce an enhanced immunological response
- The particles offer a prolonged and controlled presentation of the antigen to the immune system
- They are found to be equivalent to Freund incomplete adjuvants (FIA) protecting against different infections



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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Topical drug delivery system

Liposomal drug **Free drug**

Advantages of lipid nanoparticles applied in topical delivery system :

1. Increasing drug permeation through stratum corneum
2. Lowers skin irritation caused by drugs and byproducts
3. Extends the effective time within the skin by interaction of phospholipid bilayer with the similarly structured cell membrane. Drugs can be readily released from extended efficiency
4. Due to increased retention in the skin, the amount of drugs which enters the epidermis/dermis and reaches systemic circulation is lowered, mitigating toxicity.
5. For hydrophobic drugs, liposome formulation increases overall solubility without the use of irritative solvents

Advantages of liposomes:
 - Prolonged drug permeation
 - Prolonged residence time
 - Prolonged drug activity

Labels in diagram:
 - Stratum corneum
 - Epidermis
 - Dermis
 - Blood supply

UoA (University of Alberta) logo and text at the bottom left.

So the next application is topical drug delivery system so we can see the difference between the free drug as well as liposomal drug and the free drug it is entering through the skin and it is reaching the blood supply which will induce the systemic toxicity. In case of liposomal drug it will reduce the irritation and it will enhance the drug permeation and also it will show prolonged 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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Incorporating lipid nanoparticles into new cosmetic products

- Good physical stability and compatibility with other ingredients they can often be added to existing formulations without any problems.
- As lipid nanoparticles are patent protected worldwide as Lipopearls® or Nanopearls®

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 lipopearls or nanoperals or various cosmetics applications.

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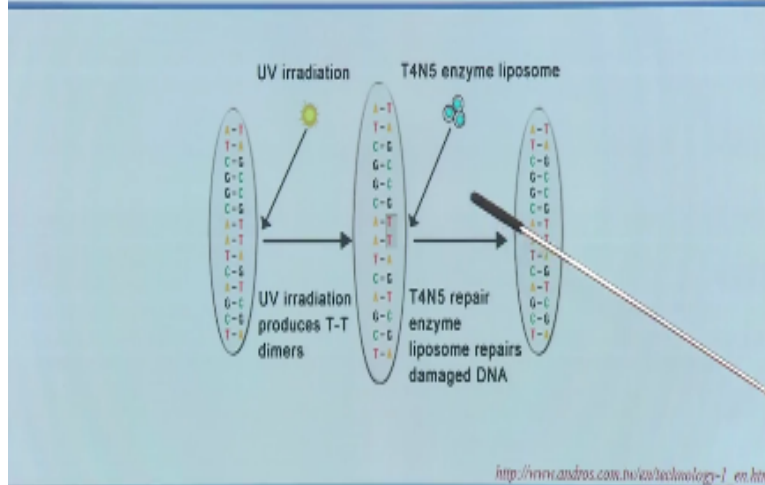
Benefits of using lipid nanoparticles in cosmetics

- Improved stability of chemically unstable active ingredients
- Controlled release of active ingredients
- Improved skin hydration and protection through film formation on the skin.

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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High-end cosmetic ingredient



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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High-end cosmetic ingredient

- DNA repair enzyme – T4 endonuclease V (T4N5) is a 16kD protein with the ability to repair DNA damage. Long term skin metabolism and UV irradiation causes Thymine (T) bases in DNA to form lesions known as T-T dimer which ages the skin and is carcinogenic.
- T4N5 removes the T-T dimer and allows DNA replicated normally, restoring healthy skin conditions. T4N5 repair enzyme also possesses anti-wrinkle, UV blocking, and whitening capabilities.
- Hydrophilicity and large molecular weight limits the permeation of T4N5. By encapsulating T4N5 in liposomes, skin permeation is increased and greater amounts of the enzyme can be delivered to cell nucleus for DNA repair.

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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Summary

- Lipid based carrier system
 - Liposomes
 - Solid lipid nanoparticles
- Applications of lipid based nanoparticles

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.

For Further Details Contact
Coordinator, Educational Technology Cell
Indian Institute of Technology Roorkee
Roorkee – 247667

E Mail: etcell.iitrke@gmail.com, etcell@iitr.ernet.in

Website: www.iitr.ac.in/centers/ETC, www.nptel.ac.in

Production Team

Sarath Koovery

Mohan Raj. S

Jithin. K

Pankaj Saini

Graphics

Binoy. V. P

Camera

Arun. S

Online Editing

Arun. S

Video Editing

Arun. S

NPTEL Coordinator

Prof. B. K. Gandhi

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