Science and Technology of Polymers
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Lecture - 29
Polymeric Nano materials and Devices (Contd.)

Thank you. Let us see the last part of these nano materials, polymeric nano materials and devices.

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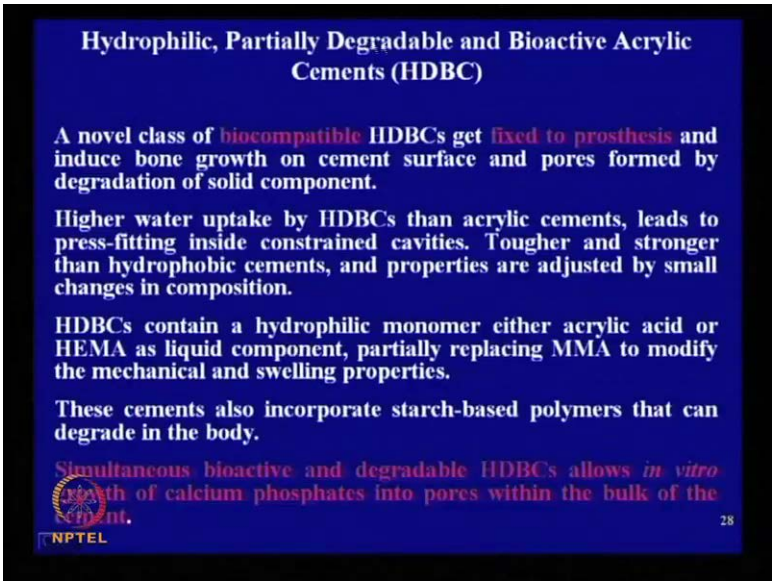

Now, this slides shows the title of the slide is hydrophilic, partially degradable and bioactive acrylic cements. Look at the key words. It is hydrophilic property, partially degradability, that is another property. Bio activeness is another property and this is the material. So, we can think of some material which can provide, so many different properties. Till now you have seen these different systems, hydrophilic hydrophobic for making nano devices, all those things for delivering drugs in nano dimension, all these things.

Now, we are thinking of the matrix. We are thinking of this support, we are thinking of the carrier, so these are the things. So, a system may be hydrophilic and you have to make it degradable, partially degradable you know the (( )), means how to make a system degradable. If you take hydro carbon, it is not degradable. If you take non hydro carbon polar materials, it is degradable. So, you can make a system partially hydro carbon type,

partiality non-hydro carbon type and you can do it. So, this way you can get partially degradable hydrophilic, so HDBC bio degradable composite, hydrophilic degradable bio active composite.

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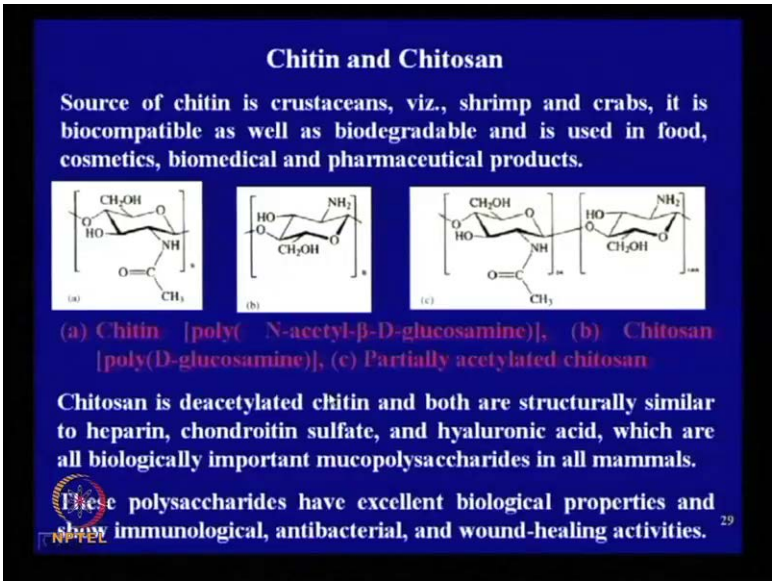

What are the materials? You can think of this chitin and chitosan. What is the source of chitin? Do you like lobster, prawn, crabs and shrimps? The cells of those things contain chitin. There is a natural occurring polymer having such formula. You see, these groups are their cardboard like (()) with some substitutions, acetyl groups. Now, this chitosan is a deacetylated chitin. Chitosan is a deacetylated chitin.

Now, this chitosan or chitin is found extensive use in biomedical field. This polymer, natural polymer with little bit of modification, many different kinds of bio degradable bio active systems are been made. I am not going in detail. Just for your information, these are the steps. The formulas in structures names are given here. You see, later on it is not difficult to understand. So, chitin is deacetylated chitosan.

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Due to low toxicity, chitin is inert in the gastrointestinal tract of mammals. So, this can be used for drug delivery purpose and this can be used for wound-dressing material. That means, you can make a fabric, you can draw or you can spin fiber from this chitosan molecules. You can make a fabric and that fabric can be used for wound dressing. That will be better fabric. Then cotton or other things and Then you can make a composite of hydroxyapatite chitin and chitosan which can be used for bone filling, all these things.

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Now, there are some modifications we have on this, chitin and chitosan. Sugars, dendrimers, cyclodextrins, crown ethers and glass beads and those find some unsuitable applications. So, these are all chitosan related developments and devices which can be used for various bio-medical purposes.

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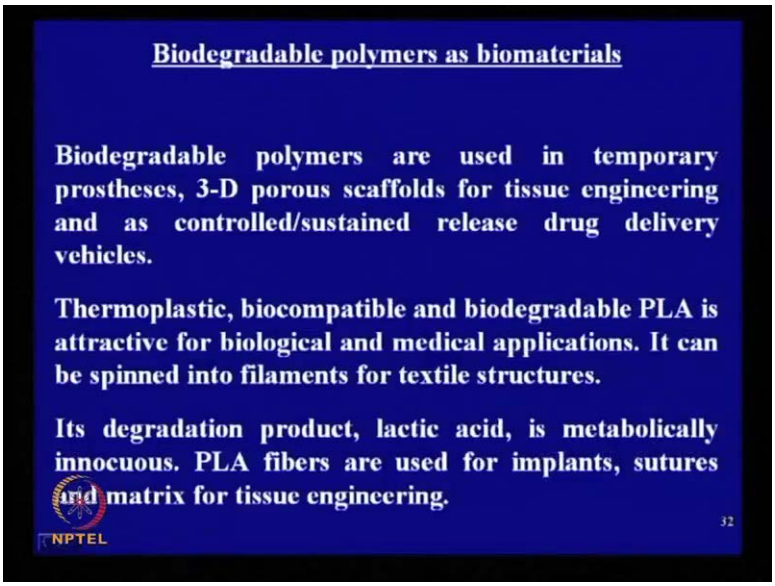

Now, look at biodegradable polymers as biomaterials. Could you tell me one example of biomedical biodegradable polymer? Clearly, you should say immediately polylactic acid, polylactic polyglycolic acid, a copolymer of polylactic acid and glycolic acid. Those are natural polyesters or say, your biodegradable polyesters. You can synthesize this poly starch. Also, this chitin and chitosan, these are also biodegradable.

So, one can use these polymers for making 3D porous scaffolds, three-dimensional porous scaffold for tissue engineering and as less controlled or sustained release of drug or for delivery purposes or drug delivery vehicles. Polylactic acid as I mentioned, polyglycolic acid there copolymers where used in implants, as sutures and as matrix materials for tissue engineering.

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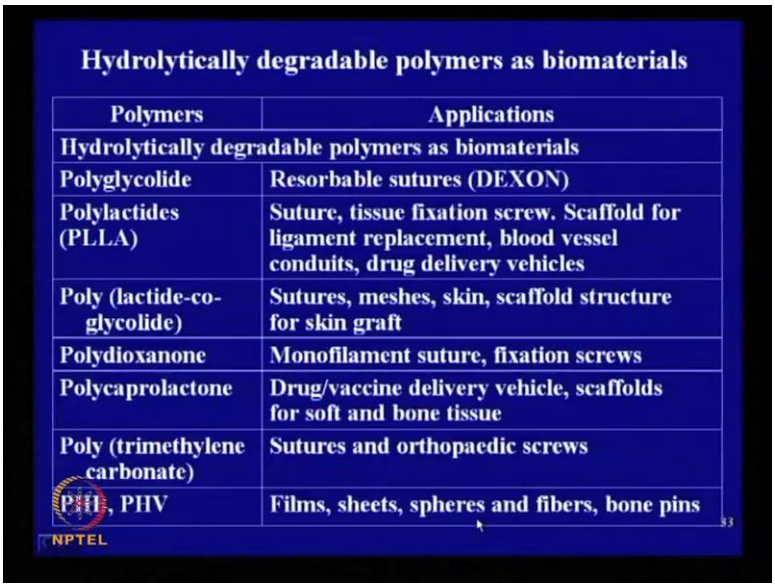

These are examples. As you see, polyglycolide resorbable sutures commercial available dexon. Dexon is their trade name of this suture. Fully observable suture need not removable after healing of the wound. Polylactides: suture, tissue fixation screw, scaffold for ligament replacement, blood vessel conduits, drug delivery vehicles, say copolymer. Lactide and glycolide copolymer: sutures, meshes for hernia repairing, hernia repairing meshes, skin, scaffold structure or for even skin graft. Polydioxanone: monofilament suture, fixation screws.

Screws are made on this polymer you see. You have seen the photograph of the screw used for bone fixation. Polycarprolactone is a good biomedical polymer, although it is little expensive. This is used in drug delivery, as vaccine delivery vehicle, scaffolds for soft and bone tissues. Poly (trimethylene carbonate): for sutures and orthopedics screws. Polyhydroxy butyrate, polyhydroxyvalerate, copolymer of polyhydroxy butyrate and polyhydroxyvalerate, these are bacterial polyesters. These are actually bacterial polyester synthesized by bacterial polyesters, bacterial polymers. This can be formed into films, sheets, spheres, fibers as your less bone pins.

So, from this list, you see large number of applications are there for which we need for polymer and these are the polymers which are been proven to bioactive, which are proven to be inert, sorry which are proven to inert in the system means, biocompatible.

They are biocompatible, bio acceptable. Sometimes, they are biodegradable chemotherapy.

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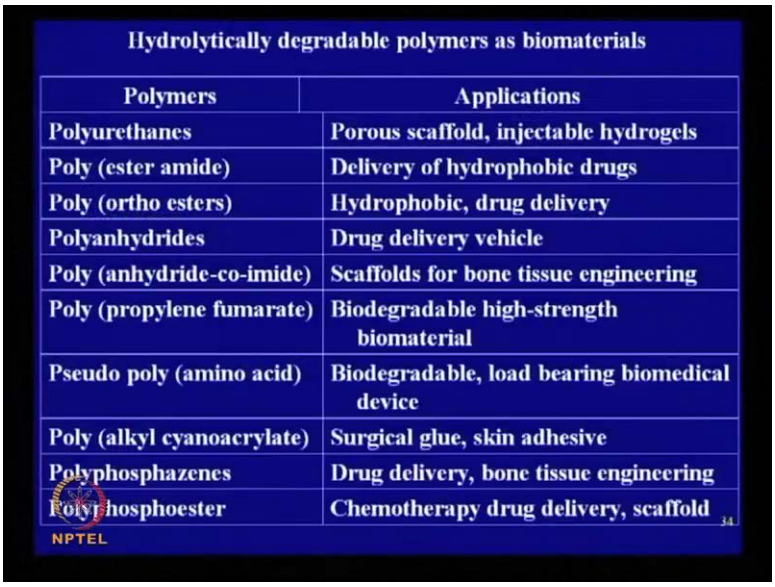

These are hydrolytically degradable polymers. Polyurethanes, you know poly ester amide, poly ortho esters, polyanhydrides, poly anhydride-co-imide, poly propylene fumarate, pseudo poly amino acid, poly alkyl cyanoacrylate, polyphosphazenes and polyphosphoester.

You see if you have this literature with you and today, if you see these are the, here is a list of polymers available for so and so applications. Today, I am not asking that you have to remember everything. No, it is not possible. Even for me also, it is not possible, but if you see these are the things available even is exposed to you. So, from that, you have seen here. You see large kind of different applications using these polymers. So, in your professional career, you may find some for your convenience that time if you need.

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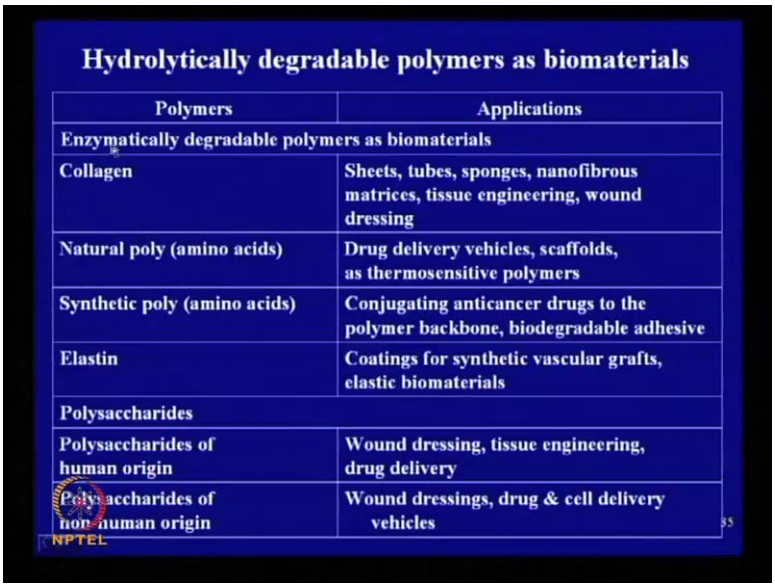

Then hydrolytically degradable polymers as biomaterials. Collagen, this collagen can be harvested from animals. Natural poly amino acids, synthetic poly amino acids, elastin, polysaccharides, polysaccharides of human origin, polysaccharides of non-human origin and you see their applications, all in bio medical applications. Now, these things today are converted into nano devices, all these things. Now, it is not easy to say in one or two hour lecture to show the design and process for making those nano devices and their applications, but what I want to say is that you can make in nano dimension in order to explode their unusual properties. These nano devices can provide us some unusual properties which are not available from macro or micro systems, where as it can be available from these nano systems.

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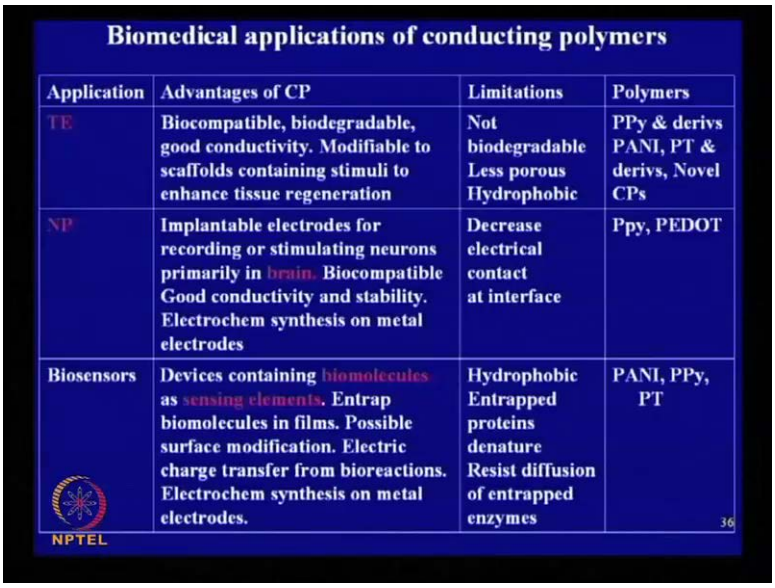

There are also applications in tissue engineering. TE means tissue engineering. NP means neural probe applications, neural artificial neural probe for sensing in senses. I will show you some photographs or the diagrams there and in biosenses also, these are there in all these cases conducting polymers. Now, you see conducting polymers are used in making semi-conductor devices. You will be surprised to see such conducting polymers are used in biomedical purpose, also in bio medical field within hard valve or making for some drug delivery or artificial muscle, artificial muscle actuation of the muscle movement of the muscle that is done artificially.

Now, if there is some paralysis due to non-functioning or melt functioning is knob that can be activated by these artificial systems using this neural probe system, using these conducting polymers. Today, these are very much used in nano medicines, nano therapies. Yes, please. It is there already. It is there. Today, you see chemo therapy. In chemo therapy, your drug delivery, chemo therapy drug delivery, this nano system is using the biggest today. We do not know, but it is been used.

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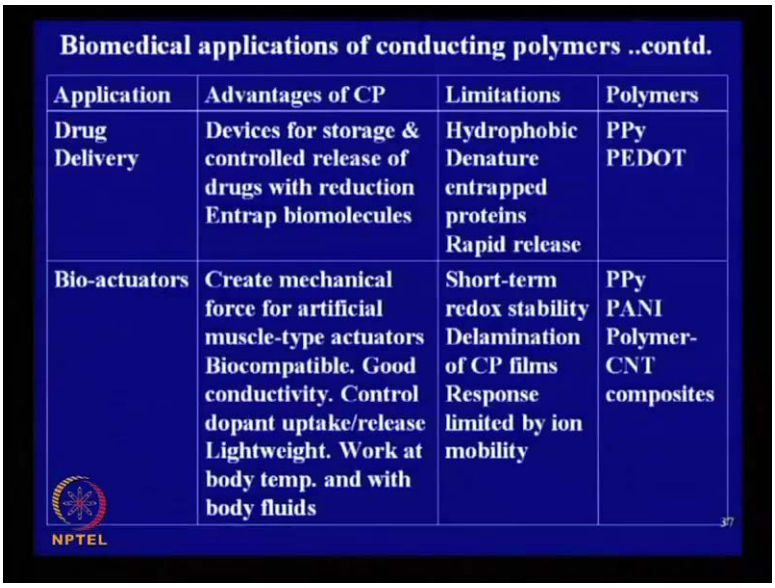

First, I like to leave here. You think of cost because my life is costlier than anything in the world. Read it. If I like to save your life, should I bother about the cost? I can sell it in my country to other country, get the money and I can save your life. That should be the motto. So, these conducting polymers, polyphenol pedot, I will show you what is that. Pedot, polyphenol, polyaniline carbon nano tubes, carbon nano tubes, these are been used for bio actuators drug delivery.

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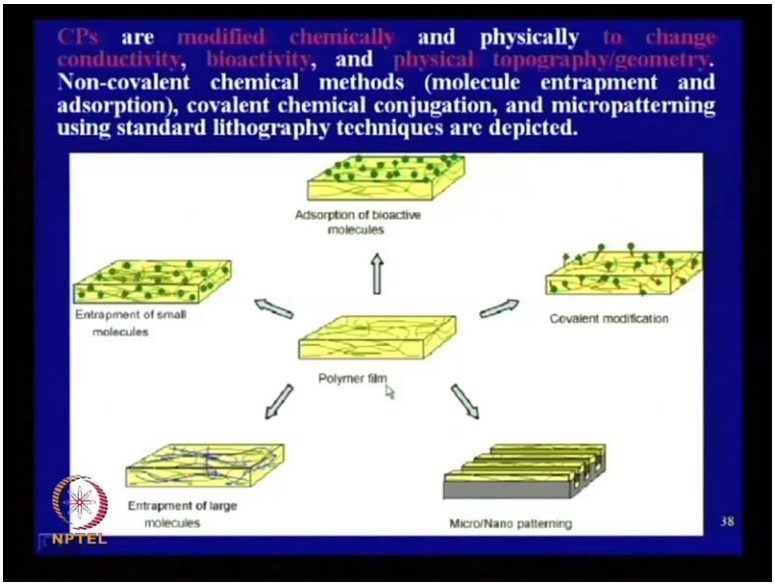

You see conducting polymers are modified chemically and physically. To change conductivity, it is not visible here. So, why you are looking back? I am reading. Please listen. Conducting polymers are modified chemically and physically to change conductivity bioactivity, and physical topography, geometry, non-covalent chemical methods like molecular entrapment and adsorption, covalent chemical conjugation and micro patterning using standard lithography techniques are depicted here. Here, you see say if you take a polymer film.

To this polymer film, you can attach some bio active molecules by various mentioned ways. Now, that attachment can be done through adsorption, physical adsorption of bio active molecules. So, this is physical adsorption of bio active molecules. This is a kind of modification, overall modification, different modifications and types of modifications. Here, those things are showed, written over here. This is been taken from a paper.

If you are interested, you come to me and I will give you the reference, the review, papers review, articles, huge paper huge review articles and lot of different references there given. So, only I have taken few things to explain before you. So, this polymer film if you want to modify in these ways using this conducting polymer, all these things. Now, that polymer film over which this bio active molecules can be adopt. That means, entrapment are fixing by physical adsorption or you can entrap inside in the polymer film, entrapment of small molecules and entrapment of large molecules. You can do micro patterning as it is done in micro electronics. You can modify covalently through primary covalent bonds bio active molecules. So, if you want to modify your polymer for suitable applications, you take this polymer having certain properties and Then you modify it, so that it suits properly to that particular biomedical application, this general thing, this general concept.

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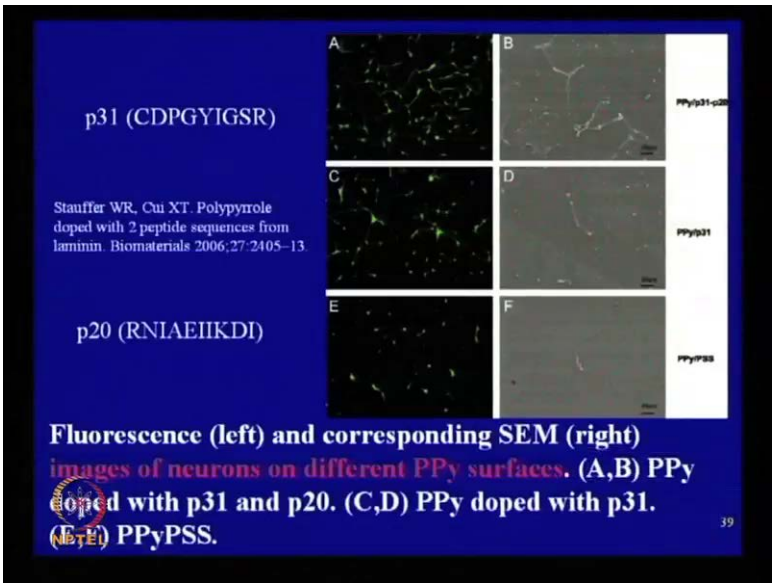

Here you see it is visible from your side. No, actually this photography is not good here. Now, here you see this, some fluorescence and corresponding images of neurons on different polyphenol surfaces. So, neurons you see blue green colour neurons made of polyphenol have been developed through some protein molecules. This is the reference. If it is not that visible, I will give you this PPT and from there you can see or you can get this. If you just download this paper, you can see this.

So, different proteins over some protein molecules, these polymers are conducting and polymers are deposited. So, conducting polymer deposited protein molecules act as neurons. You take this in a simple way. Protein molecules here, the sequences are there. These are the amino acid sequences. Amino acid sequences over the protein molecule, some conducting polymer, say polyphenol is deposited. So, conducting polymer deposited protein acts like a neuron. Now, you understand? I am not asking you to just go through hearing from me, you will understand everything or you will know everything, you will be able to do. No, just focus. I am focusing that it apathetically you think of some protein molecules over which it deposit some conducting polymer. So, protein is the substrate and you have made that protein molecule conducting like a conducting nerve.

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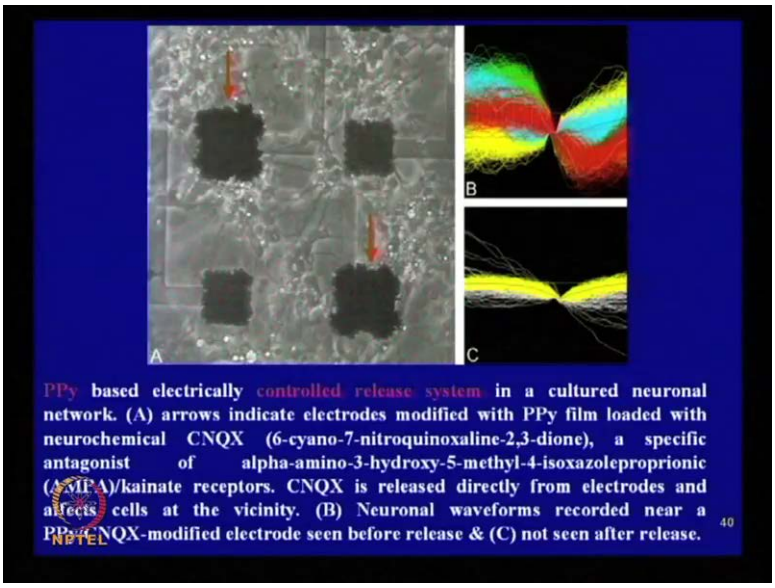

Now, here you see this is if you feel comfortable, you can look back side to that screen. You see this is a polyphenol based electrically controlled release system and this is the drug loaded system in a cultured neuronal network. Now, this arrow, red arrows indicate electrodes. These are the electrodes modified with polyphenol film loaded with some neuro chemical drug C N Q X.

So, these electrodes are covered with or deposited with some polymer, conducting polymer polyphenol in which some neuro chemical drug is deposited. So, for nerve stimulation if this device is made, so electrode is there. Now, with the help of electrodes, you can apply some potential and that application on some potential there. I am telling in crude way application, by applications or through some application, some potential that conducting polymer will release the drug, neuro chemical drug whereas, if you swallow the drug or you inject the drug, the therapeutic dose of the drug may not reach the affected side. So, the action will be slow and it will be proper, but this can help that it can provide you accurate quantity of drug release on this thing.

So, this figure shows you see a specific this. C N Q X is released directly from electrode here. These drugs are released and affect cells at the vicinity. Now, these are neuronal waveforms recorded near a polyphenol C N Q X modified electrode seen before release and after release. These are the wave form. Those wave forms have been recorded through this image.

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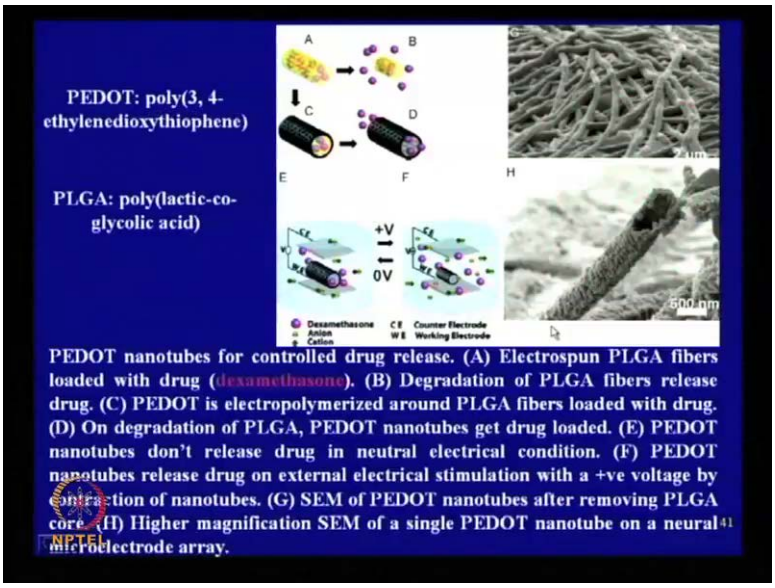

Now, this is very interesting. Now, I will tell you the essence of this thing. Now, here is a polymer poly 3, 4 ethylenedioxythiophene. These are famous conducting polymer, poly 3, 4 ethylenedioxythiophene. That means, a thiophene derivative conducting polymer of thiophene derivative poly 3, 4 ethylenedioxythiophene. What they have done in this work? They have taken poly lactic-co-glycolic acid; that means lactate glycolate-co-polyester. Please listen to me. They have taken lactate glycolate-co-polyester. It is a bio degradable polymer.

Now, suppose they have made fiber, very thin fibers, say nano dimension, nano fibers. Suppose, this P L A P G, a nano fiber, they have made. It is bio degradable. This nano fibers bio degradable drug, they have loaded with some drug. That means they have made this bio degradable fiber loaded with drug. After that they covered this drug loaded P L G A with PEDOT poly 3, 4 diethylene thiophene diethylene, sorry 3, 4 ethylenedioxythiophene.

So, what is that? They have taken a biodegradable polymer, loaded the bio degradable polymer in the drug and Then they covered that drug loaded bio degradable polymer with a conducting polymer after this conducting polymer in nano dimension. That means you are having a nano tube of PEDOT inside which there is a bio degradable polymer loaded with a drug. Once again I repeat. They have made a nano fiber of PEDOT. Within

this PEDOT nano fiber, there is bio degradable PLGA polymer loaded with some drug. So, you can say, this is a nano tube loaded with drug in a bio degradable polymer.

What they did after this conducting polymer nano tube permission? They have degraded this PLGA polymer. Then after degradation of the PLGA polymer, they got this drug loaded conducting polymer nano tube. Within the tube, there is a drug and tube is made of conducting polymer. So, what is the purpose of taking this bio degradable polymer? Only for drug encapsulation, only for holding the drug or template for the drug or something like that substrate for the drug. So, they have put the drug in the bio degradable polymer. After putting the drug, after loading the drug, they have covered the drug loaded bio degradable polymer with conducting polymer and Then they have degraded the polymer where only leaving behind only drug molecule inside the conducting polymer nano tube.

Then, what they did? They have put this device in the affected side, within the affected side in the body. Then from the external side, externally they have used two electrodes, positive and negative electrodes and applied bolt age potential. So, what they did on application of the positive bolt age is actually it squeeze the tube. On squeezing the tube, drug molecules came out of this system. So, this way drug delivery was there. Clear? These things are described in this slide, particular slide I think. Am I clear?

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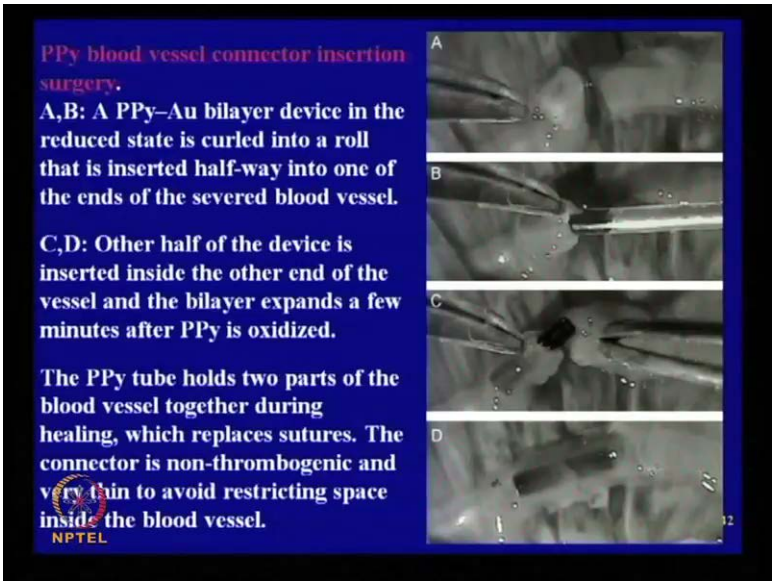

This is again another thing you see. You know connector tube. Suppose, this is a tube, this is a tube and this is another tube, this side of two tubes, one to connect. What you will do is you take a connector. Suppose this is the connector. So, we are inserting this part of the tube here. So, this tube is connected to the connector and this side also open like this. Imagine this is also open. So, you connect this side with this thing. So, two parts are connected.

Now, this is required in surgery, you say bypass surgery. In bypass surgery, what they do actually is there is some blockage in the artery. The surgeon actually removes that blocked portion and Then he takes some of that artery or vein from other parts of the body. Then they tie with stitching. That is very difficult. So, this bypass surgery, although there is be success today, but there are failure also because a blood vessel which is congested due to cholesterol deposition, now that is causing heart blockage and that blockage is removed by bypass.

That means, some bypass tube is connected now that by pass tube blood vessel (( )) tube is taken from other part of the body and that is connected. How it is connected? That tube should be obtained and this new tube should be connected to that by stitching with the help of sutures. It is easy to think, easy to discuss everything, but how difficult it is to get a success of in this surgery?

Now, what they have developed? They have developed a connector made of conducting polymer. What is this? They made a polyphenol gold bilayer device polyphenol over which gold film is there. So, in this bilayer device, now this bilayer device in this reduced state is called. So, here the oxidation reduction phenomenon is exploited. Reduced state it is called in to a roll that is in once it is curl into a roll. It looks like a tube and that is considered as a connector.

That is inserted half way into one of the ends of the severed blood vessel. Now, other half of the device is inserted. Same way insert the other end of the vessel and the bilayer expands a few minutes after polyphenol is oxidized. So, this way in case of when it is in reduced state, it is curled and found a tube. Then it is put in the one side of the vessel and in the other part of the tube is also put inside and others part of the vessel and Then it is oxidized. On oxidation it expands.

So, it is fixed to the blood vessel tightly without any stitching. So, it connects the two parts of the blood vessels. So, this blood vessels connectors are made from such conducting polymer gold by that devices exploiting there oxidation reduction or there mechanical responds obtained from object from this oxidation reduction phenomena nano medicine. Just I will show you some photographs. I will explain you. Read these lines as these are self explanatory. Keep patience if you read it and you will understand because I have already described and explained the basics of all these things.

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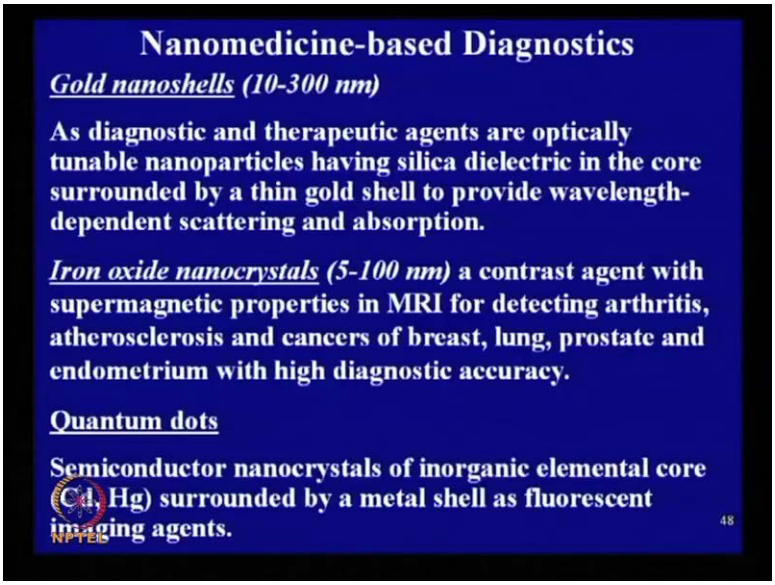

Nano medicines based diagnostics. Gold nanoshells as diagnostic and therapeutic agents are optically tunable nanoparticles having silica dielectric in the core surrounded by a thin gold shell to provide wave length-dependent scattering and absorption. So, in the diagnostic for the purpose, one can take a silica core which bears like a dielectric over which if there were shell made of gold that can provide scattering wavelength dependent scattering, so that can be used in diagnostic or as if probe, say endoscopy probe in order to get the image. So, this optical property, optical phenomenon is required. I do not know the details. I am not an expert in this field, but whatever I understand that some electric properties are regulated. Optical properties are regulated with the help of these nano devices.

Then, iron oxide nano crystals, a contrast agent with super magnetic properties in MRI for detecting arthritis. If there is some arthritic problem mean pain in the bone and the

joints etcetera, doctors prescribe MRI test, so atherosclerosis and cancers of breast lung prostate and edometrium with high diagnostic accuracy. So, here the nano material is iron oxide nano crystals. Do you know what is their material? What is the device? MRI. You heard this MRI. Now, today we have little information that yes, these are the materials, say gold nano shells iron oxide nano crystals are used in MRI test MRI device. Quantum dots semi: conductor nano crystals of inorganic element like core having cadmium mercury surrounded by metal shell for fluorescent agents.

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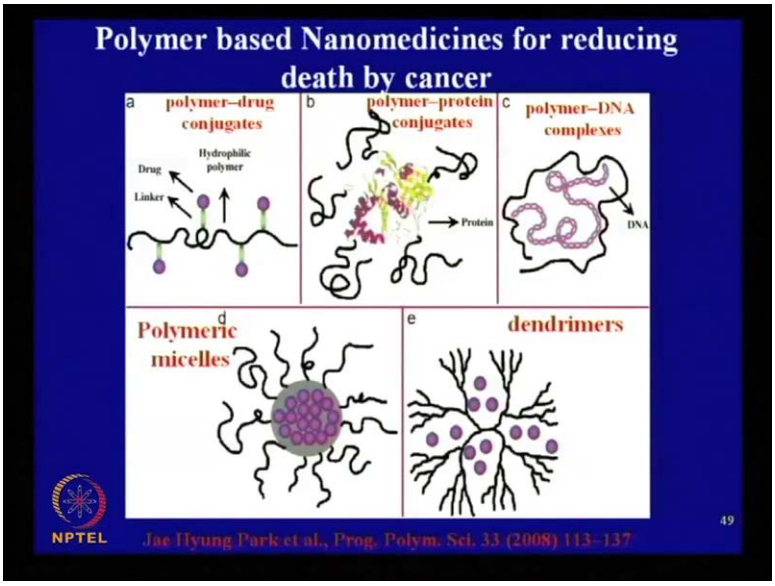

This is very interesting polymer based nano medicines for reducing death by cancer. Have a look into this. Actually, this shows some polymer drug conjugates. So, this is the polymer molecule which is hydrophilic polymer. These are the drug molecules. So, drug molecules are conjugated to polymer attached through link to polymer through some linker for that. So, drug master have some functional site exploiting the functional site present in drug as you less in polymer.

So, drug could be conjugated to polymer molecule and polymer can have either hydrophilic characteristic or hydrophobic characteristics. Again, you think of this, your emulsion depending on whether this polymer chain hydrophilic or hydrophobic and the hydrophilisity, hydrofluisity of the drug conjugated drug molecules. You can make a system of emulsion, nano emulsion now, if this is emulsified.

So, it is available in the form of fluid. If it is put in the blood vessel, in the blood system that to be carried, so the blood vessel to be circulated through the entire body. Now, if there is some affected side, there can be of some involvement of different pitch, different temperature, and different surface characteristics at the affected side. What will happen? If this system reaches, this linker will be broken releasing the drug in other parts of the body. That linker will remain stable, but in the affected side, this linker will be broken and drug will be released. This is the concept here. You see in this case, polymer drug conjugate, some proteins are also used as drugs. In that case, protein can be conjugated to polymer. This is the protein and it is conjugated to polymer. Then enters system in nano dimension can be used as drug where your drug area or drug delivery system.

Then, sometimes DNA is used as drug. If that DNA can be complexed with polymer, you know what chemical complex is. You know what kinds of bonds are present in chemical complexes. You know complex molecules. So, this DNA molecule can be just encapsulated or somehow enclosed by complexing, by complexation all these things. So, that will carry this, polymer system will carry the DNA molecule to some place within the body or polymeric micelles. This is the drug. A cell has been formed by the polymer molecules. So, this system as such can be used for drug delivery.

Again dendrimers. What are dendrimers? You know there is a polymeric system hyper branched, super branched supra molecular systems. Dendrimers is a core center. It has large number of branches. They are produced and living behind some spaces inside. Now, that space can be used as template. Sometimes, it can be used as in encapsulation, by virtue of this, your physical adsorption of all these things. So, this is a system.

Passive tumor targeting. Please read it. There is no time to read all these things. Passive tumor targeting slowly passive tumor. This is not active passive tumor present is honor of this passive tumor. A patient sometimes is unaware of the passive tumor. This is required only in diagnostics system. I do not know whether there is a tumor or there is cancer cell. We do not know, but if it is actually activator or somehow, it gives some symptoms, then you go to the doctor and doctor prescribes so many different tests and diagnose and Then analyzes all those things, pathological tests. Then only, one can come to know whether there is a tumor cell or not, but it remains in passive form. Now, that passive if there is in the passive tumor or not, that can be targeted by virtue of these nano devices.

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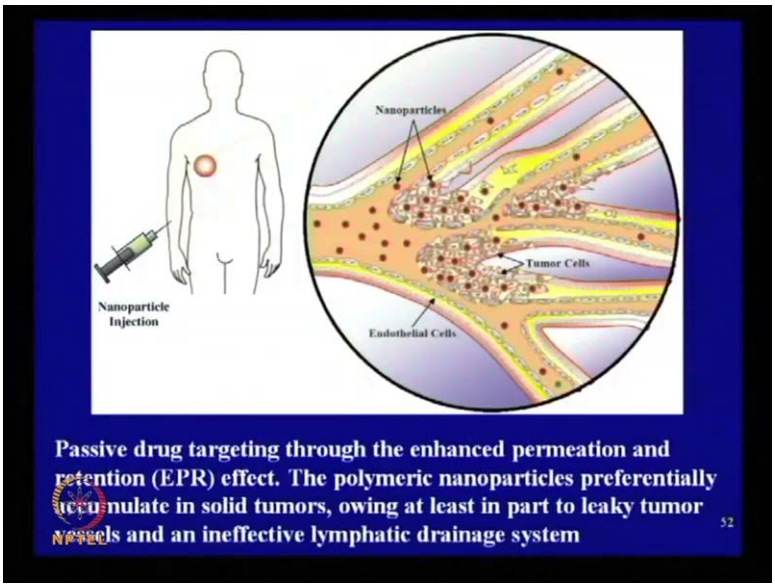

Passive drug targeting. Please read it and you will understand. Now, here you see this passive drug targeting through the enhanced permeation and retention EPR effect. The polymeric nanoparticles preferentially accumulate inside the tumors, owing at least in part to leaky tumor vessels and an ineffective lymphatic drainage system. Here you see this is the tumor site. Now, nano particle is injected for passive targeting. Look at him. Now, what is there? What are these nano particles?

Nano particles contain some drug or something, some agents. It will reach the active side, all in that effected side. If there is any tumor cell, this will release those agents there. If there is no tumor site, then suppose in crude way I am telling. I am not your medical expert. These things, suppose there is some tumor cell. We do not know how to diagnose. You see if something here is some nano particle is made into emulsion and that is injected and if there is some tumor cell, it will be deposited only over there.

Then, by some imaging system, if it can be detected, yes those nano particles are deposited at some place. It will only deposit at that place if there is tumor, if there is some cancer cell. If there is no cancer cell, it will not be deposited. It will break created through the system if there is only affected site. If there is any tumor cell, if there is any cancer cell, all these things will be released and deposited over there. Then outside you have a camera.

So, for example, the x-ray, and intestinal x-ray, how it is done say, barium sulfate suspension is solved assented. What is the practice? You know probably this thing. Then this barium sulfate will be deposited and this x-ray, OPEC and only that portion, this your some barium sulfate, that you can get the image by x-ray deviation. Same kind of thing is injected into the system. It will carry, it will circulate through blood. These nano particles, you see nano particles separated through blood and if there are tumors cells, it will deposit only over there. It will see to get there. Then through imaging, we can detect. Yes, it has been deposited there. That means, these portions are affected a site. Then people will go for and Then they will diagnose. Yes, if it is a cancer patient, that tumor is malignant, not to be cured.

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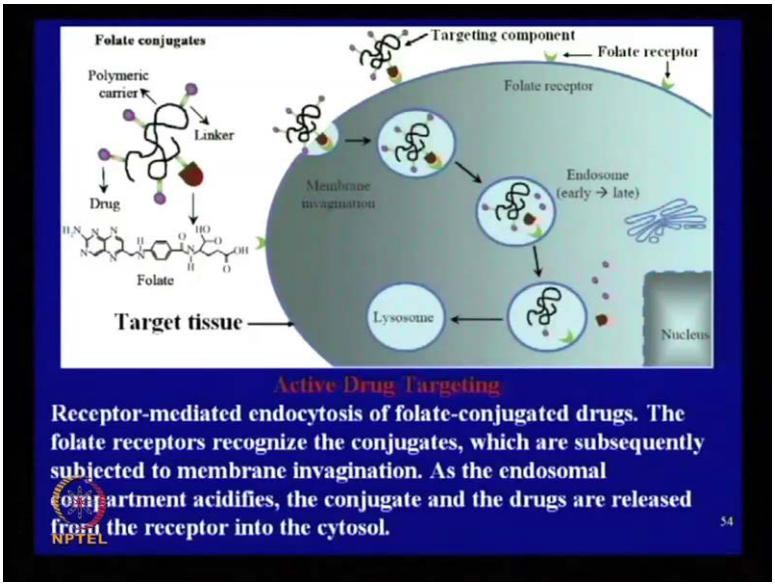

Active drug targeting. Receptor-mediated endocytosis of folate conjugated drugs. It is very interesting. The folate conjugates which are subsequently subjected to membrane invagination. As the endosomal compartment acidifies, the conjugate and the drugs are released from the receptor into the cytosol. You see this means a polymer molecule. This is a polymer molecule. Now, through this polymer molecule, drugs are attached through linker, suppose these are anti-cancer drugs. So, these anti-cancer drugs if it is circulated in through the blood in the form of nano emulsion, then it will be circulated throughout the entire body. Now, there might be some affected site having cancer cell.

Now, if the cancer cells have some receptor site, then this is identified actually like camera or something like that or what is that called this equidity process. Today these are metal detector. Suppose, it is a metal detector, so it is actually after injection. So, it will go through the membrane into the cell. Now, if there is only receptor, folate receptor, this is receptor. This is the folate connected to the polymer to which drug molecules are connected. So, this is a system of polymer and drug containing some folate or some detector like metal detector and here is a receptor. So, only if this receptor is somehow here, you see inside is a receptor.

These are showing, only symbolizing these looks like this is actually receptor to which this should be attached. Here, it is fixed to the size and sep here. So, this is membrane vagination of the system comes inside, fix to this and Then within this region, if there is some acidity or something like that here, you see as the endosomal compartment. This is the endosomal compartment. In the endosomal compartment, the conjugate, it is acidic or it acidifies. In that acidic involvement, the drugs get released. Also, detector is released and ultimately, what happens is we get this drug release at the affected site.

So, this is a model. With the help of this model, this active drug targeting and targeted delivery, how it is can be done is shown. So, this is a system containing polymer through the drug ejectors, through the linker and it is again connected to a detector and there will be receptor which will recognize only this and not the others. This receptor, folate receptor will only recognize the folate, not others.

So, when it flows, when it circulates or moves inside, it will catch. That means affected site must have the receptor of this folate if there is and only if there is. Suppose, if there is a cancer cell, so cancer cell have this folate receptor. If there is cancer cell, it will catch and Then in that involvement, this acidic involvement, this linker will be dissolved and drug molecules will be released. So, drug is actually reached to that specific site targeted delivery if we can achieve this 100 percent success cancer recovery will be there. Recovery from cancer is not a problem today.

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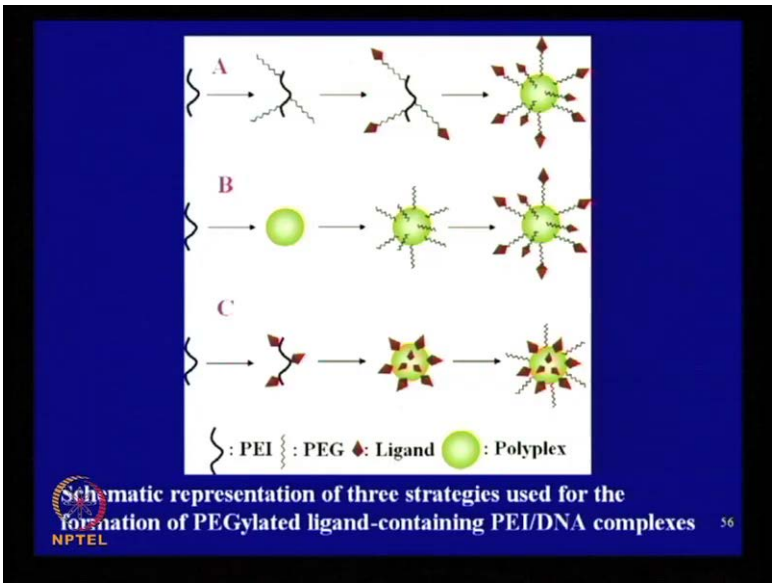

Polyplex, PEG, ligand means polythene glycol to poly attachment of some drugs, some polymers to polyethylene glycol. You know polyethylene glycol. So, what are soluble? Polymer hydrophilic polymer. Polymer is water soluble. If there is a little bit of molecular weight beyond certain limit in water is insoluble, but is hydrophilic because of present of oxygen atoms.

Now, to these polyethylene glycol polymers, some drugs can be attached. You see there are various ways, strategies of ligand complexes. This polyethylene imine p e I polyethylene imine DNA complex. If this DNA is used for some therapeutic purpose, so that DNA should be connected through polyethylene imine polymer again which should be connected to with, should be taken help of this polyethylene glycol polymer. So, this is polyethylene glycol to which other polymers are attached. These are drugs. You see this polyethylene imine polyethylene glycol, say ligand polyplex. So, polyplex is a device for drug targeting and delivery.

PEG is grafted to polyethylene imine. PEG functional groups are located at the end of the chain for chemical conjugation to ligands. Polyethylene glycols have been active sides to which these ligands are bound by chemical reaction to which DNA molecules are complexed for DNA. Complexing of DNA, you have seen in other case. Complexing of DNA, it needs some polymer of your chemical structure and configuration for DNA complexation again for carrying such polymer at DNA complex to a affected site. It is

grafted to that polymer, grafted to polyethylene glycol to make it hydrophilic. I understand you are getting impatient.

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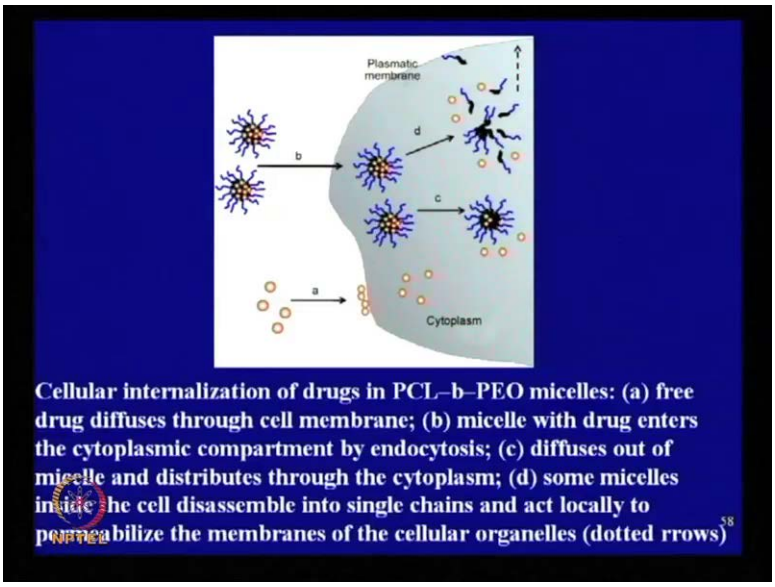

Cellular internalization of drugs in polycarprolactone polyethylene oxide micelles. Look at the micelle. This thing I have already covered that much. This is a core cell diagram for drug delivery core cell. This is the cell, this is the core, this is the polymer molecules attached to this core, here is the drug and this is the drug in the core.

Thank you.