Science and Technology of Polymers
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Lecture - 26
Stimuli Responsive Polymers and its Application (Contd.)

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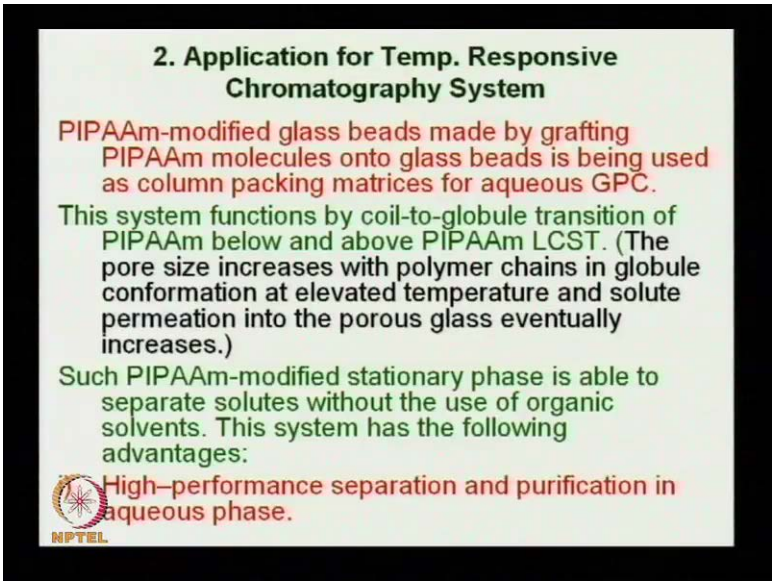

Now, let us see the application of such thermo responsive polymers in chromatography system for separation of very active or sensitive molecules, sensitive systems. Now, this PIPAAm poly n isopropylacrylamide modified glass beads. Glass beads are modified, glass beads surfaces are modified with this NIPAAm polymer. We can say NIPAAm polymer, NIPAAm polymer can be also called as NIPPAm polymers. NIPAAm n isopropyl acryl amide NIPAAm polymer.

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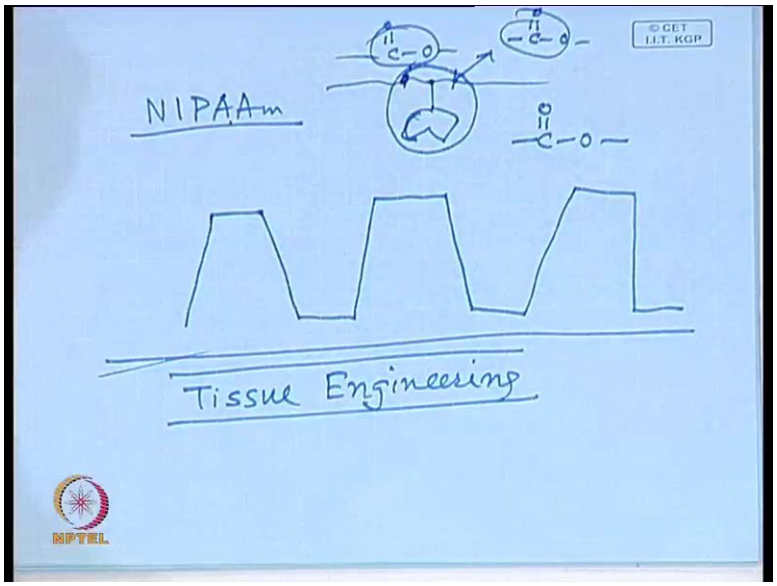

So, this NIPAAm polymer can modify this glass beads, and which can used as column packing matrices for aqueous gel permeation chromatography without involving any organic solvent, GPC. You know GPC system is used for separation as well as separation and purification as well as for evolution of molecular weight and molecular weight distribution of polymers.

Now, this system functions by coil to globule transition of PIPAAm below and above their lower critical solution temperature LCST. The pore size increases with polymer chains in globule configurations, you think of a bead, porous bead over which these polymers are coated, what happens? If it assumes the globular configuration pores are obtained. So, that way it says the pore size increases, pores gate opened so the pore size increases that way, pore increases with polymer chains in globule conformation at elevated temperature due to shrinkage of the polymers.

Hydrophobic nature transition to hydrophobic nature and solute permeation is encouraged through the porous glass and which gradually increases due to such change in phase. Such, PIPAAm modified stationary phase is able to separate solutes without the use of organic solvents. So, if the organic solvents could be avoided, then separation of bio active molecules becomes very easy, because organic solvents denatures or destroys the bio active molecules, where these organic solvents are not recommended. This system has the following advantages.

What are the advantages? Number one is high performance separation and purification in aqueous phase.

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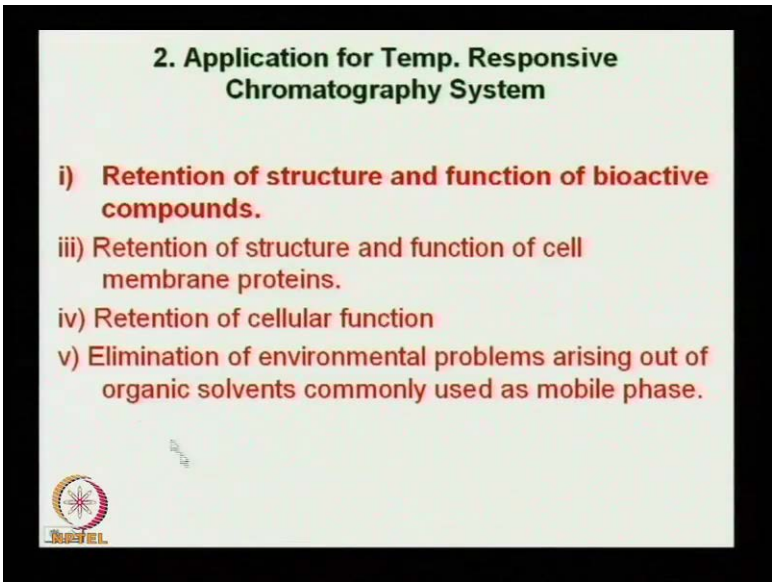

Two, retention of structure and function of bioactive compounds, neither the structure or the function of bioactive compounds and molecules are altered; then they can retain the structure and function of cell membrane proteins, cell membrane proteins. Cell membrane of the proteins, cell membranes are made of protein molecules, protein molecules. So, their structures and functions are kept altered or retained. The retention of cellular function, elimination of environmental problems arising out of organic solvents commonly used as mobile phase. So, use of such NIPAAm polymers as modifying agent can provide such advantages in chromatographic separation systems.

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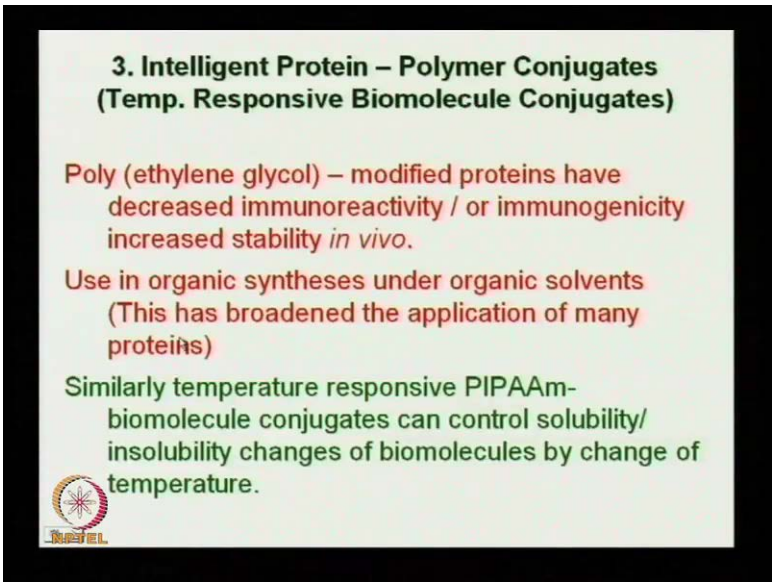

Polyethylene glycol modified proteins have, decreases the immunoreactivity or immunogenicity and this increases stability, in vivo stability of the system. Use in organic syntheses under organic solvents actually these are little, it needs little elaboration, you may not be interested. So, you can skip these portions, this may not be suitable for you. Those who are interested for biological applications, biological separations or other things they can go in detail. Similarly, temperature responsive PIPAAm bio molecule conjugates can controls solubility, insolubility changes of bio molecules by change of temperature. Following are the characteristics of such systems.

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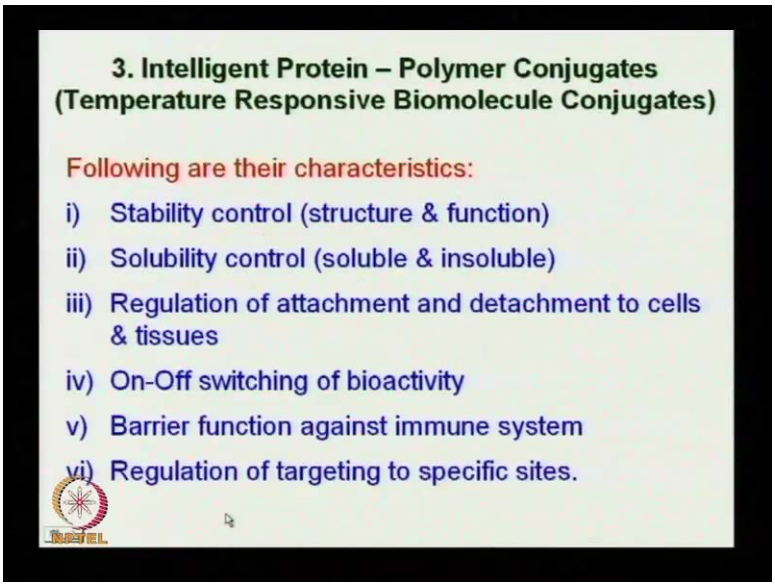

They control the stability through structure, controlling through alteration of structure and their functions. They control the solubility of the system becomes soluble or insoluble through copolymerization of the polymer. Regulation of attachment and detachment to cells and tissues that is also done. On-off switching of bio activities can be developed. Barrier function against immune system can be developed. Regulation of targeting to specific sites drug delivery that also, that is also possible.

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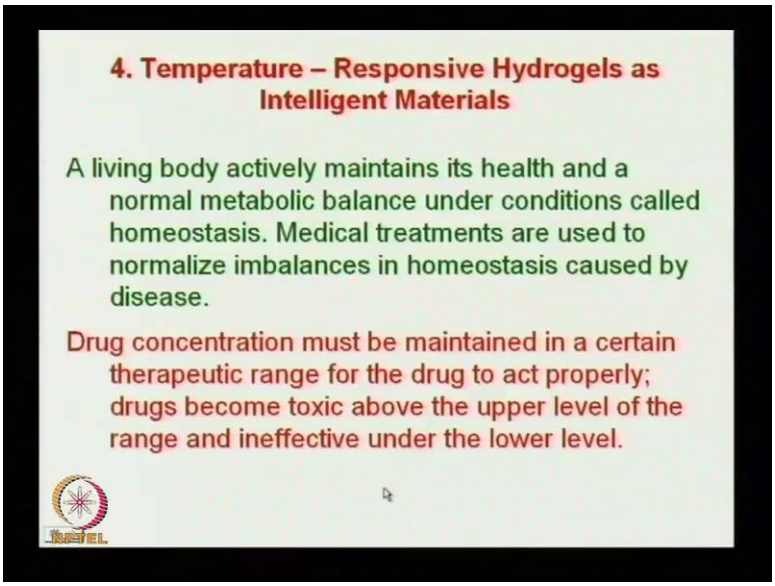

Now, a living body actively maintains its health and a normal metabolic balance under conditions called homeostasis. Maintaining normal healthy physiological functions is known as homeostasis. Deviations from such normal homeostasis is called disease that occurs due to disease. That medical treatments are used to normalize imbalances in homeostasis caused by disease. Now, that is done by drug incorporation and drug concentration must be maintained in the certain therapeutic range as I mentioned for the drug to act properly. Drugs become toxic above the upper level of the range and becomes ineffective under the lower level. That means appropriate dose should be given, it should reaches the target site, it should not affect the other parts of the body etcetera, that is the requirement.

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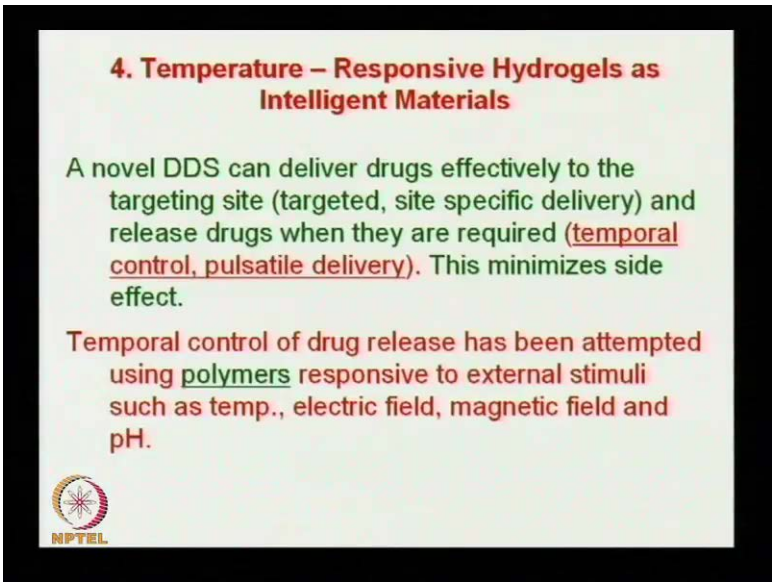

A novel drug delivery system deliver drugs effectively to the targeting site called targeted or site specific delivery and release drugs when they are required. That means temporal control means how much time, minimum time is required to release the drug. Control of that time is known as temporal control and then it starts the drug release for certain quantity of drug is released which is required, the therapeutic dose is released after that it should be stopped pulsatile delivery. That means there can be for certain period of time drug should continue to release then after that period it should stop the release again there may be a pause for say few minutes, few seconds and again it should start release of the drug, continue for certain period, then stop.

This way drug release for such certain period, stop. So, it can show like this, say drug release, then stop, again starts release this way it can show this kind of release and stopping like this. This is called pulsatile profile, pulsatile profile, pulsatile release profile of drugs. This minimizes side effects. That means once drug is released that drug starts fighting with disease only consumed by the affected tissues, not by others, if it needs further amount quantity of drugs then that is released in the second cycle of the release profile, this way in terms of through pulsatile delivery we can go for control drug delivery. Temporal control of drug release has been attempted using polymers responsive to external stimuli such as temperature, electric field, magnetic field and pH.

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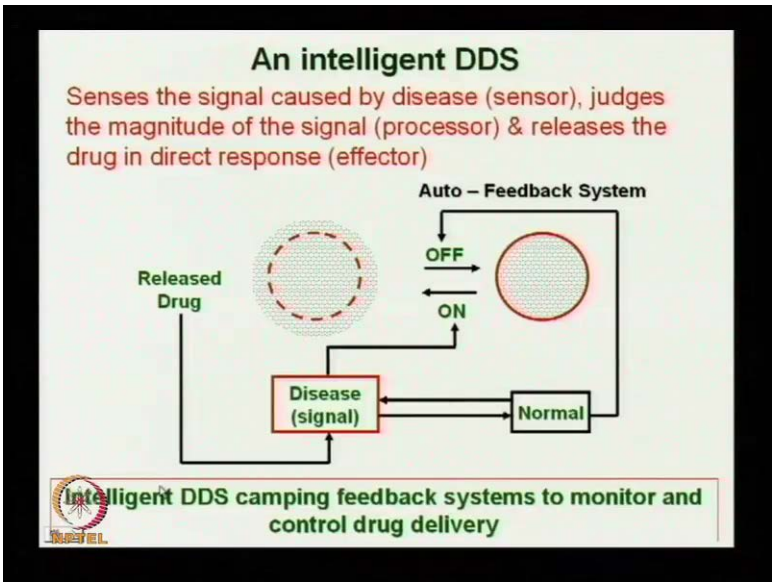

Here is a model, here is a model. Suppose, this is the drug delivery device say, consider this as spherical device having pores. Inside the pores the drug is kept loaded. So, these dots are, suppose these dots are drug molecules, drug particles inside and outside surface is coated with such polymer which can acts like molecular valve. So, what happens if the system, if the centre system receives a signal, disease signal. Now, that disease signal means that signal due to change in temperature, change in temperature, if there is certain disease body temperature will change. That change in temperature gives a signal as a sensing signal. Once, that sensing signal is received by this device that will switch on the device means that will direct these molecules to open the valve means it should be hydrophilic.

That means if the temperature decreases, if the temperature decreases the molecules can swell and open the valve. Here, you see in case on stage, on stage, switch on stage the drug molecule, these valves are opened, valves are opened and drug molecules are getting out, going out of the device. Now, after this drug molecules say insulin suppose, insulin that consumes the glucose, extra glucose in the blood and again the temperature will change in the opposite direction and a signal will go to the system then it will say now you should close the valve, system should get off.

So, that is that means from the disease if some signal received as normal the situation homeostasis has become normal then that will give a feedback through auto feedback system, it will ask the device to close the valve that means switch off the device. So, it will come back here. So, this way pulsatile release of drug can be released released and your stopping release of drug can be done, this is known as intelligent drug delivery system. Intelligent drug delivery system in actually this is (( )) controlling, it should be controlling feedback systems to monitor and control drug delivery.

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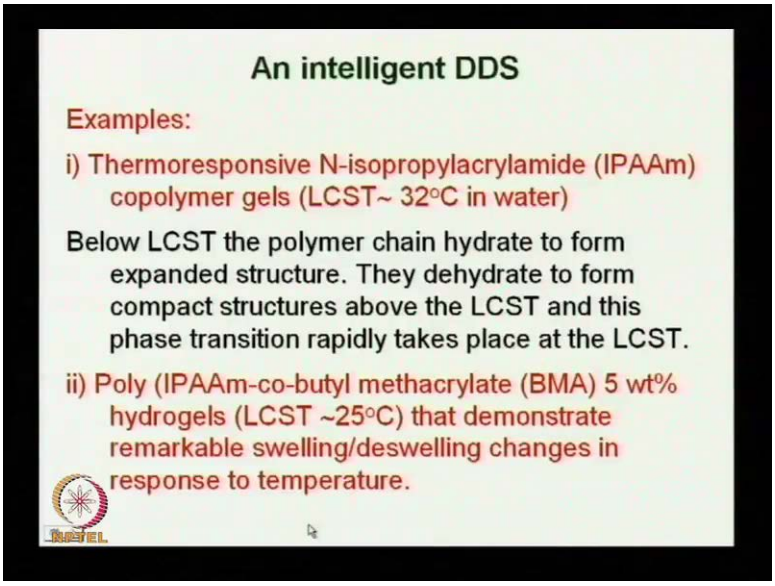

There are some examples of polymers N isopropylacrylamide, copolymer gels, copolymer gels using certain percentage of butyl methacryl that is not mentioned over here. Say, in this case here it is mentioned 5 weight percent butylmethacrylate. So, the LCST lower critical solution temperature of this particular polymer with the copolymer, comonomer its LCST is 32 degrees Celsius, above this temperature it becomes hydrophobic, below this temperature it becomes hydrophilic. Now, this LCST temperature can be regulated or changed by altering the composition of this polymer and the comonomer concentration, comonomer nature, comonomer chemical type. So, you see in another case you find the LCST minus 25 around 25 degree, that demonstrate remarkable swelling, deswelling changes in response to temperature.

So, we have flexibilities. It is not that it is rigid to only one temperature. Depending on the temperature signal or temperature that occurs or arises as a result of one disease say if there is some stomach disorder you find sometimes there is fever, if there is some injury, physical injury, operation there is some increase in body temperature, why? You know? So, there is some, if the doctor knows that for so and so disease for so and so reason the body temperature changes to that level. So, that is why if there is some temperature history of the patient, known temperature history of the patient and if the doctor can correlate the change of body temperature with the specific cause of a disease specific disease he can diagnose a suitable drug and there that encapsulation of the drug can be decided or judged by people like you, those who know this polymer, who are making this drug delivery devices.

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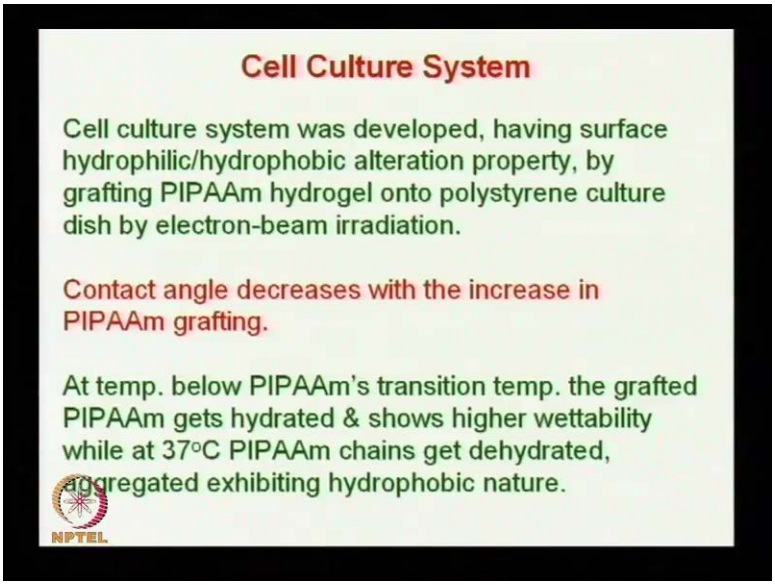

These are few applications; I will show you in other chapter, cell culture system as I was mentioning you. Normal polystyrene dish is used for culture of cells or tissues. Today, tissue engineering is a well known keyword, tissue engineering. What is tissue engineering? Now, cosmetics surgery you know cosmetics surgery that cosmetic surgery is done by grafting process. How that grafting is done? The tissue is collected from some other part of the patient and it is grafted to the affected site.

That is a kind of treatment, cosmetic treatment, cosmetic surgery, but today that is painful affairs. Today, now that tissue instead of taking from other part of the body if that could be developed artificially, in artificial way by through tissue culture system using what is that called stem cells, technology through stem cells technology, I am not conversant in that field, but stem cell technology through using embryonic cells. So, these cells are used for tissue culture. So, for that tissue culture or tissue engineering some scaffold is needed, skeleton is needed.

You know for making an idol skeleton is made for giving a support using some woody, stems as well as some straw and other things over which then hydroplasted clay and other thing are added and then idol is made. So, some skeleton is required. Now, that skeleton is called as scaffold. Now, that scaffold can be made of these polymers, all right, this way tissue engineering is done. In other cases say myocardial tissue, if there is problem in the myocardial tissues on the heart, heart muscles suppose heart muscle.

The property of heart muscle it should be beating you see, it should be beating like this, contraction expansion, contraction expansion function should be there in the muscle. Now, that muscle is artificially made using the stem cells. How it is done? There skeleton, use of skeleton is little difficult. Now, this technique, this technique has been followed for making cell sheets like a ply this one sheet of cell tissues, engineered tissues. This one is engineered kept aside, another tissue sheet is engineered, kept over it, another tissue is engineered kept over it.

So, thin sheets of tissues when they are assembled one over the other a thick muscle is created and it has been found that this tissues which are cultured, you are artificially developed they have beating characteristic, they have some electrical communicating power, electrical power transmission characteristics as well as what is that called? New muscularization means muscular tubes, blood vessels are also accommodated over there, those can be created over there. So, they have shown some success in such artificial tissue engineering using this system. What is this?

In order to understand that thing just you consider this polystyrene tissue culture surface. You know polystyrene tissue culture disc is made of polystyrene, is made of polystyrene. Now, over that polystyrene some nutrient broth or something like that your medium , media is given over which cells are incubated, some strains are give, your cells are incubated over there and kept in

the incubator that means temperature, humidity, carbon dioxide, oxygen, nutrients everything that means foods and the environment all are provided to those cells.

Then they starts growing perforation cell growths are there, tissue growths are there and after certain period of that culture what we find that a sheet of tissue is formed over the disc, over this surface. Then after it is formed what we need? We have to harvest it, you have to take out that sheet either by some forceps or by some other technique. Now, those tissues get added to on to the surface through those cell membrane proteins. Those cell membrane protein actually make themselves the tissues bound with the culture surface.

So, that has to be ruptured or broken. For that some enzymatic treatment is given. That is known as trypsin or other enzymes. So, once those enzymes are given that enzymes actually break those membrane proteins and the cells can be taken out of the surface and can be lifted. Now, during that process what happens it damage the cell, it damages the confluency of the cell and majority of the cell membrane proteins are damaged, all these problems are there.

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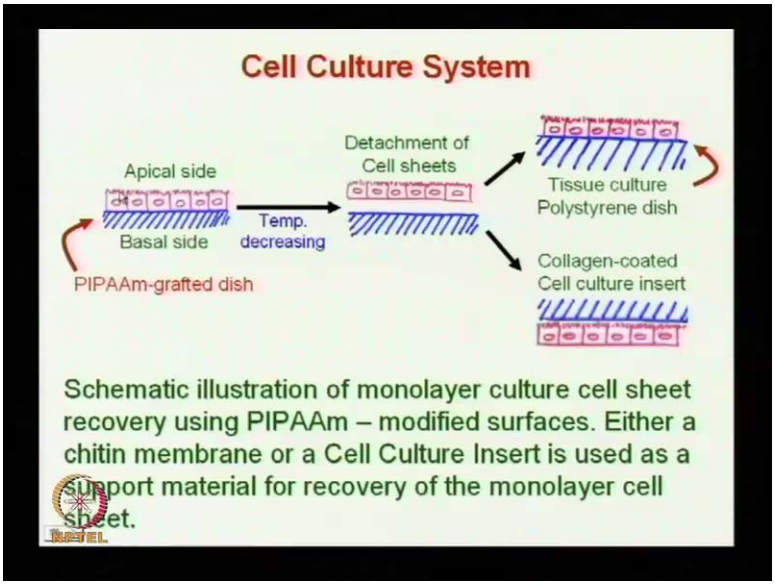

So, these things are discussed over here. Little bit, you will get the concept if you read it. Now, here you see. Let me show you this. Explain this diagram here. Suppose, this is a tissue culture surface, tissue culture surface. Then some tissue or cells are grown, these are the cells which are

remaining side by side. Now, such type of arrangements is called as confluency, cells confluency. So, that you can say this is a confluent cells sheet, all right. Once, this confluence cells it is made, found then it should be detached from the surface. So, this way, this way it is cells are, cell sheets are detached. Now, tissue culture polystyrene dish is this. This cell is formed and collagen coated cell culture insert is there of course, that is little different. So, this way, try to understand this portion we want to get this lift out this tissues sheet.

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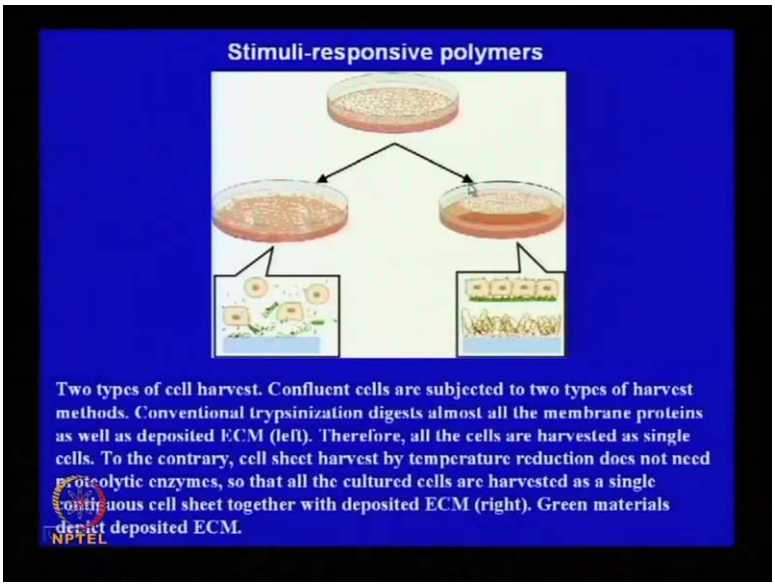

Now, here you see, here you see this is a polystyrene disc over which cells are grown. Then in order to take out this cells or cell sheets some enzymatic treatment in the left side, this enzymatic treatment is done. What happens? The cells are separated and damaging this cells also. On the contrary if the tissue culture disc is coated with that NIPAAm polymer, NIPAAm polymer, what happens?

The NIPAAm polymer covers the surface over which this tissues are grown then without any enzymatic treatment by simply changing the temperature, changing the temperature of the culture disc, this cells can be lifted from the from the surface of the disc where we just compared these two. Here the cells are ruptured or these proteins are broken, all these things are due to enzymatic treatment. Actually, some extra cellular metrics ECM these are also damaged,

all these things are damaged, but here it is not. It is maintained. This is the advantage of the tissue culture.

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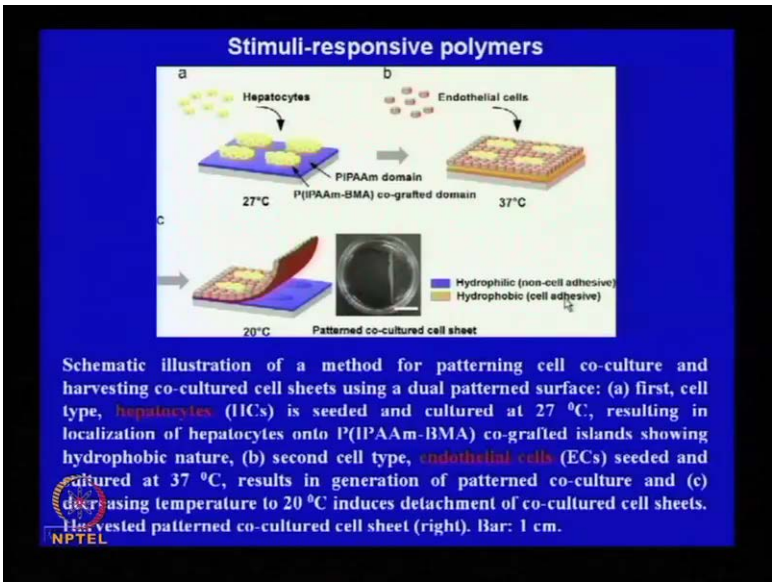

Here you see, patterned patterned cell culture. That is done in microelectronics in integrated circuits. Some circuit patterns are developed, the technique is there, technology is there, today people are making. In tissue culture also this has been made possible by virtue of these polymers, characteristics of this polymers. Here you see these are the yellow colour cells are hepatocytes cells and these brown colour cells are endothelial cells. Now, over a surface, over a surface if we want to have a pattern like this hepotocytes cells in a definite pattern and endothelial cells is another pattern.

Then that is possible if the surface is modified with this NIPAAm polymer. Now, this is actually this this is actually your blue portion is PIPAAm domain and this portion is actually a copolymer of the PIPAAm and bultyl methacrylate grafted polymer domain. And in this case the LCST is 27 degree Celsius and in this case LCST is 37 degree Celsius, this case it is 20 degree Celsius. So, there are three different cases, this one, this one and this one. So, these three different LCST are used for three different cases so ultimately what happens? We can get this patterned growth of tissue, hepatocytes and endothelial cells and that entire pattern sheet can be lifted by virtue of this LCST property of this polymer.

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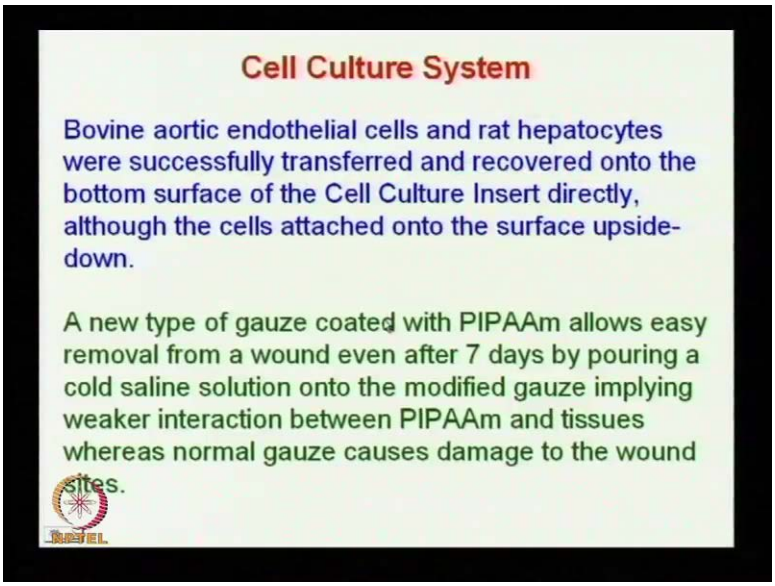

Now, here is an example. A gauze for dressing of wound, dressing of wound. So, if there is your after surgery or due to some injury, all these things. So, it needs dressing of the tissue surface in order to prevent from external bacterial attack as well as giving a support for normal group of the tissue for healing, is it not? For that purpose it is actually covered with some bandage or gauze. Now, if it needs dressing for two, after some intermittent period like that some intermittent period say 2 days or 3 days, 5 days like that, what happens? So, some tissue ingrowth occurs into the gauze, bandage, is it not? It is healing; during the time of healing some tissue ingrowth can be is there into the bandage also. So, when that old bandage is removed so that tissue, engrown tissue will be ruptured that will be a severe pain to the patient, is it not? That is a problem.

Now, instead of that if that gauze is coated with such polymer by simple taking hot water of that particular temperature, it will separate out instead of adhering. So, a new type of gauze coated with PIPAAm allows easy removal from a wound even after 7 days by pouring a cold saline solution onto the modified gauze implying weaker interaction between PIPAAm and tissues whereas normal gauze causes damage to the wound sites. So, this is a very good application say for dermal wound healing, say for severely wound patients, you understand the situation. There such type of modified gauze can help treatment of wound patients giving minimum injury,

minimum pain to the patients and that injury again the second time or third time dressing injury again, that is affecting the healing process also.

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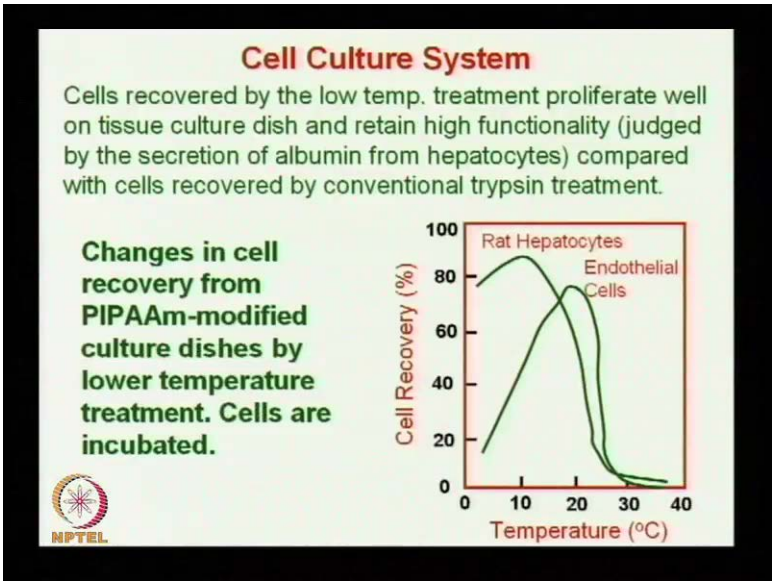

So, if that healing process kept unaffected then healing could be quicker, is it not? So, that is done by such modification. This is another application. Again, you see cells, cell recovery or harvesting by low temperature treatment proliferate well on tissue culture dish and retain high functionality judged by the secretion of albumin from hepatocytes compared with cells recovered by conventional trypsin treatment. So, it shows some recovery profile with temperature rat hepatocytes cells and endothelical cells. Let us skip all these things.

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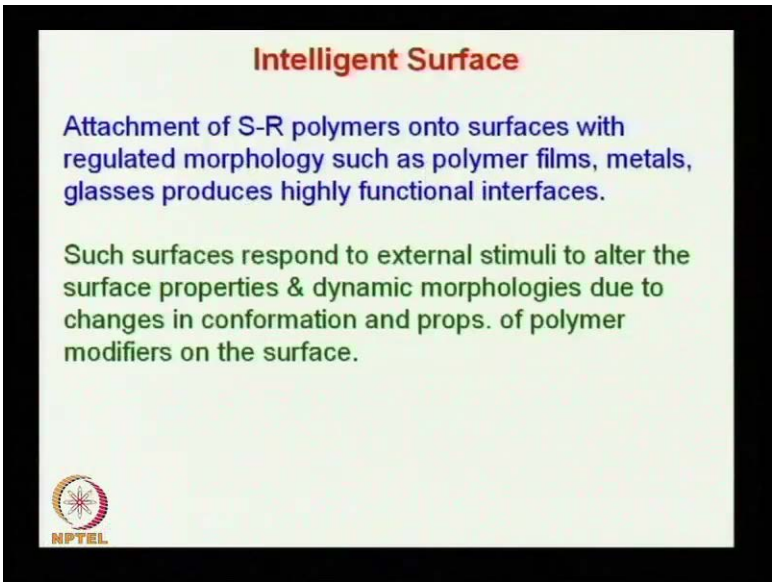

Intelligent surface, attachment of stimuli responsive polymers onto surfaces with regulated morphology such as polymer films, metals, glasses produces highly functional interfaces. Such surfaces respond to external stimuli to alter the surface properties and dynamic morphologies due to changes in conformation and properties of polymer modifiers on the surface. So, the job is to prepare an intelligent surface. If I ask how to make it if I give you some monomer, isopropylacrylamide, how do you modify the surface with that monomer, how do you do, who can say?

Student: (( ))

That is monomer. The rule of coupling is not there. The coupling agent will couple the monomer on to the surface, then what will happen? Rajesh, you are discussing something with your friend, stand up please, explain? I asked you to modify a polystyrene surface by this isopropylacrylamide monomer. I shall give you, if I give you a polystyrene dish and this monomer you tell me the method how it can be modified, not the polymer. I have given you the monomer only, how to do? You have come from BIT, yes sir. You have read polymer also there, yes sir. Then you should tell how that polymer can be developed on this thing, isopropylacrylamide is the monomer, can your friend help you, no sir. Why? You tell me how this polymethacrylimide is made from methyl methacrylamide?

Student: (( ))

So, if you just take the monomer and give BPO and you will get the polymer.

Student: (( ))

So, if it is done in presence of air will it form?

Student: (( ))

Repeat?

Student: (( ))

In presence of air polymer will be formed? No, why? Why you do not know? Why? You have done the experiment in the lab, you have read in book, you have attended so many lectures, why not? Did you ask anybody? Sit down. You have to remove oxygen from the polymerization chamber otherwise oxygen elevates the polymerization. So, nitrogen purging is required to evacuate the oxygen from the medium. In absence of oxygen only such polymerization can occur from methyl methacrylate in presence of BPO benzyl peroxide or any other initiator as you wish isobutyronitrile.

Here also this monomer isopropylacrylamide can be polymerized on this polystyrene dish using some monomer, using some initiator, but that will not do in this particular case because we have to have a grafting of such polymer on to polystyrene disc. For that you may need some electron beam or some other techniques so that some radical or some active surface is created on the polystyrene, these surface and then in presence of that moisture I sorry if you do this process in the presence of that monomer.

That monomer will start polymerization simultaneously. So, that polymer will get attached on to the polystyrene surface and you will get modification of the surface. There is kind of or modification of or a type of plasma polymerization in order to modify the polystyrene dish inside this thing. Well, such surfaces respond to external stimuli to alter the surface properties and dynamic morphologies due to change in confirmation and property, properties of polymer modifiers on the surface.

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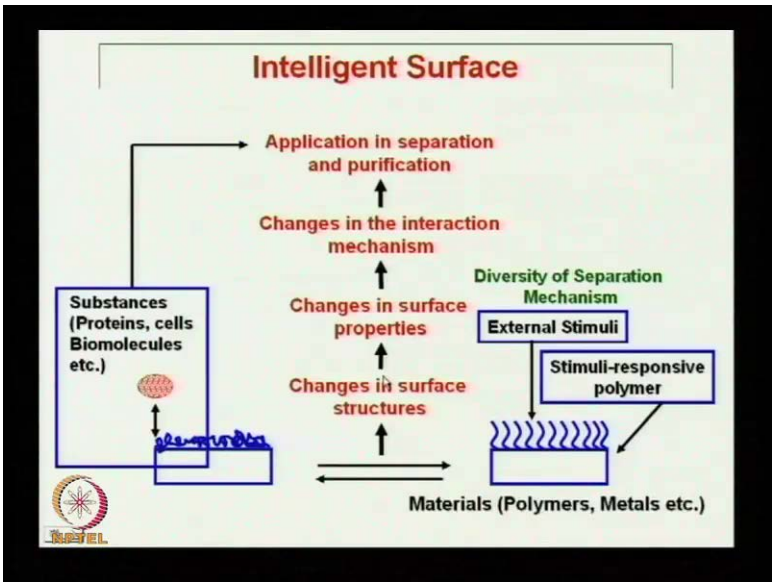

Same concept here you try to look at this model where say you can have a materials with this surface, that materials may be polymer or metal or ceramic, if you have some active site on the surface then you can attach this stimuli responsive polymer on to this surface and these polymers respond to external stimuli or stimulus say temperature or pH like that. And that help in separation and purification. I give you one another example say in drug delivery system this polyvinyl alcohol, polyvinyl alcohol can be used for making pH responsive drug delivery.

Now, in stomach, in stomach you know the pH, acidic means how acidic, how much acidic? Less than 5, it goes to less than 5 highly acidic. So, when we swallow something it passes through that highly acidic region, acidic zone or digestion or hydrolyses or breakdown of the breakdown of the food materials. Then slowly it process through the colon, the large intestine. There the pH is higher. Now, sometimes we need some drug to be released in the stomach, sometimes we need drugs to released in the large intestine at different places where the pH is, pH environments are different. So, if your drug is or your drug delivery system is responsive to such pH say at low pH the encapsulated device will not show any something like that.

So, drug will remain inside the device. When it passes that stomach or high, low pH region and enters the high pH region, there it will open because of swelling, because that only swell in alkaline pH not in acidic pH. The reverse thing can also be done, swelling in acidic pH and

deswelling in alkaline pH. So, that can be done by modifying this polyvinyl alcohol by attaching some carboxyl group or without carboxyl group. So, these are the concepts, people are working on these things and making some device.

You know you are swallowing so many different capsules or drugs, coated capsules etcetera, polymer coated capsules, sugar coated capsules or drugs, pills, how they are making, who are helping them? People like you are helping. So, if you have some knowledge you can tell something new. Here you see this due to change in temperature it can show solane to dissolane configuration.

Now, if there are substances like proteins cells, biomolecules presented by this, that can be separated or that can be purified, that can be, that can help in filtration etcetera. So, by change in surface structures, by change in surface properties, by changes in interaction mechanism for application in separation and purification. You go through this diagram and see the message, the message which can be obtainable from such diagram, from such a presentation.

Student: (( ))

You have to know the swelling and diswelling kinetics. Swelling and disswelling kinetics as well as swelling volume, deswelling volume. You have the specific volume in swollen and deswelling condition. There you know how much is the volume of the metrics in which the drug is kept loaded or encapsulated, you know the volume of the drug and if you know the ratio of the swollen to deswollen volume then you can get the size of the pores created or pores generated due to swelling etcetera and if you know the time of release.

So, this way the entire your release profile can be programmed that way. You know there are so many different variables, so act on the variables, work on the variables, this way you can make a programme so that it can give you well defined drug release, well define drug release. So, that is called targeted as well as pulsatile or controlled release of drugs. This is the concept you see how to think, you have to make a programme that way.

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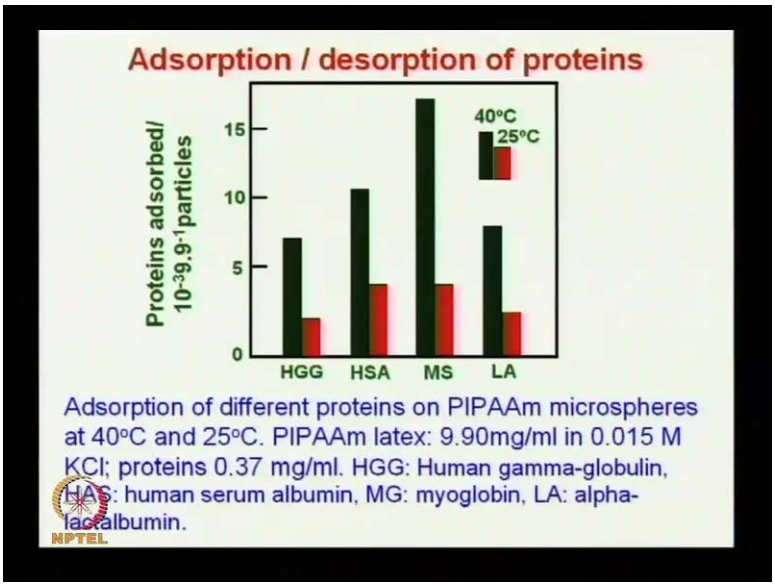

Adsorption, desorption of proteins is another application. Proteins like human gamma globulin, human serum albumin, myoglobin, alpha lactalbumin. You see at different temperatures, proteins adsorbed per 10 to the minus 3, per gram of particles actually. 10 to the minus 3 gram per gram of particles, this is not 9, this is g actually. So, (( )) made it, this turns out minus 3 gram per gram of particles. And these are the two different temperatures at which they get adsorbed on to the surface of the gel modified with such polymer, it is not very difficult to understand.

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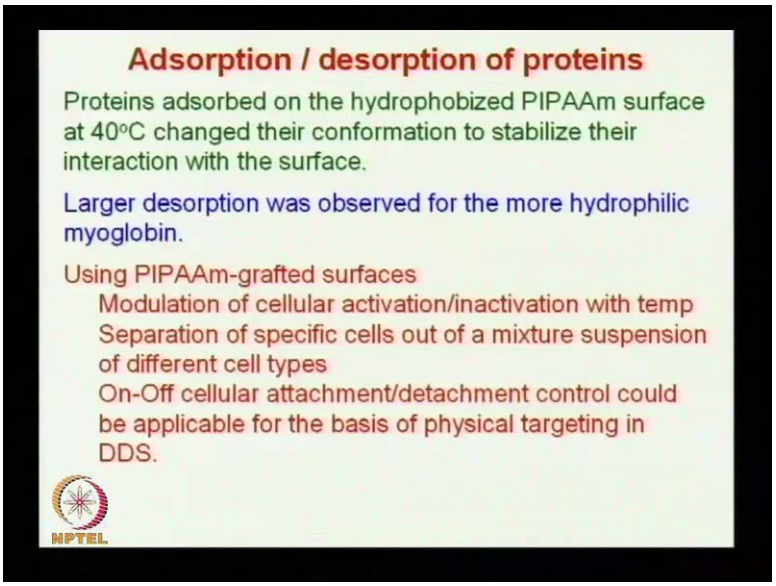

Adsorption, desorption proteins, I like to tell you some general aspects.

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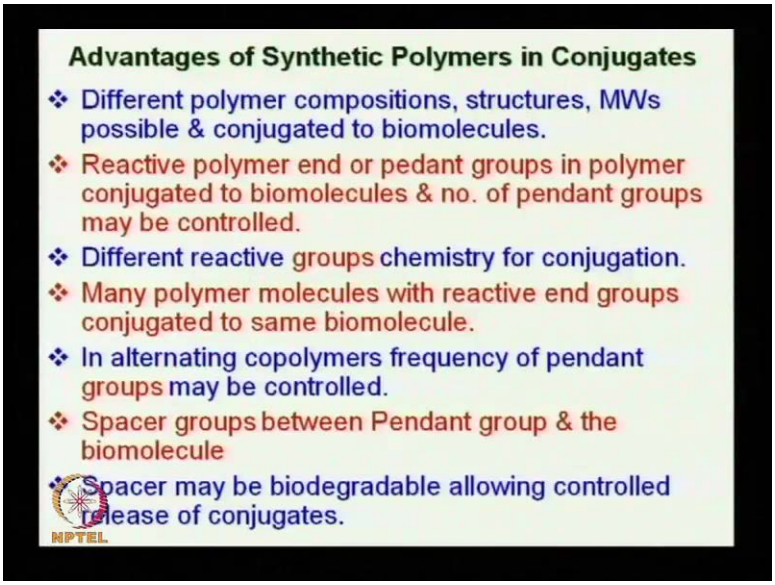

These are advantages of synthetic polymers in conjugates. You see polymer biomolecular conjugates, polymer biomolecular conjugates, natural polymers biomolecular conjugates, synthetic polymers biomolecular conjugates. Advantages of such conjugates, advantages of such synthetic polymers, disadvantages of such synthetic polymers etcetera. So, you try to

understand here different polymer compositions, structures, molecular weights which are possible in case of synthetic polymers which is not so easy in case of none, your natural polymer because in natural polymers the diversity, that diversity is not possible because a system produces such natural polymers so their molecular weight, molecular distribution remain a narrow zone and they have, when such synthetic polymers are used for conjugations or bound to biomolecules then that is also suitable for synthetic polymers.

That means it is shows some advantages of using synthetic polymers, use of natural polymers. I tell you one example, stimuli responsive system. Say, touch me not plant is there, have you seen touch me not plant? Touch me not, Lajjawati? If you touch it, Lajjawati if you touch it, its leaves are closed. After some time it again opens. There are certain plants as the defence mechanism they have some thorns or these leaves you see this Lajjawati in order to protect themselves from this your, what is that called, cattles. Otherwise, cattles will eat them.

Say by some touch or some your wind flow etcetera they close their leaves. Those cattles will emerge in there, there is nothing available. This way, this is their protection mechanism, defence mechanism. So, there is some tissues you see. There is some tissues which actually shows such changes. This is smart tissues. Then again seismonastic plants, photonastic plant, our famous scientist, who can name?

Student: (( ))

Jagadish Chandra Bose, he worked a lot on this plants. So, they are the smart tissues, smart polymers there. That means I want to say that these natural plants contains some natural polymers, if you can isolate them without denaturation then those can be used for such stimuli responsive purpose. I tried little bit. Now, there are certain plant, if you just make a sound this, there leaves will dance like this. So, that plant is there in my house, I have just some way collected, it is there.

Reactive polymer ends or pendent groups in polymer conjugated to bio molecules and number of pendent groups may be controlled and so many things are there, if you read you will understand, I tell you. This, there versatility is possible in synthetic polymers whereas this it is little bit restricted in natural polymers. And you have seen in case of this stimuli responsive

polymer, there is one side, on one end of the polymer molecule through carboxyl or hydroxyl or amino group it can be attached.

Now, if you want to attach a bio molecule you can do it in one place, one site or in multiple sites. Now, in case of natural polymer there is some limitation whereas in case of synthetic polymers you can have many more sites which you can tailor that means it creates some active sites, many more sites. Frequently, you can attach, keep sites, you can attach this biomolecules. So, those things are described over here. Alternating polymer, alternating copolymers frequency of pendant groups may be controlled. You know what is pendant group? What is pendant group? Could you tell me example of one pendent group, polymer containing a pendant group?

Student: (( ))

Polystyrene, phenyl group is the pendent group. Polypropylene, methyl group is the pendant group, like this. So, that pendant group location as well as their frequency, those can be controlled through some copolymerization. You have to design the molecule, then you can synthesize. Then some spacer can be used. Spacer, may be biodegradable allowing controlled release of conjugates. Say, you have attached a conjugates. Suppose, this is a polymer molecule, so you have attached a sorry suppose, this is a conjugate, bimolecular conjugate, active bimolecular conjugate attached to this polymer.

So, if you want to release thing from this conjugated cell say after separation you have done it, separated through such conjugation and after separation you have to again release, rewind it, recover it. How to do? Then you have to break over here. Now, if that site does not break then your purpose is lost. So, if this site contains a biodegradable group like say I tell you this way this group is there, which is hydrolytically degradable. So, here one carbon your ester group. Here, at this side again another ester group. So, by hydrolytic degradation, hydrolytic degradation this portion can be recovered. So, this is called a spacer.

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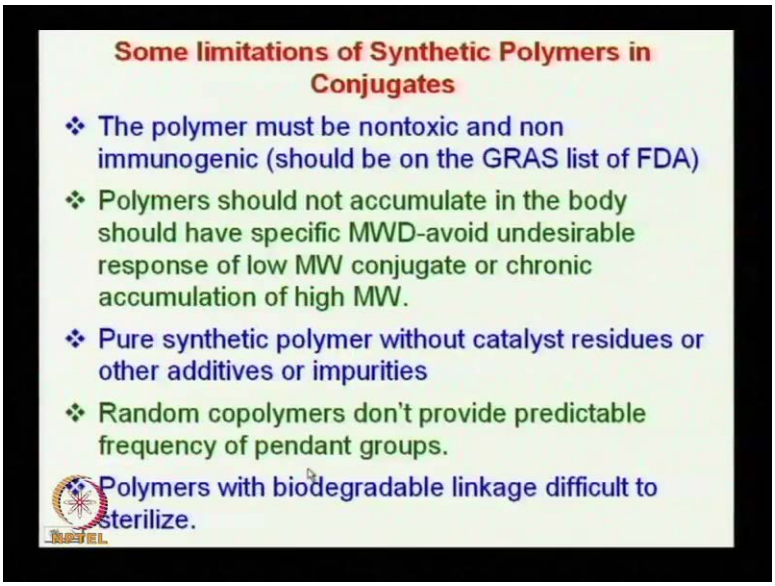

These are called as spacer here. Spacer may be biodegradable allowing controlled release of conjugates. This spacer groups between pendant group and the biomolecule, that is also possible. Some limitations, the polymer must be non toxic, non immunogenic. Should be on the GRAS list of FDA, what is GRAS? Generally regarded as safe, generally regarded as safe. That list is called as GRAS list of food and drug administration authority, food and drug administration authority, FDA. So, if your polymer is listed in that GRAS list yes you can use safely. So, this way something described over here.

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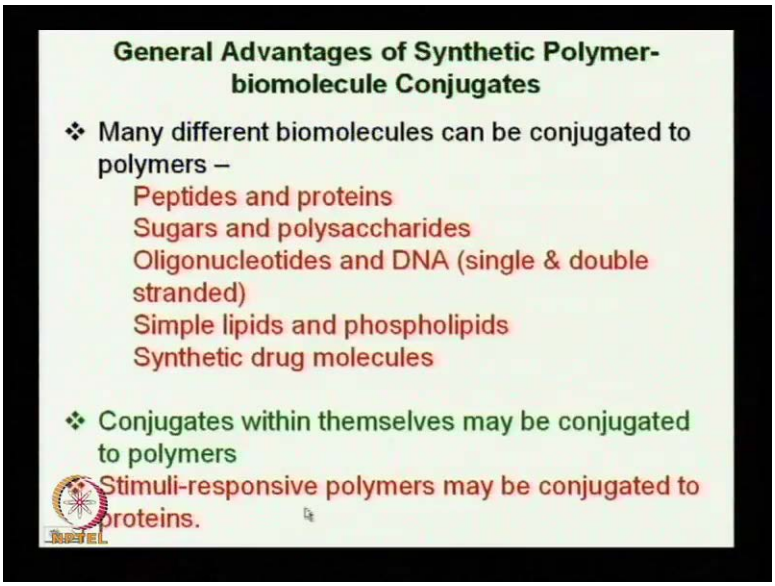

General advantages of synthetic polymer biomolecular conjugates, please read it. You will understand.

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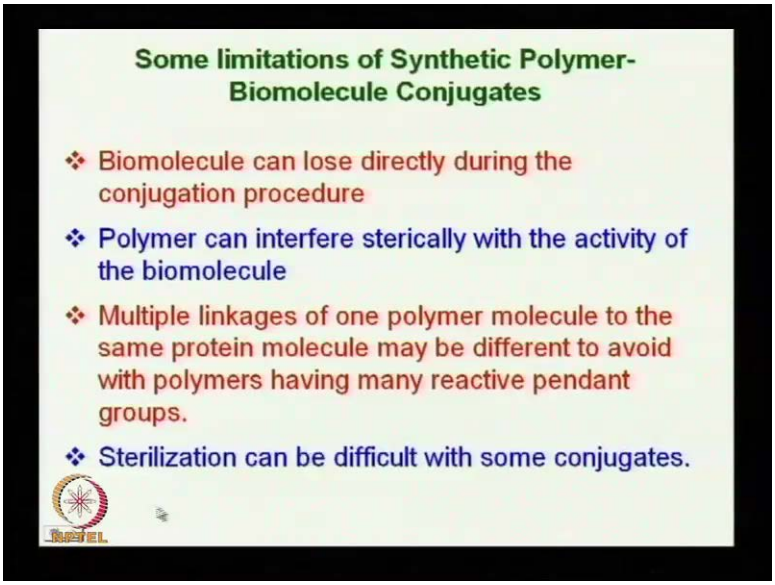

Some limitations of polymer bimolecular polymer conjugates continued where which can help in sterilization, sterilization, natural materials are not that way sterilizable, whereas synthetic materials can be sterilizable without degradation.

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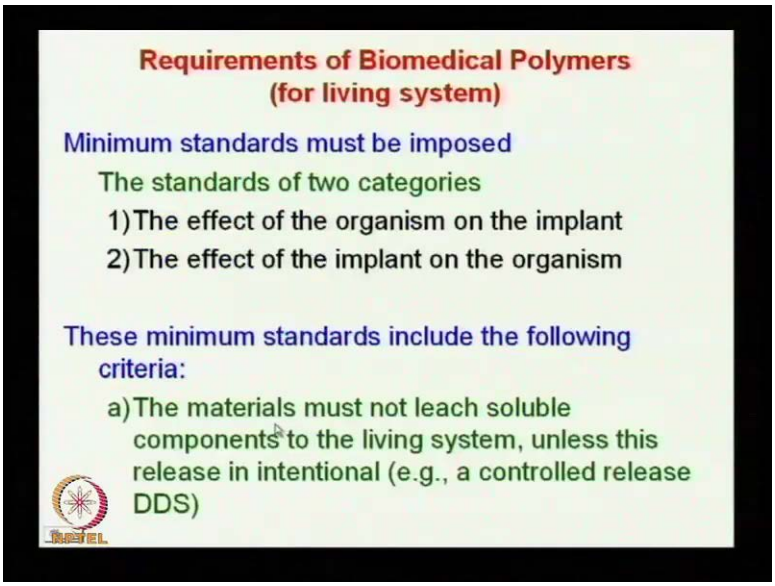

The requirements of biomedical polymers for living system, these minimum standards include the following criteria. The materials must not leach soluble components to the living system unless this release is, actually it should be is, release is intentional, a controlled release drug delivery system. For living system the material must be biocompatible, it must not degrade etcetera.

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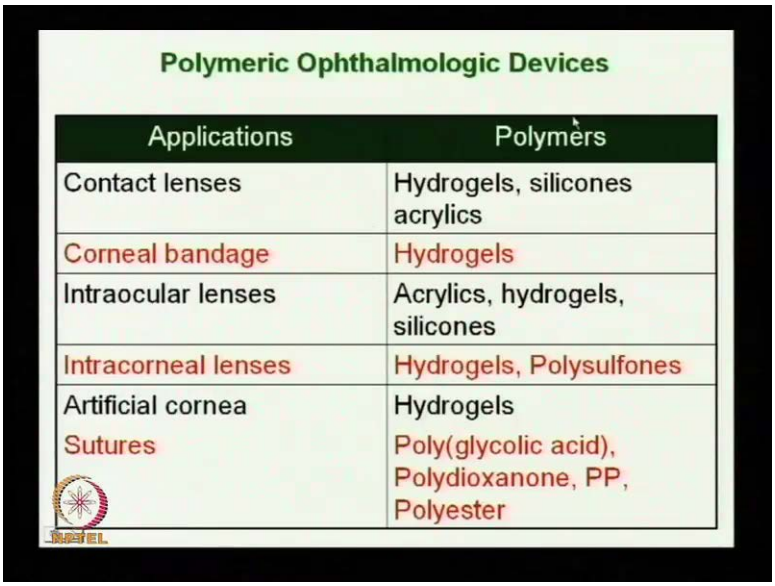

Some applications, I will cover later. Polymers have been introduced to for solid surfaces and bio molecules as stimuli responsive switching sequences. Current researches attempt to modify tissues and cells and control interaction with living systems with the help of stimuli responsive polymers which might open new applications in a wide spectrum of fields from clinical medicine to industry. That is all.

Thank you.