Tissue Engineering
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Lecture - 05
Scaffolds: Natural Polymers

Good morning, we will start with the next topic. In the last class, we looked at the extracellular matrices. So, we primarily talked about how extracellular matrices can be used for tissue engineering applications; where we talked about what are the components and we discussed what the structures are and what their roles in the ECM are.

We will move on to other materials, which can be used as scaffolds. First, we will talk about natural polymers today. I have also uploaded the slides, for the last lecture and I have edited it to give an older paper, rather than the newer paper. So, what I did was, I went back and looked at the papers, and I realized that the older paper had more detailed materials and method section.

So, I have put the older paper; it is a 2008 paper. It is about decellularizing a heart, and they have given extensive details on the protocol. I think I have also uploaded the reading material for the protocols if not I will upload that; if you are interested you can look it up, I will give that to you.

So, the group had actually published a protocols paper. People tend to do that when they have some innovative protocol; they will give the standard operating procedure for a protocol. Step by step, it will be described. That will help you with your questions whereas, in how exactly decellularization is done and the protocols paper would explain every step that can be done so that it can be reproducible.

Ok now, we will talk about the next class of materials which is studied for scaffolds, it is the natural polymers.

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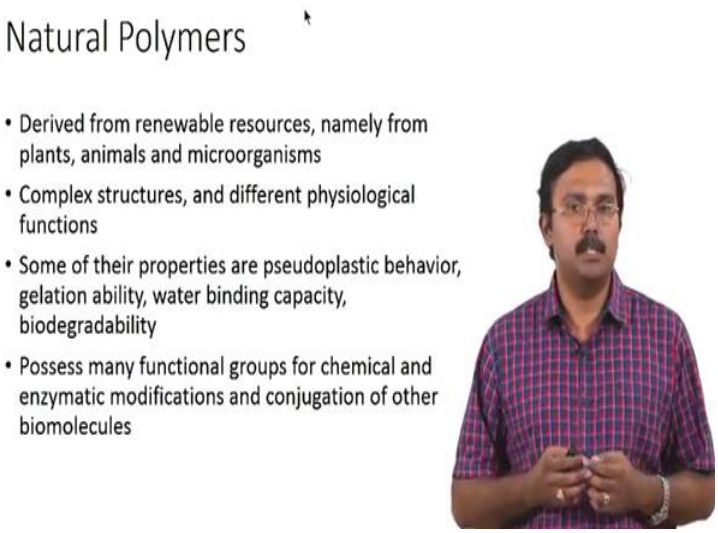

You have different types of natural polymers which are commonly used. We will talk about what they are and how they are used in tissue engineering.

A natural polymer is something which is derived from renewable resources which could be plants, animals, or microorganisms. They are complex structures with different physiological functions. Depending on which organism they are found in, they would have their own physiological functions.

Some of their properties are where they would have pseudoplastic behavior; they would have good gelation ability and water-binding capacity. They would most commonly be biodegradable; not always. See it will usually be degradable in the organism which we are looking at, but if you are going to say in humans, not all of them are going to be biodegradable.

They may possess many functional groups which can be used for chemical or enzymatic modifications or conjugation of other biomolecules. This is an important property you would want in a base material because you want to impart bioactivity to the material. The base material you use should have functional groups to which you can conjugate these molecules.

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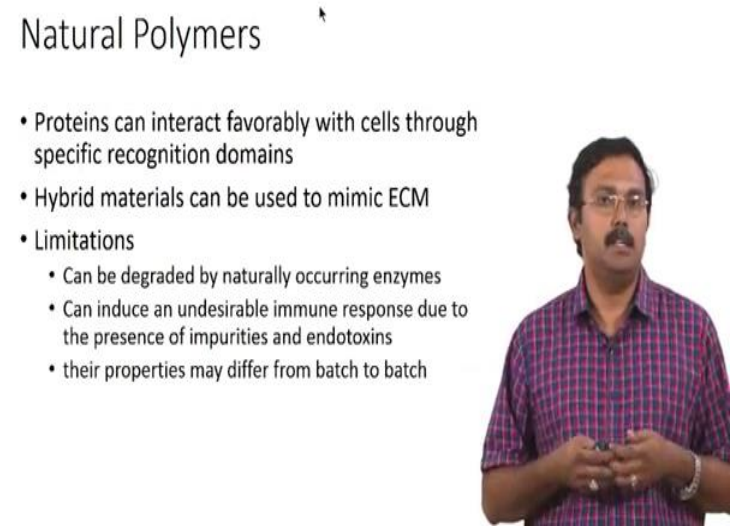

The advantage of using something like a natural polymer would be; it can interact favorably with cells through specific recognition domains because they do tend to interact with cells in the host organism where they are present. They have domains which will help in that, and if it is a molecule which is already present in your human body, then it can very nicely integrate and interact with the human body as well.

Hybrid materials have been used to mimic ECM. Basically, you take 2 or 3 natural polymers and blend them or conjugate them in a way that it would form something which would chemically be similar to ECM. These kinds of research have been done extensively over the past 20 or 30 years, and there have been varying levels of success with doing this.

The limitation would be; they can be degraded by naturally occurring enzymes which means controlling their rate of degradation becomes a challenge. If you are going to put it in a wound site, for example, you are going to have some matrix metalloproteases there, which can degrade some of these compounds. You could crosslink them in a way that they do not degrade more rapidly than your desired rate of degradation. So, that would be a challenge when it comes to this.

Another problem would be an undesirable immune response due to the presence of impurities or endotoxins because you are going to be extracting it from another place. So, there can always be some amount of endotoxins remaining. Even if it is a bacterial

culture, you can still have some of the bacterial cell wall or something which remains after purification, which can trigger immune reactions and lead to rejection of the implant.

Another problem is their property variation from batch to batch. Depending on where you get the material from, you will have a different molecular weight, different functionality, and so on. If you are looking for consistency with every step, it will be a problem.

With synthetic polymers, you have control over the chemical synthesis, which is happening. So, you can control their molecular weight and other properties to a very large extent, whereas that is not possible with natural polymers.

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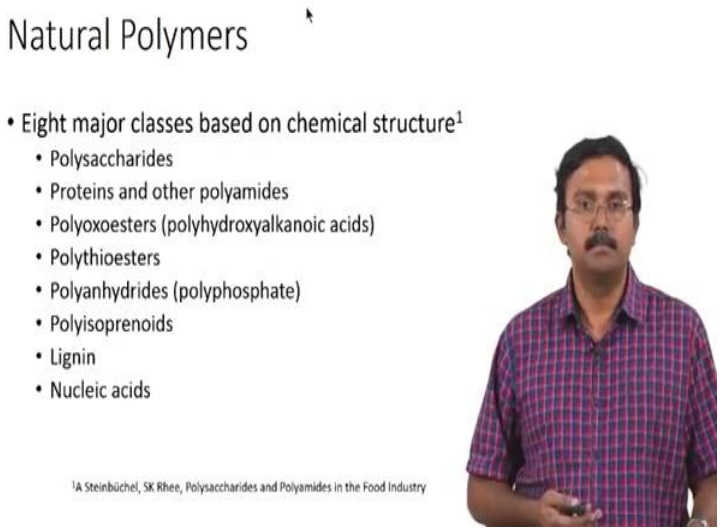

Natural polymers are classified to 8 major classes based on chemical structures; polysaccharides, proteins, polyoxoesters, polythioesters, polyanhydrides, polyisoprenoids, lignin, and nucleic acids.

Out of these, polysaccharides and proteins have been extensively studied. Because those are the components which are present in your ECM. So, they have actually been explored in depth. The polyoxoesters which would be the polyhydroxyalkanoic acids have also been studied to a reasonable level. Because they can be synthesized by

bacterial fermentation. So, that has also generated some amount of interest in this domain.

In today's lecture, we will talk about polysaccharides and only about proteins that we did not look at as part of ECM. I do not want to again talk about collagen and say that collagen can be used, right. I am not going to do that, but obviously, collagen is something people do use.

Please remember that although I am not talking about it here, it is a natural polymer which is being used in tissue engineering applications. So are other things like elastin, laminin and all that. We will not go into details of those aspects. We will talk about polysaccharides because we had not talked about them primarily when we discussed ECM. We will also have a small introduction on what polyhydroxyalkanoic acids are.

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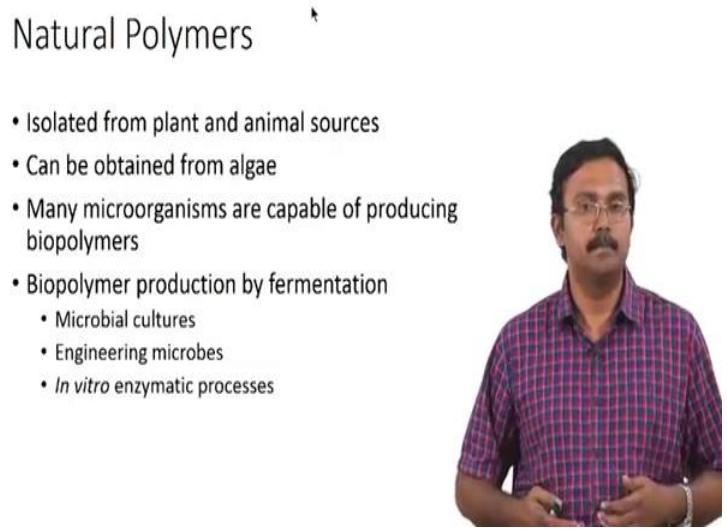

Natural polymers are basically isolated from plant or animal sources. You can also get it from algae. Sometimes microorganisms which are capable of producing these polysaccharides can be cultured, or you can use it in fermentation processes, and produce these. Biopolymer production by fermentation has been a growing field.

People try to use microbial cultures to produce different types of polysaccharides. Cellulose is one common example, where bacterial cellulose has been extensively

studied. In our department, Professor Guhan Jayaraman works on developing metabolically engineered strains for producing hyaluronic acid.

There are different ways people do it, and there are also enzymatic processes which can be used as fermentation processes. Instead of using the whole microbe, people can try to use enzymatic processes for creating these polymers. There are different processes studied for so many different materials, and you are ultimately looking to get consistency. This kind of fermentation where you may have better control over the production can limit the batch to batch variations which you are always worried about.

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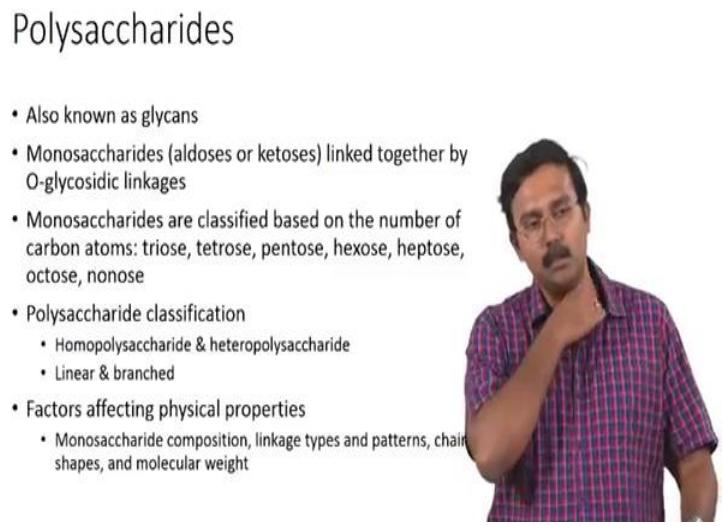

We will first start to talk about polysaccharides. They are also known as glycans. Polysaccharides are nothing but bunches of some monosaccharides which are linked together. The monosaccharides could be aldoses or ketoses, and they are linked by glycosidic linkages. Monosaccharides are classified based on the number of carbons. So, you would have triose, tetrose, pentose, hexose, heptose, octose and nonose, and so on. These are the monosaccharides, which are the building blocks for the polysaccharides.

Polysaccharides can be classified based on the composition of monosaccharides as homopolysaccharides or heteropolysaccharides. Homopolysaccharide would have only one monosaccharide as a repeating unit. A heteropolysaccharide would have multiple monosaccharides as repeating units.

It can also be classified based on the structure, whether it is a linear chain or a branched chain. If you have a branched chain, then it can have better mechanical properties in some cases. But the degradability will probably be reduced when you have a branch chain. You would have to find optimal levels for use in your application.

There are different factors which affect the physical property of a polysaccharide; obviously, the monosaccharide composition is one thing. You can also have linkage types and patterns, chain shapes, like the linear chain or branch chain and so on and the molecular weight of the material itself. You might have these polysaccharides which can start from maybe 50, 40, 50 kilodaltons to all the way to few megadaltons. So, if you are going to have that kind of range, based on the molecular weight, there will be many physical properties which will change.

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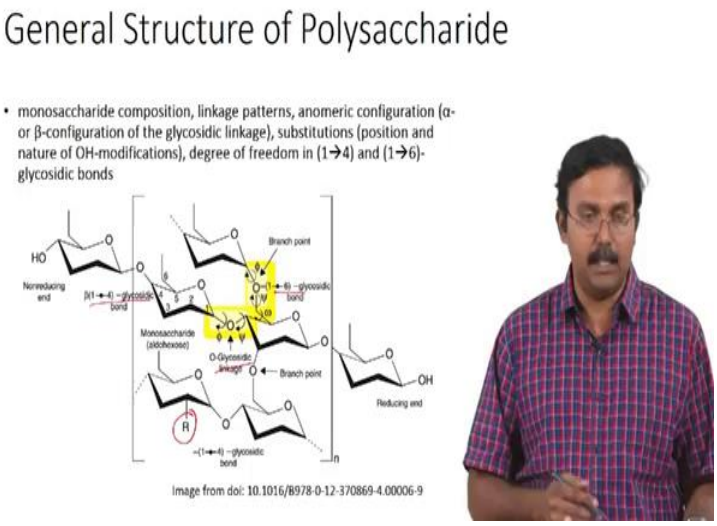

This is a general structure of a polysaccharide. So, what you look at here is different monosaccharide compositions that can be there, and you also have different linkage patterns. You have 1-6 glycosidic bond here, you have the O-glycosidic linkage general and beta 1-4 glycosidic bond and so on. You can also have different substitutions in the position of the hydroxyl group.

You have a hydroxyl group here. So, here you can have different substitutions with the R, which could be any group and you can also have different degrees of freedom because of these glycosidic bonds. This is a general structure, and you can actually keep changing

this, based on the groups which are there in the monomers. You will get different polysaccharide structures.

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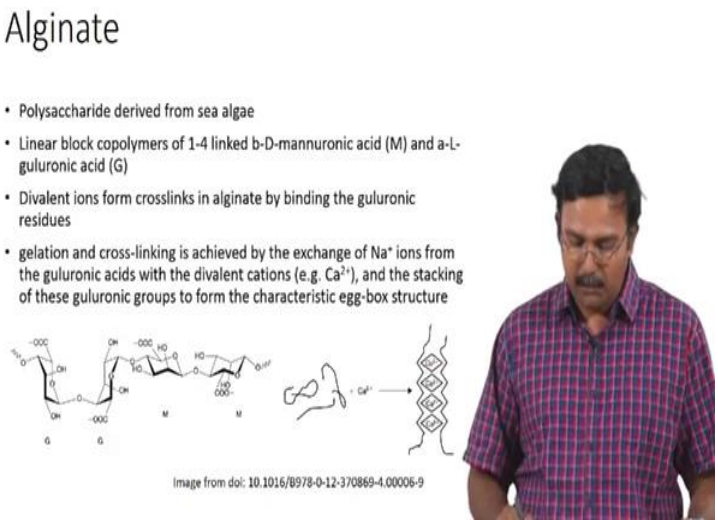

We will start with alginate. So, alginate is something all of you are aware of, right. You would have used it even if not for biomedical applications; you would have used it in some enzyme entrapment experiment. You would have taken alginate solution in sodium salts and then mixed it with calcium chloride to get alginate beads.

These are very commonly used in different applications. Biomedical applications also started looking at this for cell encapsulation and techniques like that. Alginate is a polysaccharide which is derived from sea algae, and this is a linear block copolymer of 1-4 linked beta-D-mannuronic acid and alpha-L-guluronic acid. The divalent ions can form crosslinks in alginates by binding to the guluronic residues.

So what happens is, during gelation and crosslinking the sodium ions which are there, get replaced with the calcium ions and results in the formation of something like the egg-box structure which is shown here. So, these separate links then get crosslinked because of the presence of the calcium ions results in the formation of crosslinking, and thereby, it forms a strong gel.

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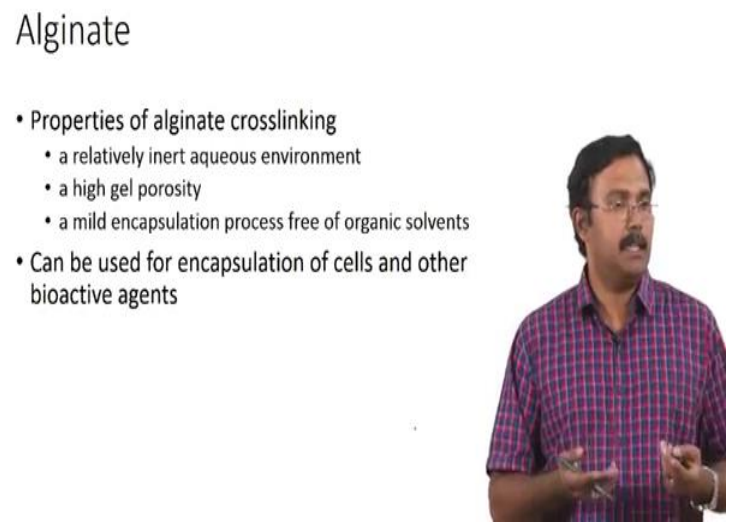

The advantage of something like an alginate crosslinking is the relatively inert aqueous environment. You do not need harsh conditions to create these kinds of crosslinking, which means it would be conducive for biological materials like cells, enzymes, and so on. It also has a very high gel porosity. It is a very porous gel so there can be very good mass transport. That means the material can come in and leave. Cells which are entrapped would get enough nutrients to survive in when encapsulated by calcium alginate beads.

As I said, mild encapsulation process, which is also free of organic solvents makes it conducive for biological applications. This is used for encapsulation of cells. People have studied encapsulating different types of cells using calcium alginates so that they can deliver cells to a site. Other bioactive agents you can try to load; growth factors and other molecules.

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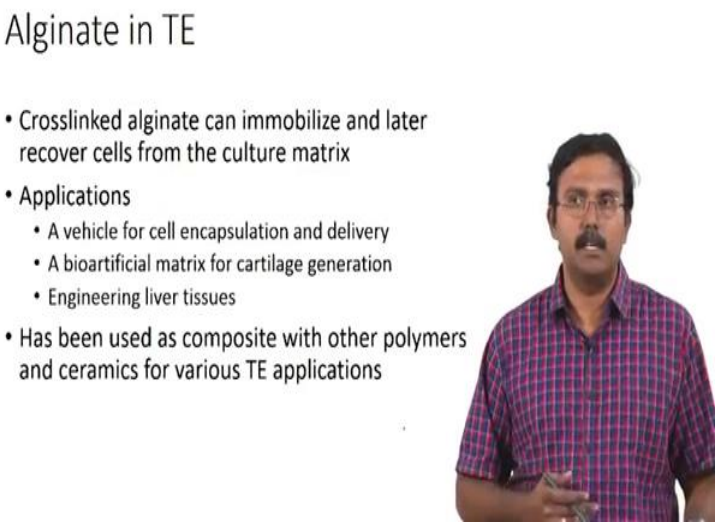

Crosslinked alginate can immobilize and also later recover cells from the cell culture matrix, and because of this, it is used in delivering cells; basically, it is used as a vehicle for delivering encapsulated cells. People have tried to use alginate beads as a bioartificial matrix for cartilage regeneration and also for engineering liver tissues. There are different papers on these; I am not going into the details of each of these things, I am just telling you these are the applications which have been used.

You can always go back and refer to literature, try to figure out how exactly people have used this. Obviously, most of these would not just be taking alginate and using it. There will be some level of modification, some other polymers being blended and so on. So, you would want to go back and read up on that if you are interested, ok.

But this can be used as an introduction for you to understand, this is sufficient. As I said, it is commonly used as a composite with other polymers and also with ceramics for tissue engineering applications. See, most of the polymers will always be tried, blended with ceramics when they want to use it for bone tissue engineering because the polymers themselves will not have the desired bioactivity and the mechanical properties. So, you try to blend them to form composites with ceramics.

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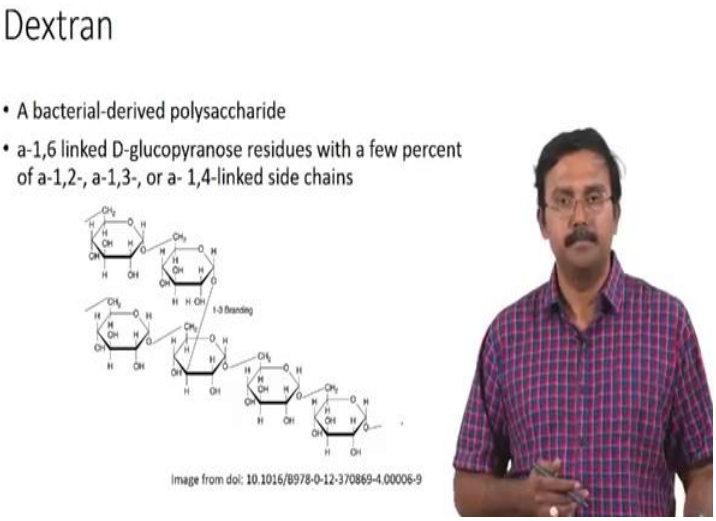

Dextran is another bacterial derived polysaccharide. You have alpha-1,6 linked D-glucopyranose residues with a small percentage of alpha-1,2, alpha-1,3 and alpha-1,4 linked side chains. This is the structure of dextran. Dextran is commonly used for different applications. So, can you think of a common application, where dextran is used; alginate, you all know. Similarly, you have also used dextran somewhere, not in medical. You would not probably think of that, but I am talking about something where some experiment that you might have done; protein purification.

Student: Sephadex.

Sephadex is actually made of dextran.

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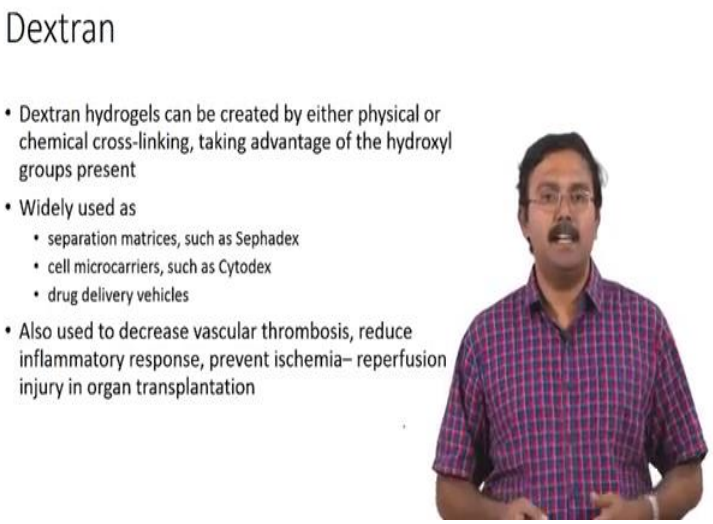

Dextran hydrogels can be created either by physical or chemical crosslinking, taking advantage of all the hydroxyl groups that are present. As you see here, the structure shows a lot of hydroxyl groups that are present. So, you have hydroxyl groups everywhere. Because there are so many hydroxyl groups, it is easy to crosslink them. You can have simple hydrogen bonding as physical crosslinking to form nice hydrogels.

We will talk about what hydrogels are and how they are formed in a later lecture. Right now, I am just talking about the materials that can be used, and then we will talk about how they are being fabricated. During that time, we will talk about hydrogels.

These are widely used in separation matrices which is the Sephadex. Sephadex is one common example where dextran is used, or it is also used as cell microcarriers, its commercial product named Cytodex; is used for cell delivery. It has also been explored as drug delivery vehicles.

These dextran has shown that it has very good hemocompatibility; so, it has been used for reducing vascular thrombosis and reducing inflammatory responses, preventing ischemia and reperfusion injury during organ transplant. Dextran has been extensively used in biomedical applications even before tissue engineering. Because there is so much promise and with biocompatibility, people have tried to explore dextran for tissue engineering applications as well.

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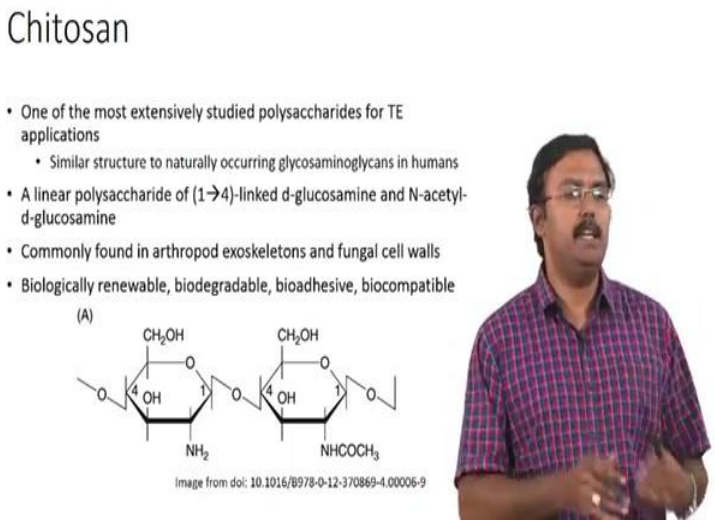

Another polymer which is very commonly studied is chitosan. I think just behind collagen; chitosan is the highest researched material. If you search for publications related to chitosan in tissue engineering, you will find thousands of them. There are many studies which have worked extensively on chitosan; simply because it has a very similar structure to naturally occurring glycosaminoglycans in humans. And it is a lot easier to get, compared to other polysaccharides which are not readily available.

Hyaluronic acid you can get it, but hyaluronan do you know where you get hyaluronan from? If you have attended seminars from Guhan's lab, you would know. Hyaluronan is taken from rooster comb. Can you imagine the quantity you would actually be able to get from that, right? It is not very easy to get that. Its extraction process is quite painful. There are also commercial processes where streptococcus is being used for the production of hyaluronan.

Guhan's lab works on, trying to use Lactococcus for production. Streptococcus is used in commercial cases, I think. But Lactococcus is a nonpathogenic strain compared to streptococcus. So, they are trying to use Lactococcus.

Anyways so, chitosan is not like that; chitosan is found in arthropod exoskeletons and fungal cell walls. So, you can very easily get chitosan. All the shrimp shell which you throw away has chitosan. Actually, that has chitin and chitin can be processed to get

chitosan. Because of this, there is a lot of abundances when it comes to chitosan and reasonably inexpensive.

It is also biodegradable, bioadhesive, and biocompatible. For these reasons, people have explored chitosan extensively, and it is basically a linear polysaccharide of 1-4-linked glucosamine and N-acetyl-glucosamine.

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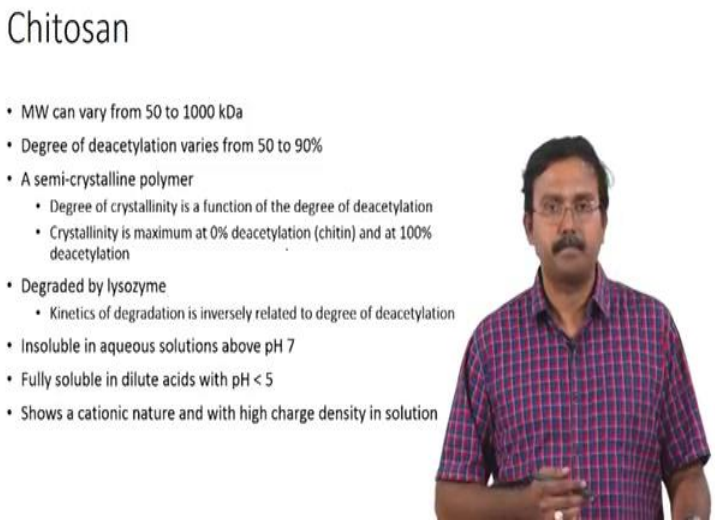

The molecular weight you get can actually range anywhere from 50 kilodaltons to 1000 kilodaltons, and also you have deacetylation of these. Chitin is acetylated; so, when you deacetylate chitin, you will get chitosan, and the degree of deacetylation can vary from 50 to 90 percent. It is a semi-crystalline polymer, and the degree of crystallinity is a function of the degree of deacetylation.

It is actually very high at both 0 percent deacetylation and 100 percent deacetylation. In between, it is a very semi-crystalline material. As I said, it is a biodegradable material because it gets degraded by lysozyme. Lysozyme cleaves the glycosidic bonds and degrades the chitosan.

That kinetics is inversely related to the degree of deacetylation. The higher the degree of deacetylation, the lower will be the degradability. It is insoluble in aqueous solutions above pH of 7, and it is fully soluble in dilute acids with pH less than 5. So, you can increase temperature, and you can play around with the solubility conditions to dissolve

it even around neutral pH. It shows a cationic nature and has a high charge density in solution.

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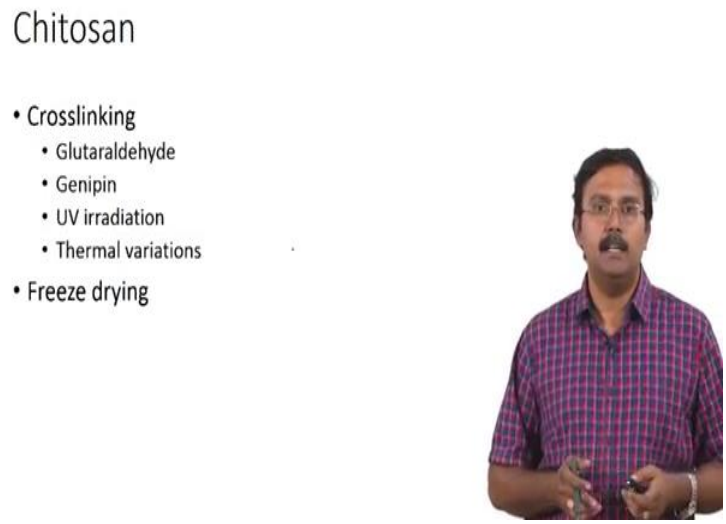

These are the major properties of chitosan. And this chitosan molecule is crosslinked when you want to prepare gels. There are different ways you can crosslink it. Glutaraldehyde is a very common crosslinking agent, which is used extensively for crosslinking because it has two aldehyde groups.

Genipin is another crosslinking molecule which is also used. UV irradiation and thermal variations can cause physical crosslinking. These are some of the techniques which are used for crosslinking and chitosan is primarily processed using the freeze-drying technique to prepare scaffolds. So, what is freeze-drying?

Student: Lyophilization.

That is another name for freeze-drying. So, what is the process?

Student: Like the water molecules get sublimed, leaving the solid-state.

So what happens is, you reduce that pressure enough so that water does not have to evaporate, but it just sublimes. Ice just sublimes to form water vapor. The advantage of doing something like this is, you would be able to create pores. The ice which is there, if it immediately goes into the vapor phase, the space occupied by the ice is going to be left

empty; leaving pores. These porous structures are going to provide the porosity for the cells to attach and grow. So, that is one use of doing lyophilization. That is why people try to lyophilize scaffolds when they prepare it.

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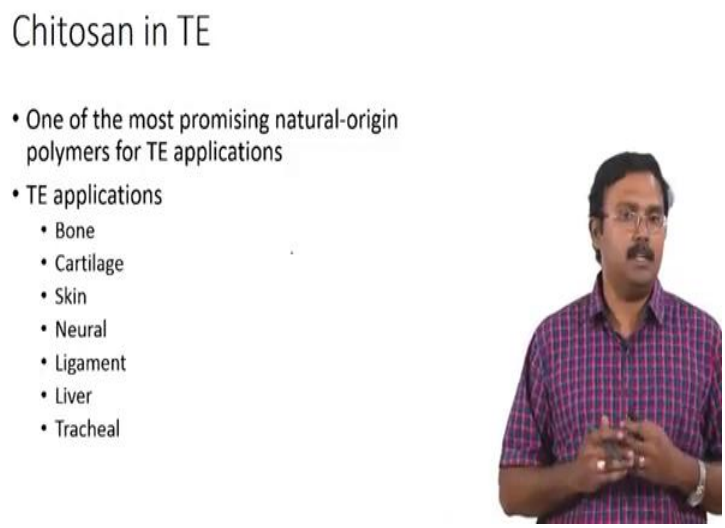

Chitosan has been used in different tissue engineering applications. It is identified as one of the most promising natural-origin polymers for tissue engineering applications. It has been looked at for different tissue engineering things. For bone applications, primarily is used along with some ceramics because just using chitosan is probably not good enough for the mechanical properties.

It has also been used for a lot of soft tissue applications. Again, it would be blended with other materials, and composites should be prepared. All the materials we talk about are a pure component, pure polysaccharides, and proteins. However, current research almost always uses composites. You would rarely see just one material being used and that is because your ECM itself is not a single material right, it is a mixture of things.

If you are trying to emulate and mimic the ECM, you cannot just use one material and think that will actually give you the exact property of the ECM. It does not work that way. Different things which people have worked on are skin, neural, ligament, liver, and tracheal tissue engineering.

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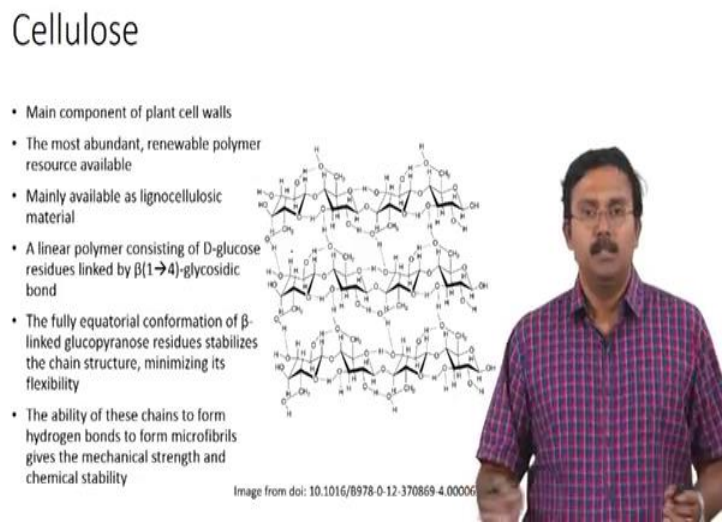

Cellulose is another molecule which people try to work on. This is one of the non-biodegradable molecules, in the sense that it is not degradable in your body. You can use cellulase to degrade it. If the organism has cellulase, it can degrade it, but we do not, and it cannot be degraded in vivo in humans.

It is the main component of plant cell walls, and it is the most abundant and renewable polymer resource available. It is primarily available as lignocellulosic material. You would have to separate the lignin from the cellulose to use it for many of the applications, which in itself is a big challenge. There is extensive research going on about how to separate lignin from lignocellulosic material.

This has a linear polymer consisting of the D-glucose residues, which are linked by beta 1-4-glycosidic bonds. So what happens is, these chains are actually stabilized by the formation of the beta-linked glucopyranose residues, and once these chains are stabilized, then the flexibility of the material decreases and these chains can form hydrogen bonds amongst each other to form microfibrils giving it the mechanical strength and the chemical stability. So, that is why it is very strong; it has very strong mechanically strength.

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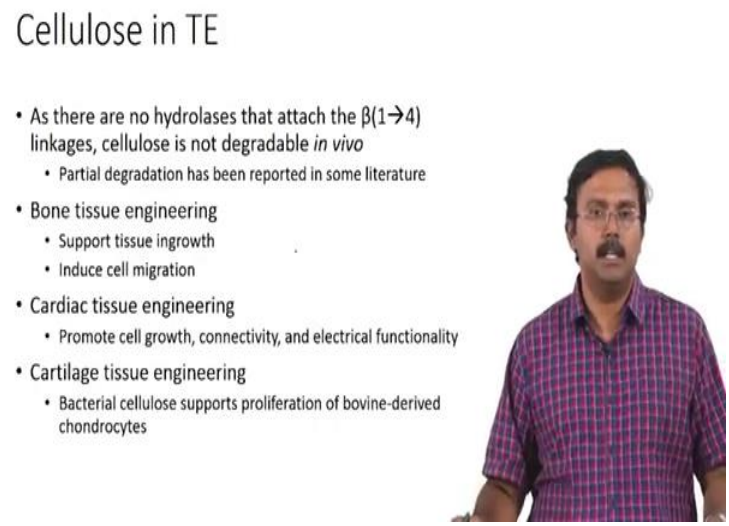

Cellulose in tissue engineering; people have tried to use it for different tissue engineering applications. Although it is not degradable. People have actually seen that partial degradation can be obtained in vivo. So, there is some literature which suggests partial degradation, but there are no hydrolases in your body which can actually degrade these linkages and therefore it is non-degradable in vivo.

People have tried to use this for bone tissue engineering and shown that cellulose actually supports bone ingrowth and also induces cell migration. They are showing some kind of bioactivity when it is used for bone applications. Cardiac tissue engineering applications have also been shown to have promise, because they show cell growth, connectivity, and some electrical functionality while using cellulose as the major component of the ECM, of the scaffold.

People have used it for cartilage tissue engineering; bacterial cellulose has been shown to support the proliferation of bovine-derived chondrocytes. Again these are all preliminary studies; some of them would be only in vitro studies, some of them would probably be some small animal studies, it is not like they have actually taken it for commercialization. So, please do not think that oh, these are all things which are completely proven. No, it is just initial studies that have shown, this is what its properties are, and there is always a chance of failure at different levels.

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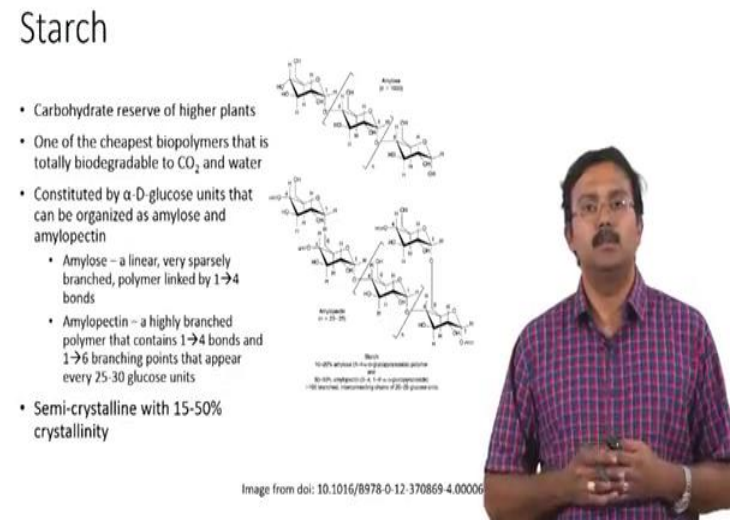

Starch is another carbohydrate molecule which is actually a carbohydrate reserve for higher plants, and it is one of the cheapest biomaterials available that is also biodegradable; it is completely degradable to form carbon dioxide and water. Because of this, it is an interesting material to work with. It contains alpha-D-glucose units that can be organized as amylose and amylopectin. Amylose is a linear very sparsely branched polymer; which is linked by 1-4 glycosidic bonds and you have amylopectin which is highly branched polymer that contains 1-4 bonds and 1-6 branching points, and it appears for every 25 to 30 glucose units.

Because of this, the structure itself is reasonably branched when you are talking about starch. Again, starch has also been used in different applications; I have not gone into the details. Starch has been used along with other molecules, other polymers for showing some tissue engineering applications.

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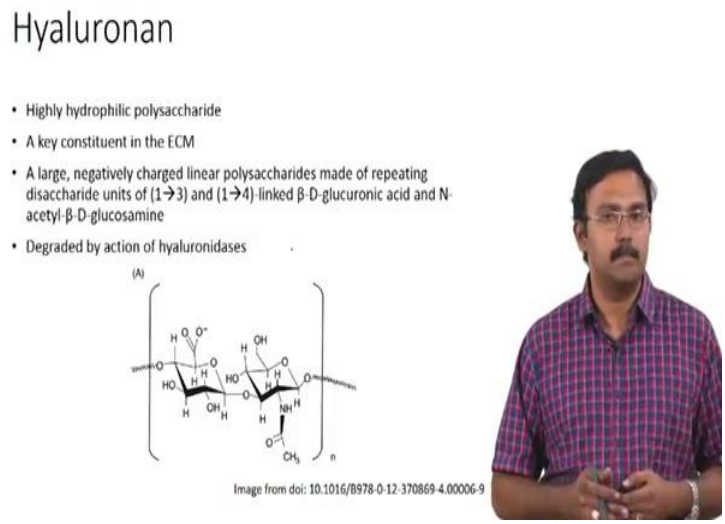

Hyaluronan is a highly hydrophilic polysaccharide. Amongst the polymers which we have discussed until now, hyaluronan is the only polymer which is actually present in your body.

Sorry.

Student: Sir, what made researchers think that starch could be used for tissue engineering?

It is biocompatible; see, any time material is biocompatible, you might want to explore its potential right. So, if it is not biocompatible, it cannot be used at all, right. When you know that it is a biocompatible material and it is completely degradable, you know for sure it is not going to cause any harm; so, you want to see whether it can have desired functionalities. When people explore; sometimes you see desired functionalities, sometimes you do not. In some cases, there will be positive results during in vitro studies which will get published. But eventually, when you take it further, you would realize at some point, its application has to stop because you cannot take it further for a clinical application. I do not even think 1 percent of whatever is reported as publications can actually be translated to clinical products.

You would see publications on every application, you will see thousands of publications on bone tissue engineering, thousands on cartilage tissue engineering and you probably

have like 3 products in each. That is because it is not going to translate that well. There is going to be a lot of hiccups and most of the times what happens is people study things in vitro, right. So, when you study in vitro many a time, you also use cell lines instead of using primary cells. So, you are going to have differences from cell line to the primary cell and then into a small animal, and then you take it to a large animal and then to humans. There is just so much chance of failure from what is published to what is becoming a clinical product.

But it is important to explore every material which has the potential to become a clinical product. That is why people who work in this domain will always start with anything they believe is biocompatible. That is why in our lab, we started working on isabgol. Isabgol pretty much nobody had worked on.

So, it is a polysaccharide. It is used primarily as a food supplement. You might have heard Sat Isab or Metamucil. So, these are products which you can buy off the shelf; it is very cheap, and it is soluble in water and people just dissolve it in water and drink it. It is a fiber supplement actually.

In our lab, we decided we will use it and see what happens right, and it showed some positive results; obviously, we have a long way to go, to know whether it can be taken much further. Similarly, glucomannan, so many things are studied because they show promise; not because we know for sure it will work in the final stages. Here, I am only talking about materials which have been reasonably well studied.

There will always be thousands of papers where thousands of different materials have been explored. I cannot actually go into details of all of them. It is not practical. You can go and look up biopolymer tissue engineering, and you will probably get like twenty thousand hits, and I am pretty sure not all of them will fall within the 6 or 7 materials which I have identified here, right.

People work on so many different things; people try to use so many different sources for things. And even if I am going to use the same material; so a glucomannan is a glucomannan, but it does not always behave that way because if it comes from one plant, it could have a certain property compared to another plant. Then you have to look at what would be the effects of using that separately. So, you would have different studies.

Hyaluronan is a key component in your ECM. It has a lot of biological functionality. So, it makes sense to, try to use it for your tissue engineering applications. It is a large negatively charged linear polysaccharide, made of repeating disaccharide units containing glucuronic acid and N-acetyl-glucosamine.

This can be degraded in your body by the action of hyaluronidase, and because of this, it is degradable, and it is not a problem. You can use it for any tissue engineering application.

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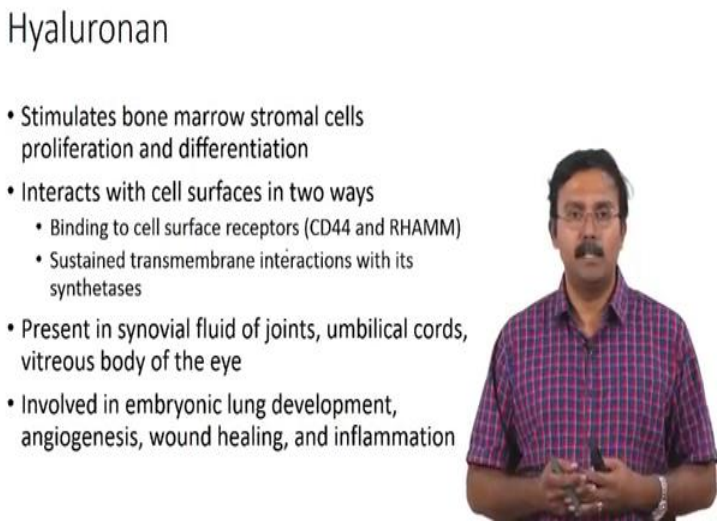

People have shown that it has very desirable bioactivities, it can stimulate bone marrow stromal cells proliferation and differentiation. It also interacts with cell surfaces; people have understood how it interacts with cell surfaces.

There are actually two ways; one is by binding to surface receptors CD44 and RHAMM. So, RHAMM is receptor for hyaluronic acid-mediated migration. And, it also has a sustained transmembrane interaction with its synthetases. Because of these things, it can interact very nicely with cells, and it will help the cells to attach to the surface.

This is commonly present in your synovial fluid joints, umbilical cords and vitreous body of the eye and so on. Hyaluronic acid (HA) is very commonly seen in these applications, in these parts of your body. It has also been proven to be involved in the embryonic lung development, angiogenesis, wound healing, and inflammatory processes.

Because you have the understanding of where it is present, you try to design tissue engineering applications where you can actually use this.

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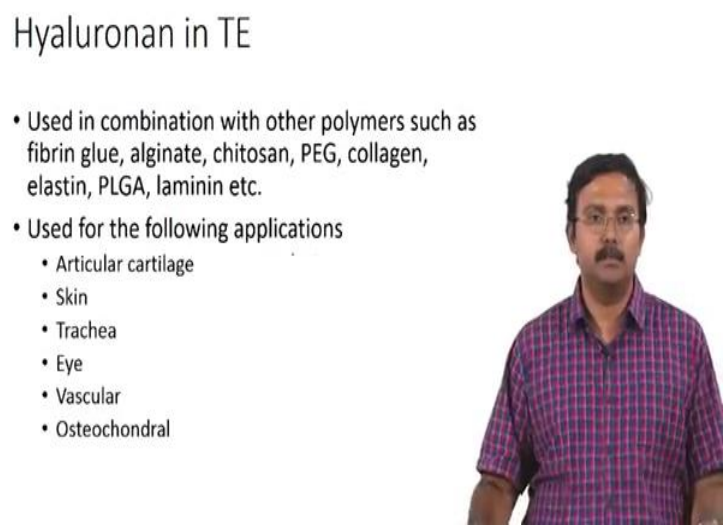

This HA is most commonly used in combination with other polymers. Like, it could be fibrin glue, alginate, chitosan, PEG, collagen, elastin, PLGA, laminin many different things. HA is just a component along with it, and it is effective for cartilage, skin, trachea, eye, vascular applications, and osteochondral applications and so on. It is reasonably effective for these things, as a blend or in combination with other polymers.

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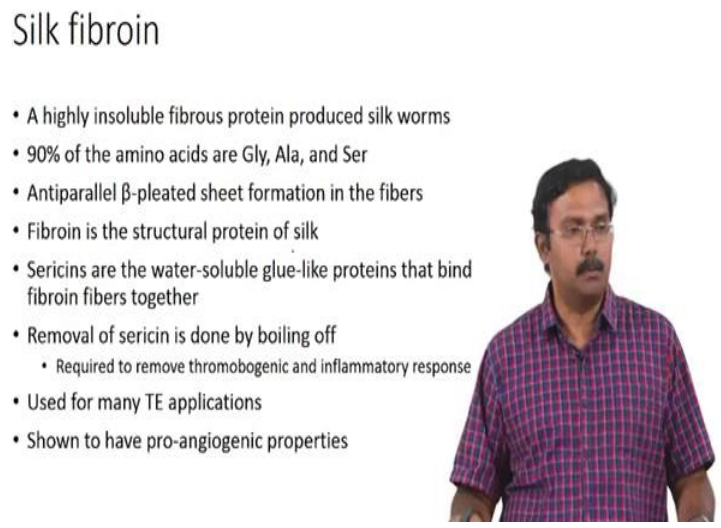

These are the polysaccharides. So, then the other class which is said is proteins. So, I am not going into collagen, elastin, laminin which we dealt with in reasonable detail as part of the extracellular matrix. So, we will talk about other proteins which are used. Here, I have only talked about silk fibroin; there are other proteins as well, which are used.

Keratin is one example; keratins have cell adhesion sites which help in cell attachment. Because of this, keratins have also been studied. Keratins from different source like from human hair, from sheep wool and so on have been studied for tissue engineering applications.

Silk fibroin I am talking about here because it is one of the more extensively studied molecules. There are a few groups within our own country and in the world which are focused primarily on silk fibroin for different biomedical applications. Professor S C Kundu and his student Biman Mandal are people who have been working extensively on silk fibroin in our country. And Professor David Kaplan is the person working on silk fibroin in the US. These people have been working on it for maybe a few decades now, and they have explored so many different avenues for silk when it comes to tissue engineering.

Silk is a highly insoluble fibrous protein that is produced by silkworms. Bombyx mori silk fibroin is what has been extensively studied. But Professor Kundu and Biman Mandal here are also working on something that is native to India; which is a non-mulberry silkworm. They work on non-mulberry silkworms and see how the silk fibroin of that is applicable for tissue engineering applications.

90 percent of the amino acids are glycine, alanine or serine, and these have antiparallel beta-pleated sheets which form the fibers. The silk contains two proteins; one is fibroin which is a structural protein of silk, and you also have another material which is a sericin. Sericin is a water-soluble glue-like protein that binds fibroin fibers together.

Sericin is usually removed before you use fibroin for a tissue engineering application because sericin can cause thrombogenic and inflammatory responses. Removing it is quite simple because sericin is water-soluble and fibroin is not; all you do is just put it in water and boil it. So, sericin will get dissolved, and fibroin will remain.

You take out the fibroin, and this is used for many tissue engineering applications again in combination with other materials. Recently within the last few years, it has shown to have pro-angiogenic properties. They have actually established the mechanism through which silk fibroin can actually provide pro-angiogenic properties, and this widens the horizon for the field, for this material because you can now use it in, along with other materials where you want revascularization to happen.

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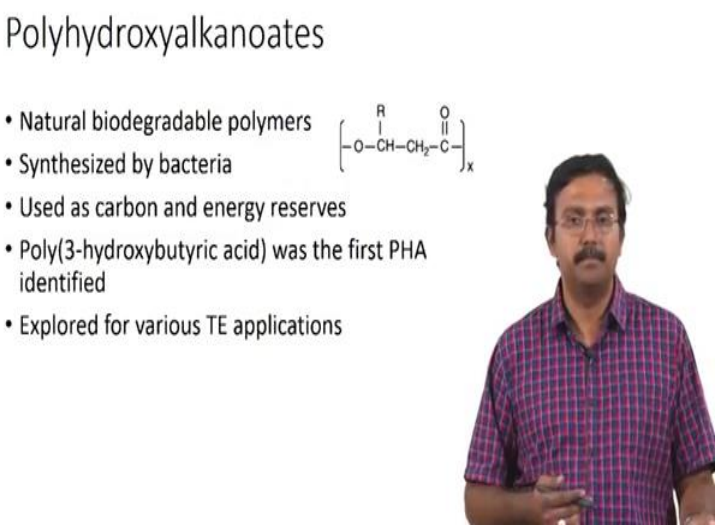

The last class of materials, which is the polyhydroxyalkanoates; are natural biodegradable polymers which are synthesized by bacteria. These are used as carbon and energy reserves. The first PHA to be identified was polyhydroxybutyrate which is also called as PHB, and this has been explored for various tissue engineering applications. Right now, a lot of work is being done on fermentation processes for producing PHBs and the other types of PHAs as well. You can look up what is all going on in this domain.

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For this lecture, this is the reference I had used. There is this chapter from a book called tissue engineering. A bunch of people edited it, and the authors for this chapter was also a bunch of people. The chapter is called natural polymers in tissue engineering applications.