Medical Biomaterials
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Lecture - 34
Biopolymers-Proteins / Hydrogels

Hello everyone, welcome to the course on medical biomaterials, we will continue on the topic of biopolymers; mainly proteins and we will then transform to another important biomaterial that is called hydrogels. So, we were talking about in the previous class about proteins what are these proteins they are the condensation polymers made from amino acids and polyamide.

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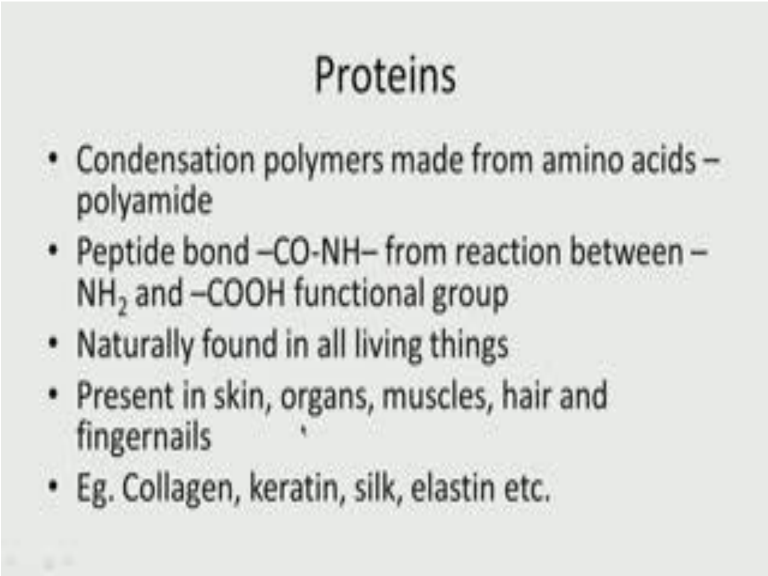

So; obviously, they have the peptide bond or the amide bond that is C double bond OON, there is a reaction when you have between NH 2 and COOH that is the acid you end up having this particular trade bonds. So, in nature we have proteins found in abundant and they can be used as a biomaterial like skin organs muscles hair fingernails. So, lot of biomaterials protein based biomaterials are found for example, your collagen, keratin, silk, elastin all these are different types of protein based biomaterials.

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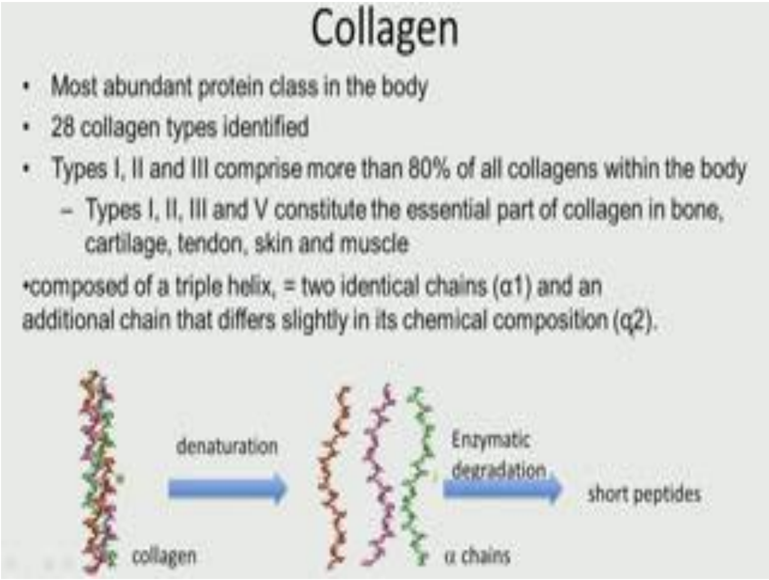

In the previous class, we talked about these collagen, collagen is most abundantly found protein in the body it has got a triple helix structure. So, it has got a 2 alpha 1 and in between you have a slightly different alpha 2, it forms a triple helix, it can get denatured and they get separated out and if there is an enzyme they can get degraded into smaller peptides there are 28 collagen types that are found, the type 1, 2, 3, is found 80 percent of all collagens within the body and. So, it is found in bone cartilage tendons skin muscles its composed as a set of triple helix like this alpha 1 chain and alpha 2, alpha 2 is slightly different in chemical composition.

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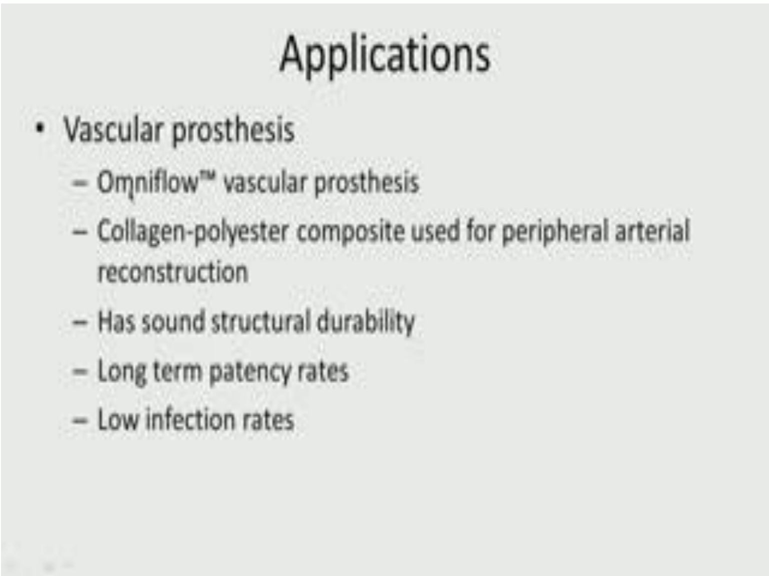

So, lot of applications it is used in vascular. So, already there is commercial product in vascular prosthesis collagen polyester composites used for peripheral arterial reconstruction it has got very good structural durability long term patency low infection rates then it can be used as addition barrier membrane.

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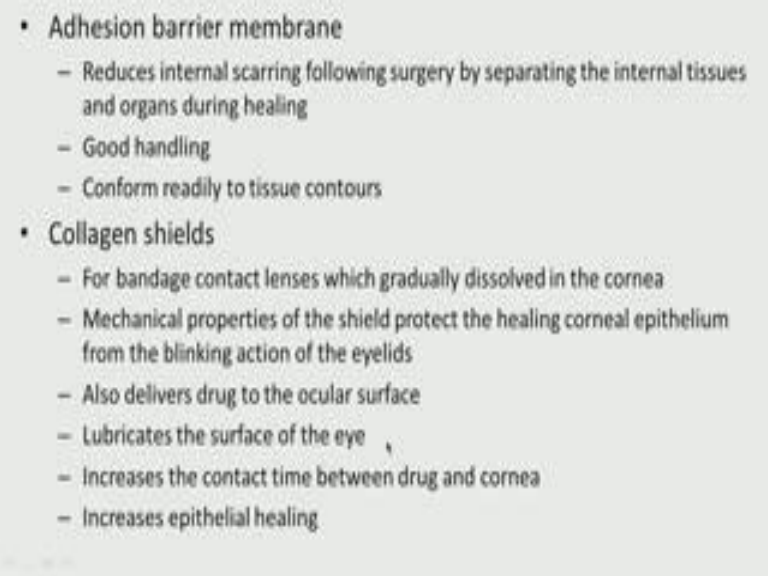

So, we can reduce internal scarring following surgery by separating the internal tissues and organs during healing, it is got good handling properties it can be contoured to the tissue and that is the beauty of it collagen shields. So, we can have bandage contact lenses which gradually dissolve in the cornea mechanical properties of the shield protects the healing corneal epithelium from the blinking action of the eyelids it can be used for delivering drugs it lubricates the surface of the eye increases the contact time between drugs and cornea increases the epithelial healing.

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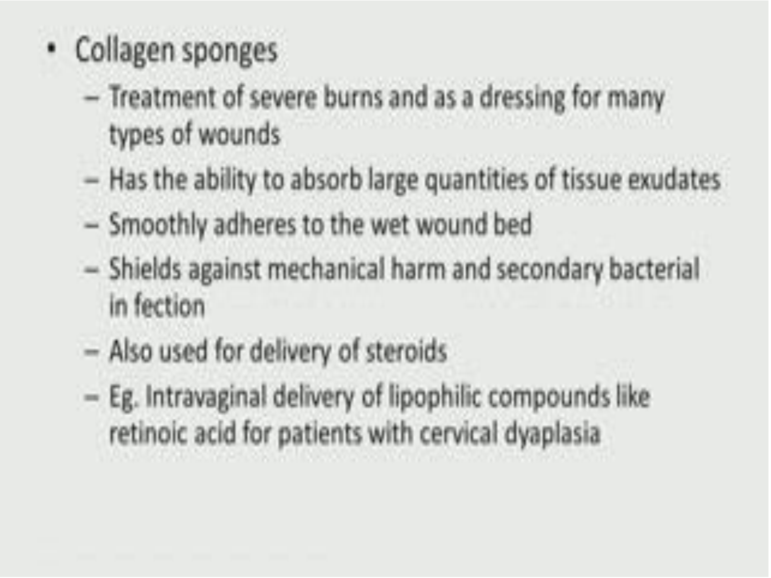

Then comes collagen sponges its very good for severe burns used as a dressing for any type of wounds, it can absorb large quantities of tissue exudates smoothly adheres to the wet wound bed shields against mechanical harm secondary bacterial infection and it can be used for delivery of steroids for example, intravaginal delivery of lipophilic compounds like retinoic acid for patients with the cervical dyaplasia.

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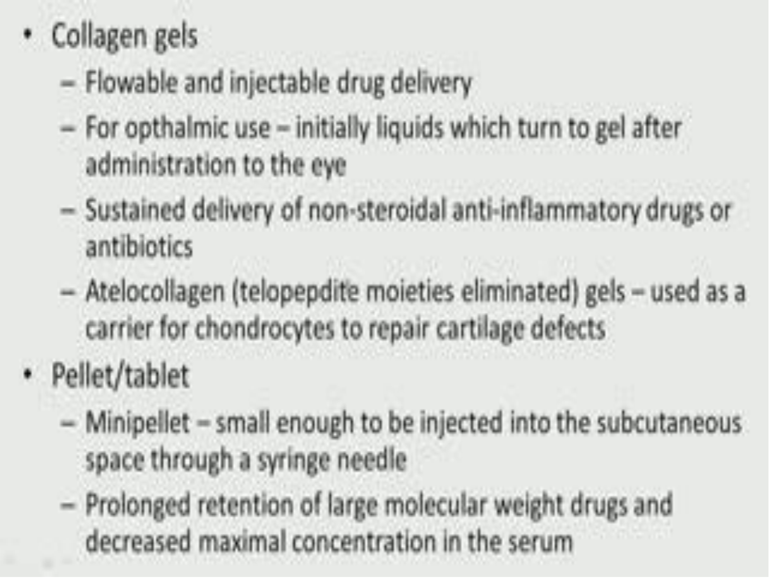

Then comes collagen gels it can be flowable or injectable drug delivery system for ophthalmic use initially it is in the form of a liquid which turns to gel after administration to the eye it can be used for sustained delivery of a non steroidal anti inflammatory drugs for inflammation pain joint or even antibiotics then atelocallagen gels used as a carrier for chondrocytes to repair cartilage defect. So, it is quite widely used because the cartilages contain primarily collagen hence it is used repair of such then it can be made in to pellets or tablets mini pellets small enough to be injected into the subcutaneous space through syringe needle prolonged retention of large molecular weight of drugs and decreased maximal concentration in the serum. So, such administrations are also possible of collagen.

But the problem of collagen is there could be cross contamination because the collagen is obtained from bovine. So, there could be bovine related diseases which may get transmitted to the human. So, that is one worry about using collagen in large scale.

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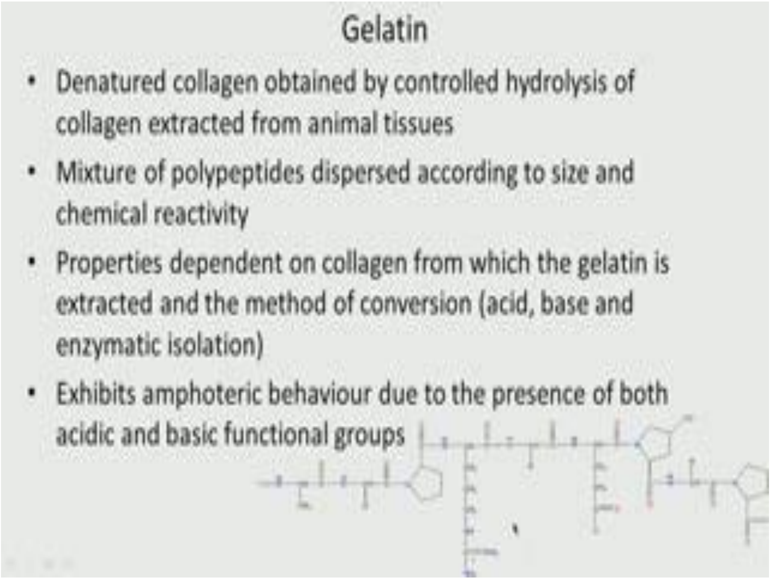

Then comes gelatin this is found from collagen it is a denatured collagen obtained by controlled hydrolysis of collagen which is extracted from animal tissues so; obviously, gelatin is much more safer than collagen because you do your chemical transformation hydrolysis reaction. So, they are really linear in nature and like collagen; collagen is a triple helix. So, the linear mixture of polypeptides because you are doing hydrolysis disposed according to size and chemical reactivity. So, you can have polypeptides of different chain lengths.

The properties depend on collagen from which the gelatin is extracted and the method of conversion whether I am hydrolyzing with the acid base or enzymatic. So, this is the typical structure linear structure of gelatin it exhibits amphoteric behaviour do the due to the presence of both acidic functional group as well as due to the presence of basic functional groups as you can see it contains both acidic functional groups C double bond O as well as OH. So, it has both the properties and. So, we can encapsulate an ionic air cationic type of drugs molecules ions and so on actually.

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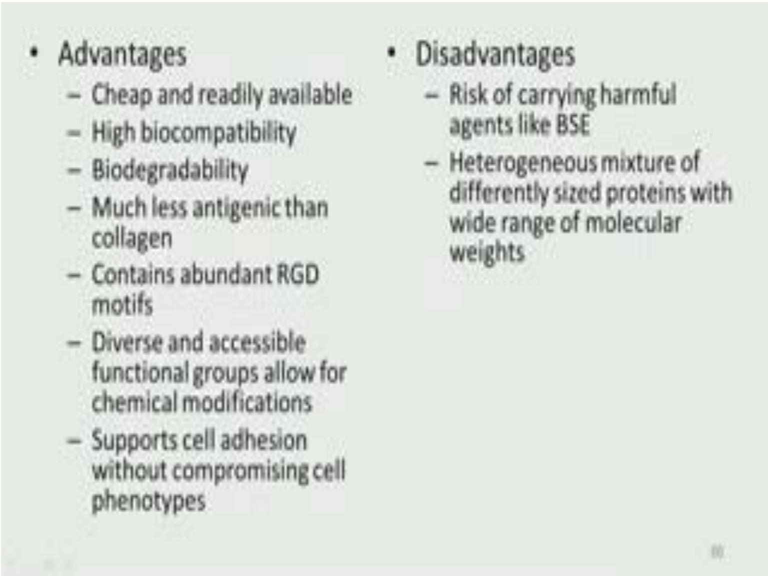

So, it is cheap and readily available very good biocompatibility biodegradable less antigenic than collagen contains abundant RGD motifs as you know RGD is a very important peptide sequence which helps in cell proliferation cells are able to identify itself and diverse and accessible functional groups allows for chemical modifications you can see so many different functional groups; so, many different functional groups. So, we can do lot of chemical modification on gelatin.

Support cell adhesion without compromising cell phenotypes what are the disadvantages risk of carrying harmful agents like a bovine related toxicity heterogeneous mixture of different sized proteins is wide range of molecular weight because I am doing hydrolysis of the collagen. So, we can have polypeptides of different chain length different molecular weights. So, that is a disadvantage. So, properties will be more of average rather than singular.

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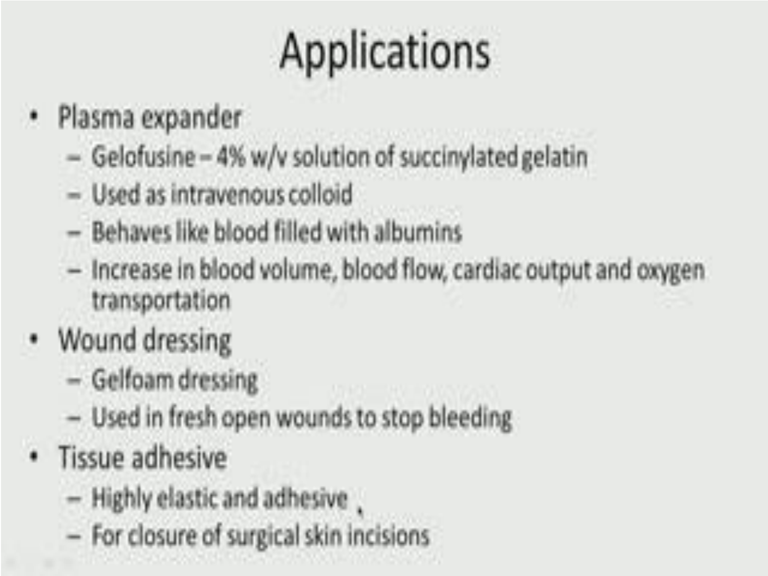

So, applications plasma expander; so, gelofusine 4 percent weight by volume solution of succinylated gelatin, so, it is used as intravenous colloid it behaves like blood filled with albumins increase in blood volume blood flow cardiac output and oxygen transfer transportation. So, we can inject gelatin in to that of course, as you know gelatin is widely used in.

Food flavoring industries and confectionaries and so on wound dressing gel foam dressing. So, it expands takes up lot of volume used in fresh open wounds to stop bleeding tissue adhesive highly elastic and adhesive.

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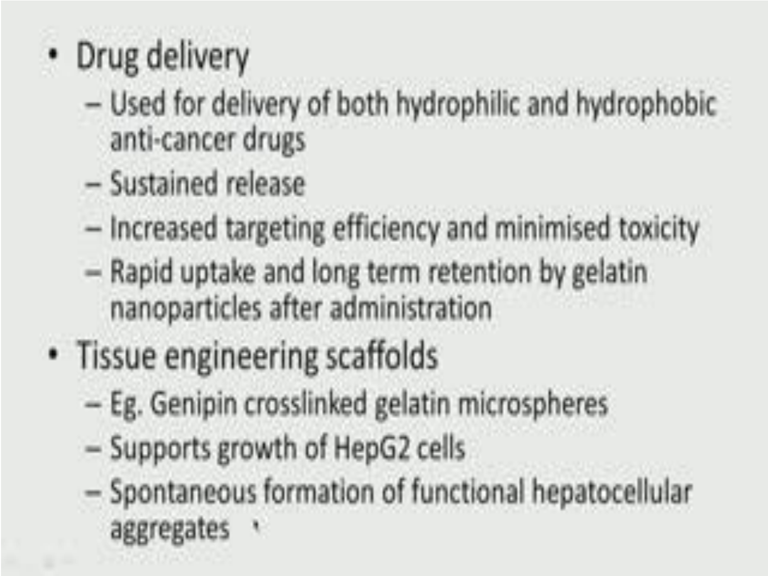

So, we can close surgical skin incision by applying this gelatin drug delivery used for delivery of both hydrophilic and hydrophobic anti cancer drugs sustained release and as I said it has got both acid; a acidic basic functional groups. So, we can have a cationic or anionic drugs encapsulated with that increased targeting efficiency and minimum toxicity rapid uptake and long term retention by gelatin nano particles after administration and tissue engineering scaffolds.

We can make scaffolds for growth of different types of tissues it can support growth of HepG2 cells spontaneous formation of functional hepatocellular aggregates.

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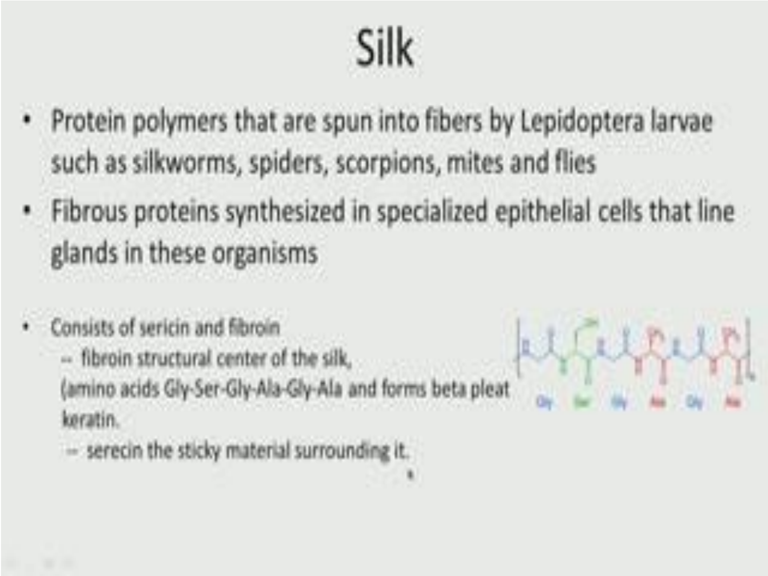

So, a lot of applications next come silk and silk as you know is used quite a lot in fabric of course, it can even be made into biomaterials it has got very good mechanical properties concile properties so; obviously, silk can have very good application in biomedical applications. So, it is a protein polymers that are spun in to fibers by Lepidoptera larvae such as silkworms spiders scorpions mites and flies.

It is a fibrous protein synthesized in specialized epithelial cells that line glands in this organism so; obviously, it contains sericin and fibroin this fibroin is the central sericin is the sticky material surrounding it this fibroin contains amino acids like glycine serine glycine alanine glycine alanine as you can see here and forms the beta pleat keratin. So, it contains fibroid that is in the central and then it contains sericin which is a sticky material surrounding it. So, silk it has got a very good mechanical properties and highly biocompatible it can help in tissue growth and also as cell scaffold.

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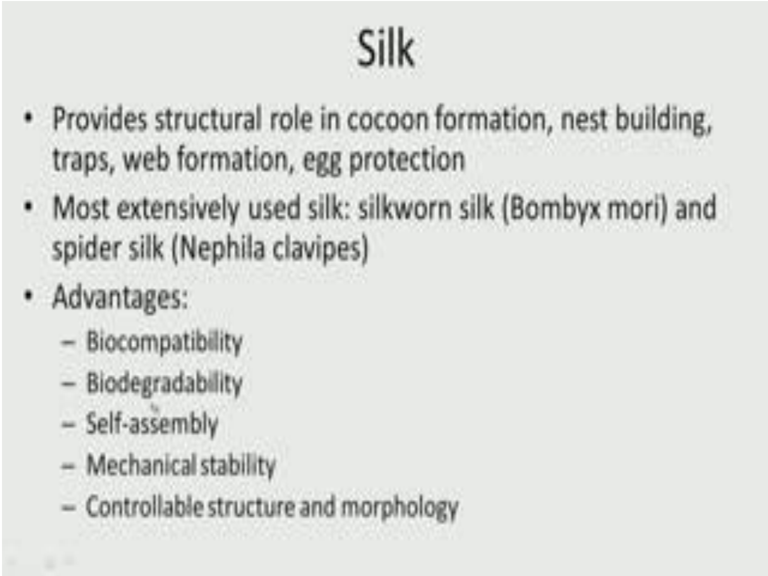

Provide structural role in cocoon formation nest building traps web formation egg protection; obviously, and produced by silkworm silk and spider silk biocompatibility biodegradability self assembly mechanical stability controllable structure and morphology. So, that is the advantage of this silk.

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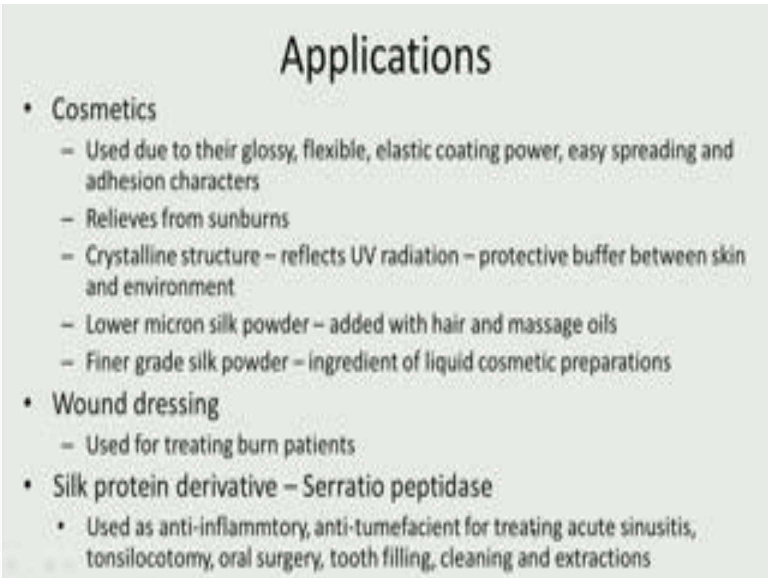

So, cosmetics used due to their glossy flexible elastic coating power easy spreading and adhesion characters relieves from sunburns the crystalline structure reflects UV radiation protective buffer between skin and environment lower micron silk powder added with hair and massage oils finer grade silk powder ingredient of liquid cosmetic preparation can be used for wound dressing burn patients silk protein derivative serratio peptidase used as anti inflammatory anti tumefacient for treating acute sinusitis tonsilocotomy oral surgery tooth filling cleaning extraction and so on.

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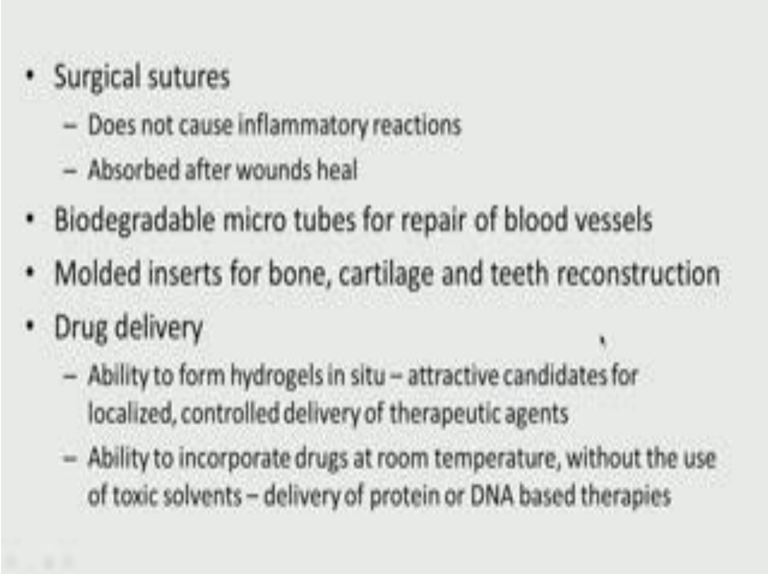

And also surgical sutures like I mentioned it has got very good tensile properties and it does not cause the inflammatory reactions absorbed after wound healing. So, its bios reabsorbed. So, it can find a very good applications as surgical sutures biodegradable micro tubes for repair of blood vessels molded inserts for bone cartilage and teeth reconstruction drug delivery ability to form hydrogel in situ attractive candidates for localized controlled delivery of therapeutic agents ability to incorporate drugs at room temperature without the use of toxic solvents delivery of protein or d n a based therapies. So, silk can find application in wound dressing surgical sutures biodegradable applications drug delivery systems and so on.

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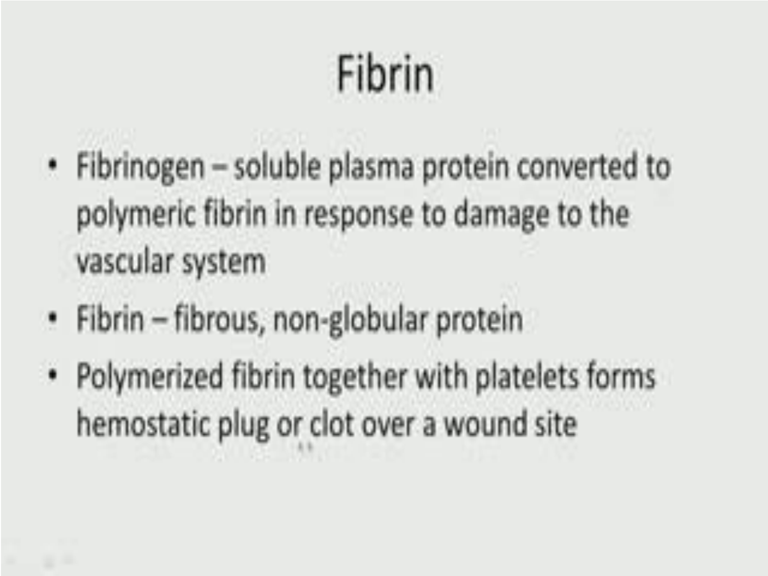

Then comes fibrin what is this fibrin is a fibrinogen this is the soluble plasma protein converted to polymeric fibrin. So, fibrinogen which is the soluble plasma protein converts to fibrin which is a blood clot especially when there is damage to the vascular system I talked long time back the fibrinogen is converted to fibrin forms the clot and closes the gap prevents the blood oozing out. So, this is a fibrous non globular protein. So, this fibrin together with platelets forms hemostatic plug or clot over a wound site.

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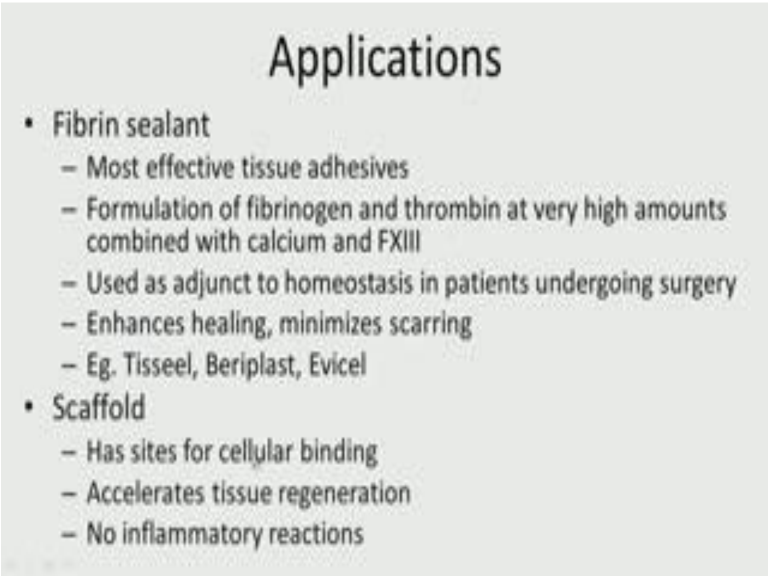

So, applications; so, fibrin sealant most effective tissue adhesive; obviously, its produced by the body. So, if you can use it as a biomaterial for sealing tissue repairs then nothing like it formulation of fibrinogen and thrombin at very high amounts combined with calcium and FX 3 used as adjunct to homeostasis and patients undergoing surgery enhances healing minimizes scarring

So lot of applications scaffold has sides for cellular binding accelerates tissue regeneration no inflammatory reaction. So, it is very good and applications especially as a sealant prevents the blood flow during surgery processes does not lead to any inflammatory reactions accelerates tissue regeneration so, a lot of proteins which are natural which can be used for tissue regeneration tissue engineering applications and as sealant and as a vascular bioresorbable material. So, we looked at biopolymers 2 types of biopolymers; one is the saccharide based polysaccharides the other is protein based; that means, they have this peptide bond and protein based or widely found in animals and natural environment. So, they also have very good applications in biomedical area.

Now, where we will look at something different they are called the hydrogels; hydrogels as the name imply can absorb lot of water and they are polymeric material which swells the presence of water. So, they can be used in areas of wound dressing slow drug release and so on.

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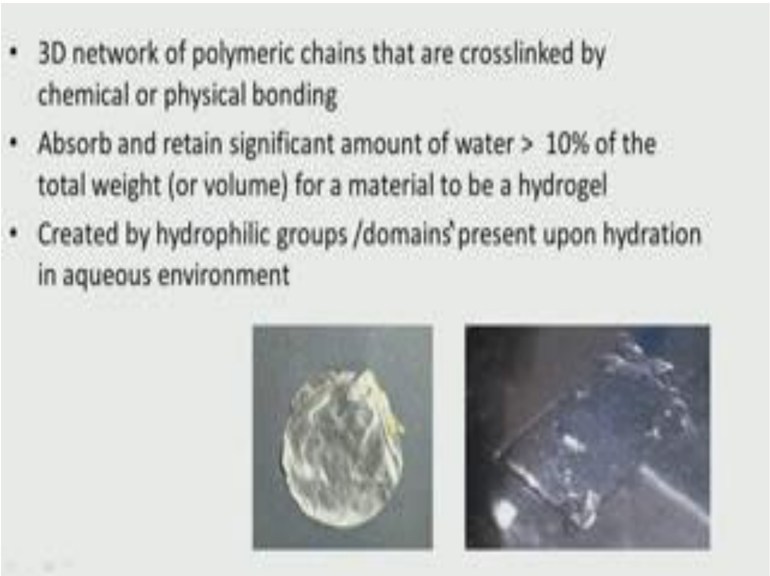

For example look at this picture, this is a polymeric hydrogel made up of cyclic beta glucan and (Refer Time: 15:37) when it is in the dry state as soon as we add water as you can see it really swells expands and reaches a very soft appearance very highly hydrophilic wet. So, they can find application especially in open wounds. So, they are 3D network of polymeric chains that are cross linked by chemical or physical bonding.

We will look at what type of chemical or what type of physical bonding that are happening in hydrogels they absorb and retain large amount of water at least minimum ten percent by weight or volume. In fact, they can go up to forty fifty sixty seventy percent well hundred percent there are many hydrogels which can retain its own weight they are created by hydrophilic groups domains present upon hydration in aqueous environment.

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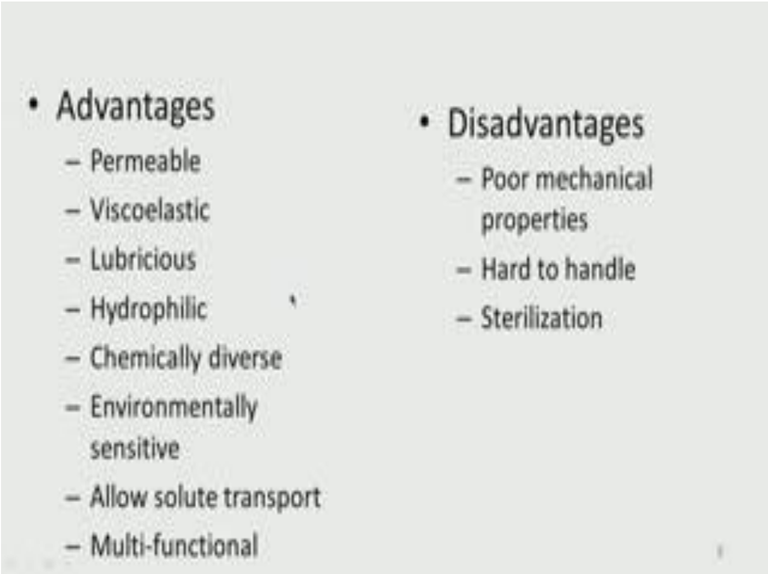

So, they are permeable viscoelastic lubricious hydrophilic chemically diverse environmentally sensitive allows solute transport multifunctional. So, we can use it for wound dressing for drug encapsulation drug delivery. So, many applications disadvantages of course, poor mechanical properties difficult to handle sterilization how do we sterilize this hydrogel that is a big issue and that needs to be thought of more in detail.

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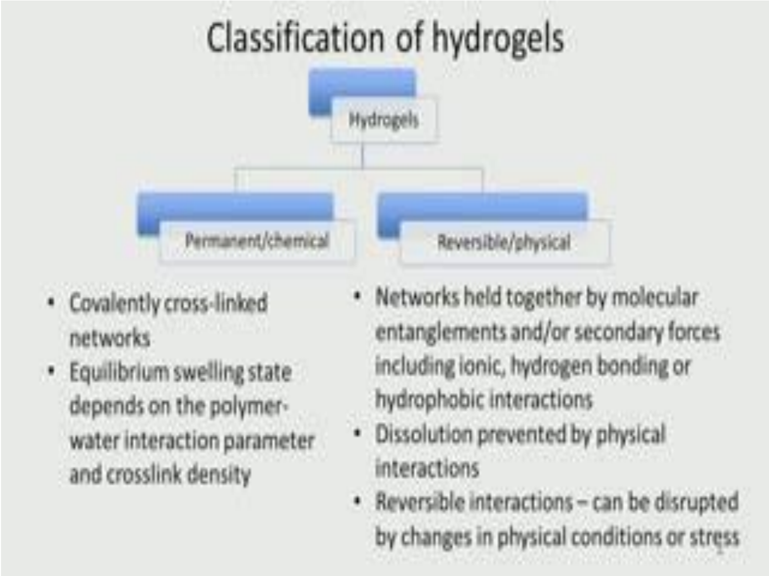

So, 2 types of hydrogels they are classified into 2 different categories permanent chemical hydrogel reversible physical hydrogel. So, the physical interactions create this type of hydrogel so; obviously, when the water is removed they come back to its original and dry state permanent that is a chemical reaction takes place so; obviously, we cannot reverse this. So, there is a covalently cross linked networks equilibrium swelling state depends on the polymer water interaction parameter and crosslink density.

So, the amount of water that can be taken up by these hydrogels depend upon what is the crosslink density now if you look at the reversible hydrogel or the physical hydrogel the networks held together by molecular entanglement secondary forces such as ionic hydrogen bonding or hydrophobic interactions we call them as non bonded interactions. So, dissolution is prevented by these forces. So, these are reversible can be disrupted by changes in physical conditions of stress. So, we can bring it back to its old form and so we this and have some advantages over these many situations.

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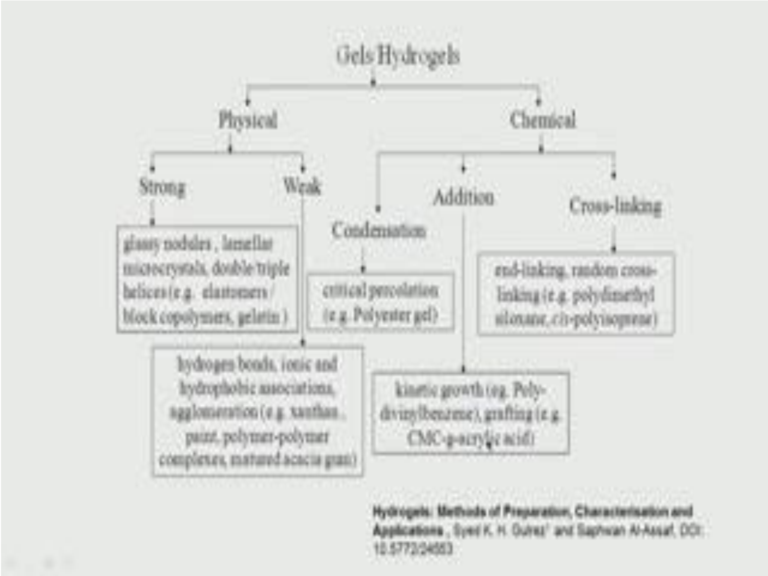

You look at each one of them physical chemical I said. So, the physical we can have strong and big types of be bonds we could be hydrogen bonds ionic bond hydrophobic bond agglomeration bonds xanthan paint polymer polymer complexes matured acacia gum is all weak strong could be glassy nodules lamellar microcrystals double triple helices elastomers block copolymers gelatin these are called strong.

Now, chemical as I mentioned before and there is a reaction chemical reaction bonds forming. So, there could be a condensation type of reaction addition type of reaction cross linking type of reaction condensation like polyester gel addition could be kinetic growth polydivinyl benzene grafting c m c that is carboxymethyl cellulose acrylic acid cross linking that is end linking random cross linking poly dimethyl, siloxane, cis polyisoprene. So, 2 types of gel the physical and chemical physical you can have weak physical forces strong physical forces the chemical could be condensation reaction addition reaction cross linking reaction.

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So, this nice table was taken up from this particular reference hydrogels methods of preparation characterization application with this d o I now the source of hydrogel it could be natural it could be synthetic or a hybrid that is combination of both sorry it could be nonionic hydrogels it could be ionic hydrogels ampholytic; that means, combination of both.

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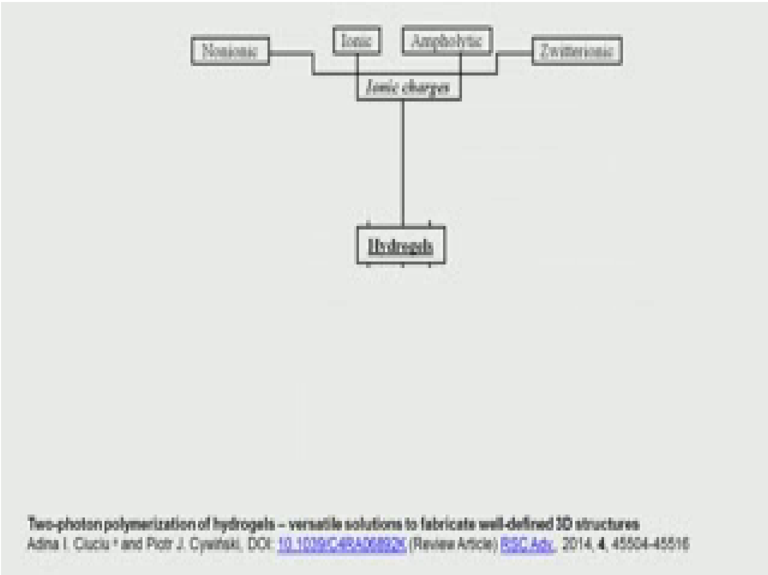

Zwitterionic, zwitter, ionic hydrogels depending upon the charge depending upon how physical or chemical depending upon the charge cross linking we can have a physical cross linking we can have a chemical cross linking.

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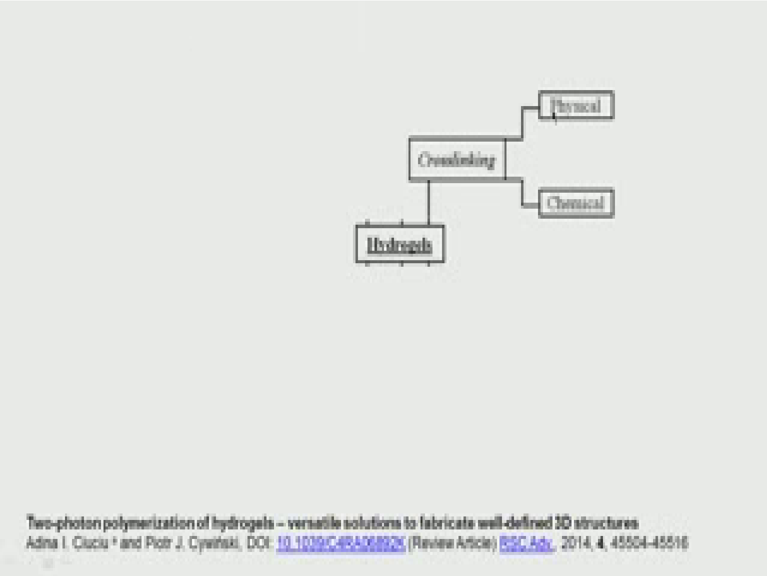

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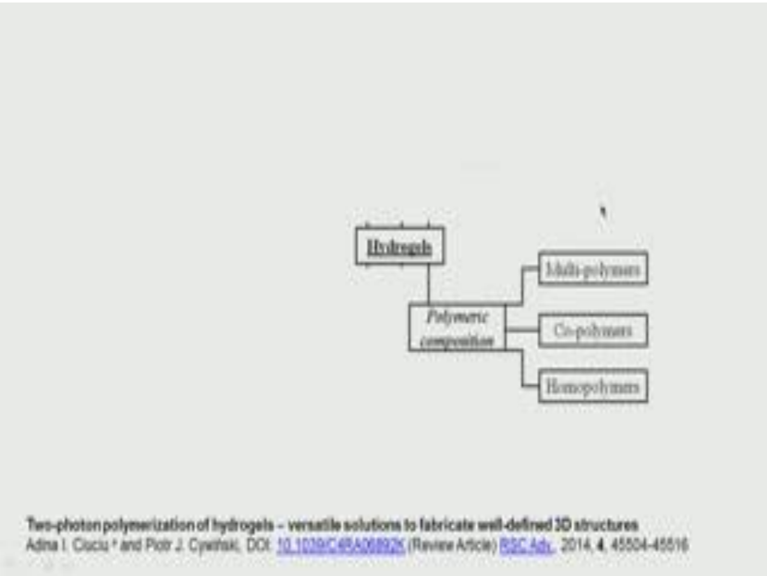

Polymeric composition we can have homo polymers; that means, only one monomer is used copolymers; that mean we can have a more than one monomers use multi polymers.

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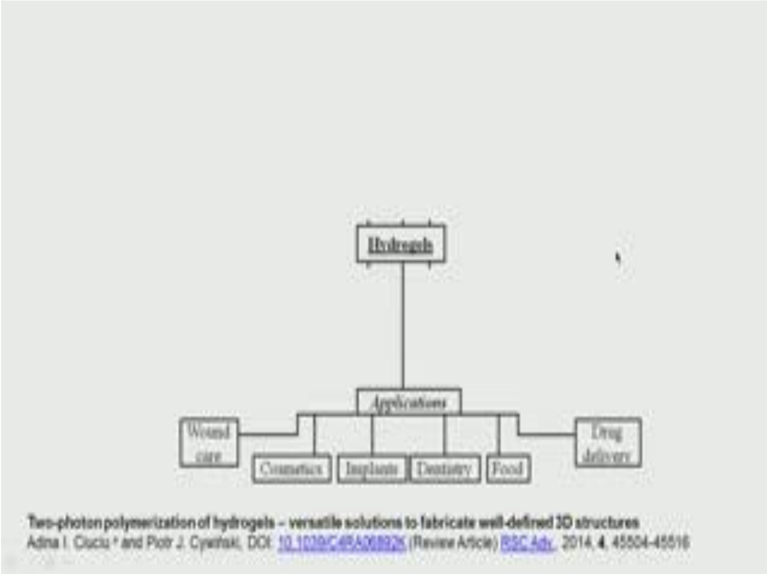

We can have many many polymers into this applications wound dressing cosmetic implants dentistry food drug delivery all these are the areas of course, as I mentioned before they have a poor mechanical properties; obviously, they can be used alone in some of these, but have to be used for example, in conjunction with the stronger and synthetic material polymer for implant applications. So, this nice looking table was taken from this particular references called 2 photon polymerization of hydrogels versatile solutions to fabricate will defined 3D structures with this DO, I can review article.

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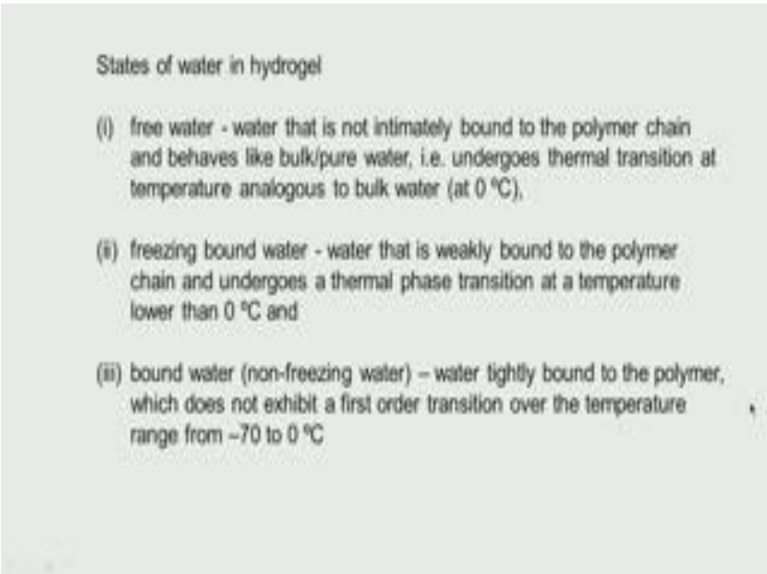

And so there is water inside this hydrogel. So, there are 3 types of water present in hydrogel very interesting, the free water it is water that is not intimately bound to the polymer this is almost like the bulk water present outside the hydrogel or pure water. So, it behaves like the normal water that is present outside. So, it undergoes thermal transition at temperature analogous to bulk water select 0 degrees then we have freezing bound water that is water that is weakly bound to the polymer chain and undergoes a thermal phase transition at a temperature lower than this free water it is called a freezing bound water.

Then we have non freezing bound water that is completely bound and it is not like bulk water or it will not freeze is like not and weakly bound water this is very tightly bound to the polymer which does not exhibit the first order transition or the temperature range from this to this these non freezing water; that means, that water will not freeze and when you bring it down to zero degree centigrade and. So, we have 3 types of water free water which is almost like the water that is present in the bulk outside then we have the freezing bound water and the water that is weakly bound to the polymer. So, it will not behave like a pure water or the bulk water, but it will have some temperature transition which will be lower than this and then we have the bound non freezing water which is very strongly bound it will not undergo any phase transition and add these condition like a water to ice and so on actually.

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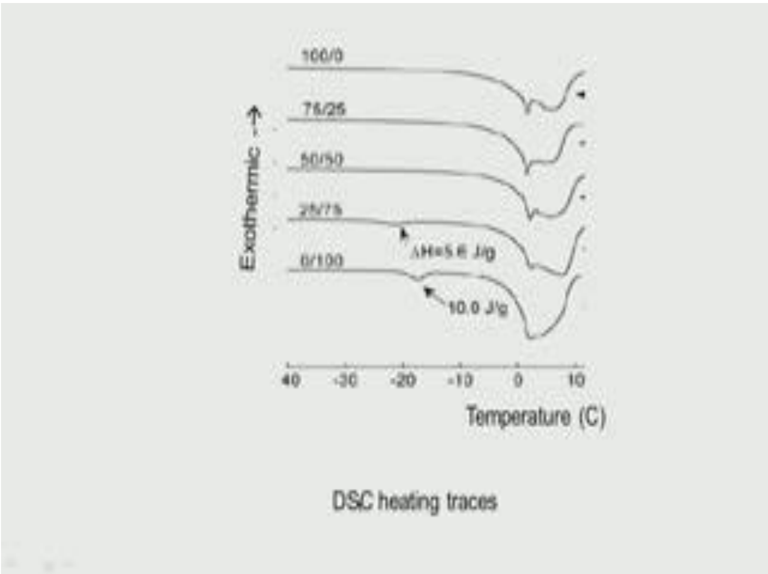

So 3 types of water and these 3 types of water could be nicely observed using a differential scanning calorimeter, so, if you look at this for example, the function of temperature exothermic. So, we can have this as the free water this as the freezing bound water and this could be de and non freezing bound water third time this is the free water which is the like a bulk water this the freezing bound water this is the non freezing bound water. So, we will continue on this hydrogel in the next class also.

Thank you very much for your time.