Medical Biomaterials
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Lecture – 08
Biodegradation and Bioresorption

Hello everyone. Welcome to the course on a Medical Biomaterial. Now we are going to talk about properties just as a Biodegradation or Bioresorption. We are going to see; what is the difference between these biodegradations and bioresorption in the human body and how it is going to help. Because in many systems we do not want the material to stay inside the body we want the material to leave body after it has done it is function. So, the properties of a biodegradation or bioresorption are incorporated into the material.

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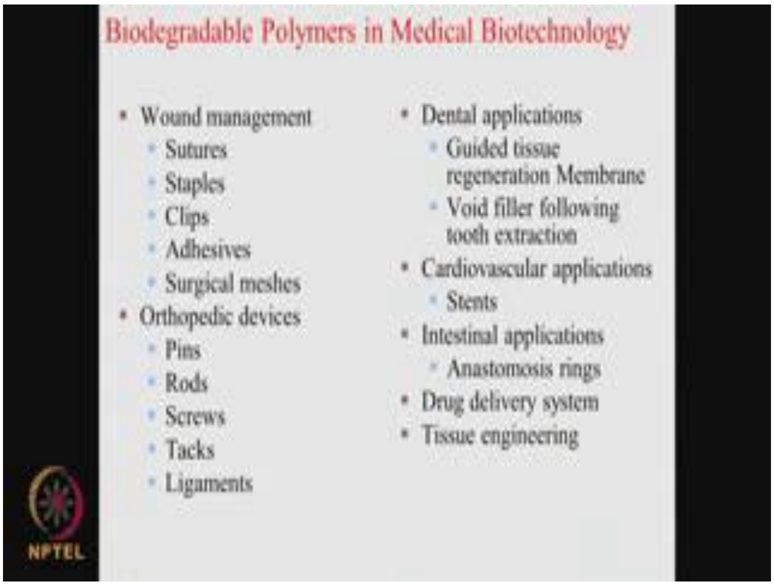

Biodegradable Polymers in Medical Biotechnology

- Wound management
  - Sutures
  - Staples
  - Clips
  - Adhesives
  - Surgical meshes
- Orthopedic devices
  - Pins
  - Rods
  - Screws
  - Tacks
  - Ligaments
- Dental applications
  - Guided tissue regeneration Membrane
  - Void filler following tooth extraction
- Cardiovascular applications
  - Stents
- Intestinal applications
  - Anastomosis rings
- Drug delivery system
- Tissue engineering

So, when do you need a biodegradable polymer in chemical biotechnology? For example, if you look wound management area sutures we want that sutures to completely disappear after the wound has yield or staples clips adhesives surgical meshes. All these once it has den it is job for example, the wound has yield there is no infection and tissue has grown we want this material to completely degraded. We do want a material which does not degrade and remain in the body forever. And ever orthopedic devices, they use quite a lot pins in orthopedic implants to keep the stainless steel or a titanium in it is position. We want the pins to degrade once the implant got in line with the bone, rods lots of rods are used screws are used. So, you want all these to degrade after it is done it is job tax ligaments in orthopedic area.

If you look at dental area guided tissue regeneration membrane void filling, so after a tooth extraction we are filling the void and we want slowly the material to grow on it is own. So, we want degradation cardiovascular application stents currently metal stents and drug eluting stents are used. And quite used ideally we would like the stent to degrade after a few months. So, that there is no titanium or stainless steel in inside. If the stents d not degrade and we have placed a stent the doctor is not able to place another stent inside the body that is one problem another problem could be sometimes starts migrating; that means, they move from one place to another and they may block some artery. So, ideally we want the stent to completely degrade after a few months and so on.

Then intestinal applications anastomosis rings drug delivery system, you are delivering drug to a targeted side and then once the drug has delivered, we want the polymeric material to completely degrade and disappear. Tissue engineering applications use scaffolds to tissue to grow. What is the tissue has grown and grown and then it has occupied the void then the scaffold material should completely disappear we do not know want the scaffold to remain? So, in all these areas we would like the material to completely degrade and come out of the system or get completely resorbed.

Now, what is the difference between biodegradation and bioresorption? There are lots differences are there biodegradation.

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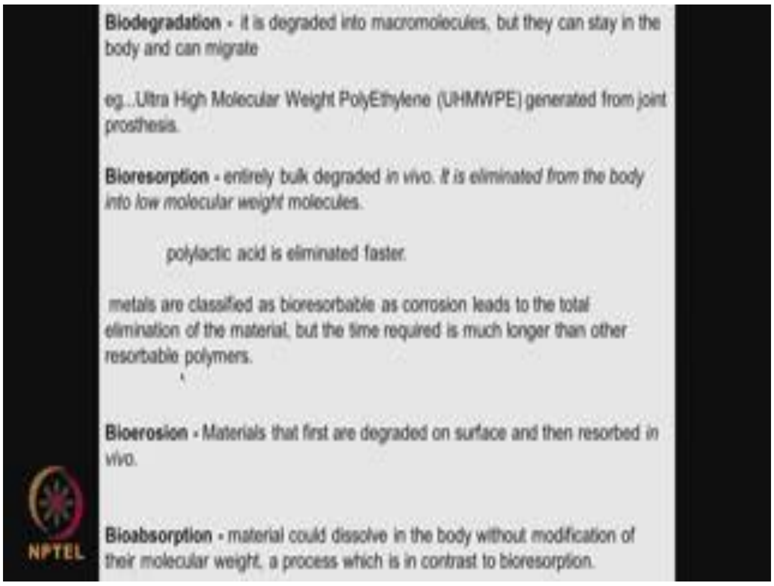

Biodegradation - it is degraded into macromolecules, but they can stay in the body and can migrate

eg...Ultra High Molecular Weight PolyEthylene (UHMWPE) generated from joint prosthesis.

Bioresorption - entirely bulk degraded *in vivo. It is eliminated from the body into low molecular weight* molecules.

polylactic acid is eliminated faster.

metals are classified as bioresorbable as corrosion leads to the total elimination of the material, but the time required is much longer than other resorbable polymers.

Bioerosion - Materials that first are degraded on surface and then resorbed *in vivo.*

Bioabsorption - material could dissolve in the body without modification of their molecular weight, a process which is in contrast to bioresorption.

So, if you have a polymer a large molecular weight polymer when it degrades it becomes macromolecule. So, a 60 kilo dalton says ultrahigh molecular weight polyethylene. For example, may degrade into smaller molecular weight may be about 10000 or 5000 or 15000 they are called macro molecules, but they may stay inside the body and migrate. So, it is degraded into smaller molecules, but it might not be completely eliminated they may be in the circulation, but still it is biodegradation. So, from may be about 60000 like I said it may come down to 10000 or 5000 of molecules of macromolecules of front molecular weights. For example, ultrahigh molecular weight polyethylene this is used quite a lot in joint prosthesis. Suppose there is joint replacement they use metal and metal interaction is not very good, because it rubs and it leads to release of fine metals. So, the use ultrahigh molecular weight polyethylene which acts sort of a lubricant; so even that gets degraded weights that is called biodegradation.

What is this bioresorption? So, the entire material gets degraded in vivo and it is eliminated from the body into low molecular weight molecules. So, if there is a 20000 molecular weight material it gets resorbed in very small molecular weight material, and that is gets eliminated completely. For example, if you take polylactic acid. Polylactic acid is a FDA approved polymer and is used in quite a lot of implant especially in drug delivery and so on. So, it gets completely bioresorbed and there is nothing left inside it goes into live and lactic acid and that gets eliminated that is called bioresorption.

So, sometimes metals are also classified as bioresorbable. So, if for exam rubbing of metal or corrosion leads to the elimination of the material. So, it may slowly come out of the body, but this could be a much longer when compared to polylactic acid bioresorption which is very fast. So, although metal we cannot call it bioresorbable, but it is still called because corrosion may lead to total elimination of the material or even rubbing of material metals can lead to final powder which may be get eliminated, but it could be much longer duration.

Then we have bioerosion. Materials are first degraded on the surface and then it is resorbed in vivo that is called bioerosion, and then bioabsorption. So, materials could dissolve in the body without modification of their molecular weight unlike the bioresorption. Please understand in bioresorption the materials degraded into smaller weight and then gets eliminated whereas, in bioabsorption the material may get the resorbed without actually degrading into smaller molecular weight material. So, these are the different types of changes that could happen materials that are placed in the body and as I said it is very important in many situations to have a biodegraded or bioresorbed polymeric material as a implant.

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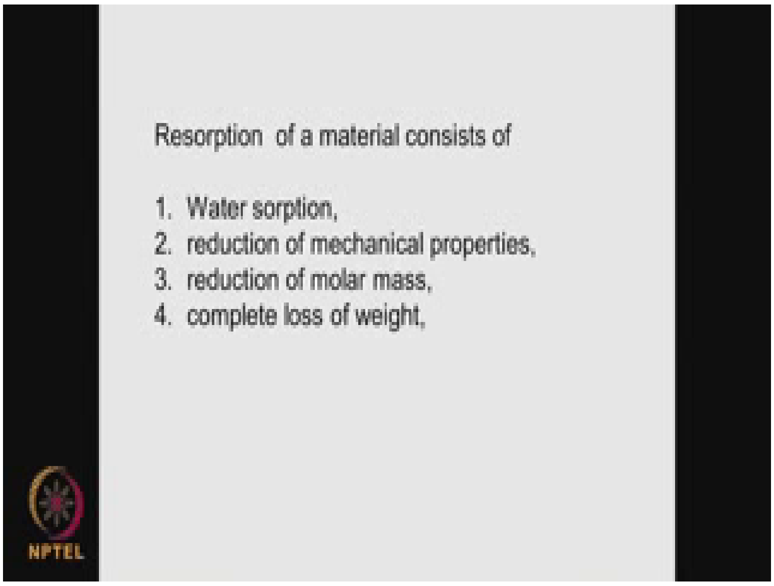

Resorption of a material consists of

1. Water sorption,
2. reduction of mechanical properties,
3. reduction of molar mass,
4. complete loss of weight,

So, the resorption of a material consists of several factors, how much water gets absorbed because water may get involved in the hydrolysis reaction. So, after it starts getting slowly degraded, there could be a reduction in mechanical properties; that means, the strength that means, the tensile strength may change modulus may change reduction of molecular mass; that means, the material may be lost in the weight, complete loss of weight. So, the material could be completely losing it is weight then it may be becoming smaller and smaller and then finally disappearing. So, that is what it means resorption.

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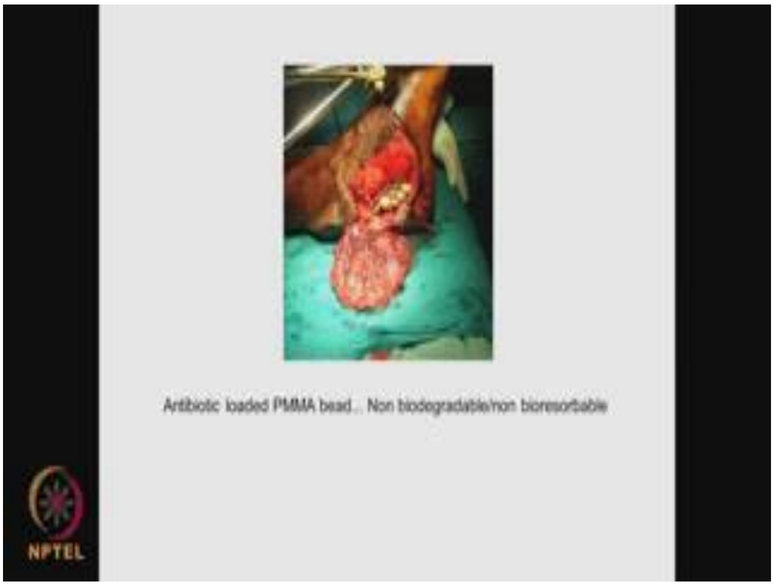

Antibiotic loaded PMMA bead... Non biodegradable/non bioresorbable

For example, I just wanted to show you a few pictures look at this. This is surgery or orthopedic surgery what they do is because there could be lot of infection, that could be happening after placing a metal orthopedic implant. So, what they do is they use a poly methyl methacrylate beads which are impregnate with an antibiotic like a meropenem for example, so they keep these beads inside and close it after doing the implant. So, the polymer slowly releases the drug the meropenem, thereby it prevents the infection and bio filling formation.

But the problem is their pmma is it does not get degraded. So, it has to be removed later on. So, they will do a small surgery to remove that. So, this is bit a painful because it is non-biodegradable or bio non bioresorbable. So, ideally one would like to have a nice polymer, which is able to take in lot of drug encapsulate lot of drug. It releases the drug say for example, within 6 to 8 weeks and then it also starts getting resorbed or biodegraded. So, the doctor does not have to perform a second surgery. So, ideally this is a courtesy this picture is a courtesy from CMCE Vellur in Tamilnadu.

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Poly urethane ureteral stent

Now, look at this this is a poly urethane ureteral stent. This is a called a ureteral stent. It is placed inside the ureter region which connects about the kidney and the ureter. So, the urine flows nicely down. Sometimes this ureter can get blocked because of infection or if there is a stone in the urine sonication is performed to break the stones. So, you need a nice opening so that the small broken powder stones can flow down. So, they place this particular material called a ureteral stent. It is quite flexible it is made up of poly urethane. So, after about 5 to 6 week the doctor has to perform another surgery to remove this.

Ideally if we have a biodegradable material, so the doctor places the material stent inside it performs it is duty and once it is performed it is duty it should degrade or bioresorbed completely. So, this is another example of where I would like to have a biodegradable material like an ureteral stent this picture. This x-ray is a courtesy from doctor Shraf of a Shri Ramachandra Medical College in Chennai.

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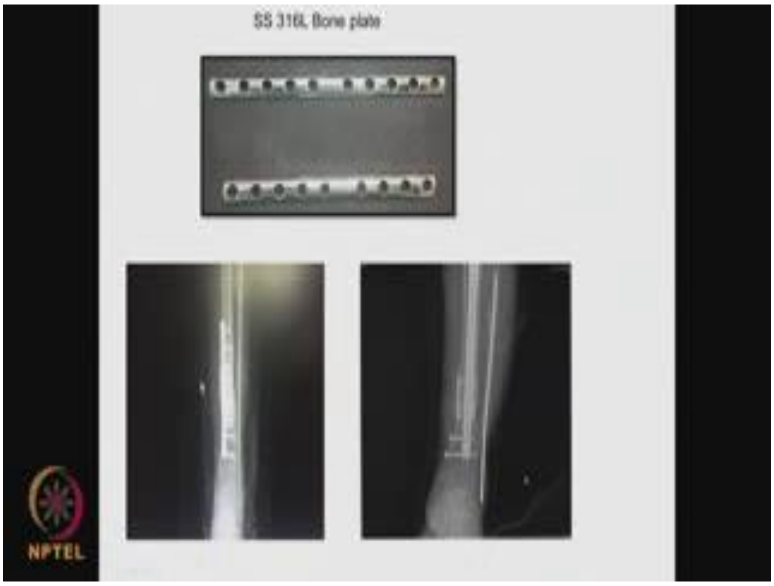

SS 316L Bone plate

Look at this these are stainless steel bone plates. So, after an orthopedic surgery these bone plates are placed inside, to connect the bones here using a screw as you can see and pins here you see. So, it is placed like this. So, the bone starts healing. The bones start growing. So, ideally after a few months if the bone plate completely resorbed, then it will be nice, they it the person will not have a foreign material plates inside, but as you know currently stainless steel and titanium plates are used which are not biodegradable.

So, they remain inside the body forever and ever. This is another place where we would like to have biodegradable bone plate, but it could be after 3 to 6 months, whereas if you look at the ureteral stent you would like to have it about 6 to 8 weeks, whereas if you look at the pmma loaded drug loaded pmma in this area. I would like the material to degrade in about 15 days.

So, you can see different types of time duration are required here you would like the material to degrade in about 15 days. Here we would like to de material to degrade after about 6 to 8 weeks and here you would like to have the material degrading after about around 6 months.

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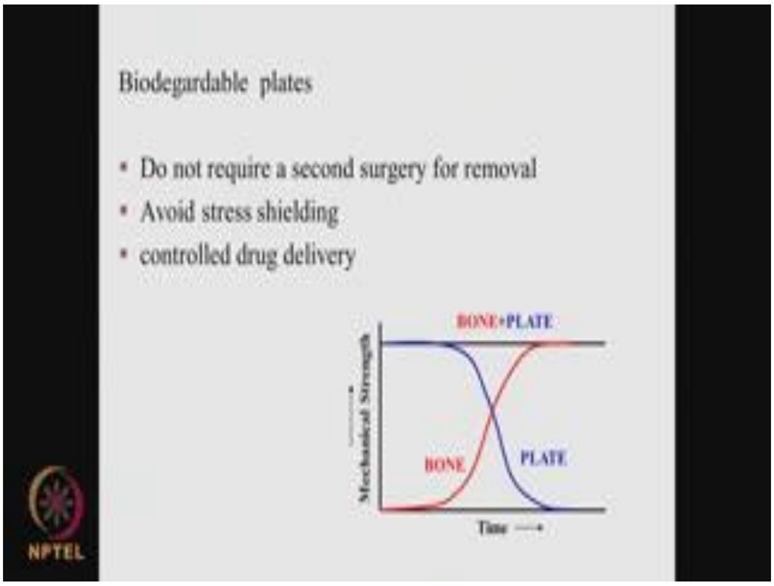

Biodegardable plates

- Do not require a second surgery for removal
- Avoid stress shielding
- controlled drug delivery

So, if you have a biodegradable bone plate we will not require another surgery for removing the bone plate generally you cannot remove the bone plate, because the bone nicely grows and muscles grows. So, absolutely it not possible we can also avoid stress shielding if the stainless steel material is not there because there will be one material that is the bone, instead of having bone made up of hydroxyapatite and stainless steel.

We can also have a control drug delivery. So, if we have a polymeric material which may degrade over a period of time which can be coated drug gets released slowly. So, it prevents the biofilm formation and infection. So, the plate takes care of the mechanical strength initially with time it degrades. So, the plate is completely useless. In the meantime, the bone starts growing. So, the bones take care of the mechanical strength requirements for the rest of the life of the patient.

So, ideally we would like to have the plate slowly degrading and later on the bone takes care of the weight and other mechanical requirements. So, these are few situations I showed you examples, where we would like to have this type of biodegradable bioresorbable material. These are courtesy the photograph which is showed are courtesy from various places like ACMC Vellur and Shri Ramachandra Medical College in Chennai.

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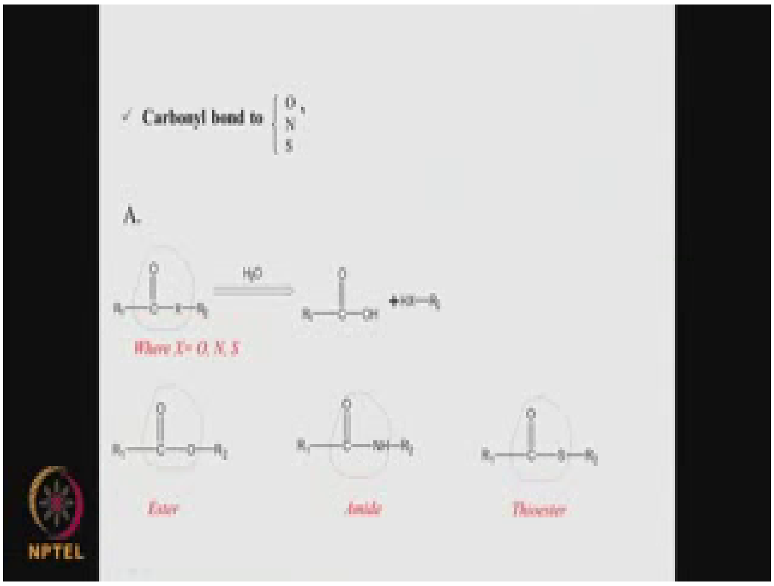

✓ Carbonyl bond to O, N, S

A.

Where X= O, N, S

Ester

Amide

Thioester

So, what type of bones in the polymer could degrade? Oxygen, nitrogen, Sulphur; for example, look at this is an ester bond you will say ester bond. So, or this could be in amide bond or this could be thioester bond. So, we have C double bond O X could be oxygen C double O X could be nitrogen C double O X could be Sulphur. So, these bonds are easily hydrolysable; that means, water can react with that may be little bit of acid or we have some enzymes. So, it can generate acid like this. So, if you have polymers which has backbones like this or linkers which has like this type of set up, they can get hydrolyzed and they can degrade slowly over a period of time. So, ester bond amide bond thioester bonds can degrade, if the polymer in the backbone has these types of bonds.

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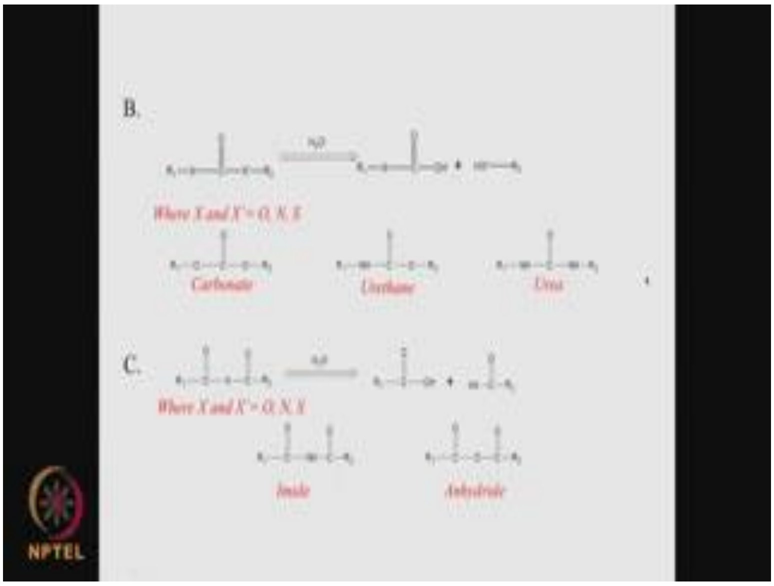

Or we can have these type of situations, carbonate these are slowly degradable unlike the previous case where we have these are faster degradable where as these will degrade much slowly. So, we can have O and O this is called carbonate. We have C double O O and O or we can have urethane C double O O N H or we can have urea N H N H and C double bond O. So, these are also hydrogen hydrolysable; that means, they can react with water, but they are slowly reacting like the previous case. Or we can have other situations like imide anhydride. Again anhydride imide they can be degrade much faster. So, we have C double O connected by O another C double bond O or C double O connected by nitrogen and other C double O or C C double O connected by S another C C double O. So, they can also hydrolyzed from acid and an ester like this. So, imide is an example anhydride is an example

So, here we can have a O O on both sides or nitrogen on both sides S on both sides with the key tone C double O. So, this can give you acid, and another hydrocarbon here whereas, these one we have C double O and both sides connected by an oxygen or a nitrogen or a Sulphur. So, these are various types of bonds systems which are biodegradable. So, if you are designing polymers with these type of backbones then they are hydrolysable; that means, they can react with water to slowly. And as I mentioned some of these bonds are degradedable faster rates, some of these bonds are degradable at slow slower rate. So, if I am thinking about 2 weeks 3 weeks degradation or if I am thinking about 6 months 9 months degradation I can design polymers a with these different backbones.

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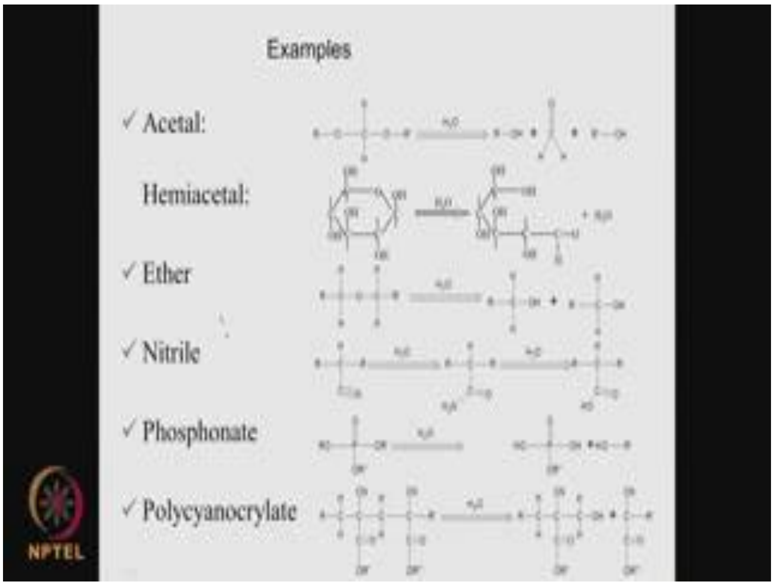

Examples

- ✓ Acetal:
- Hemiacetal:
- ✓ Ether
- ✓ Nitrile
- ✓ Phosphonate
- ✓ Polycyanocrylate

So, we have acetyl some open some examples. Acetyls oxygen on both side like this, they can degrade hemiacetal you have the ring system which are degradable ethers like I showed you here right, ethers like I showed you here oxygen these, are ethers which can degrade nitriles. So, the C triple bond N they can degrade. Phosphonate they can degrade polycyanocrylate. So, different types of bond systems that are degradable.

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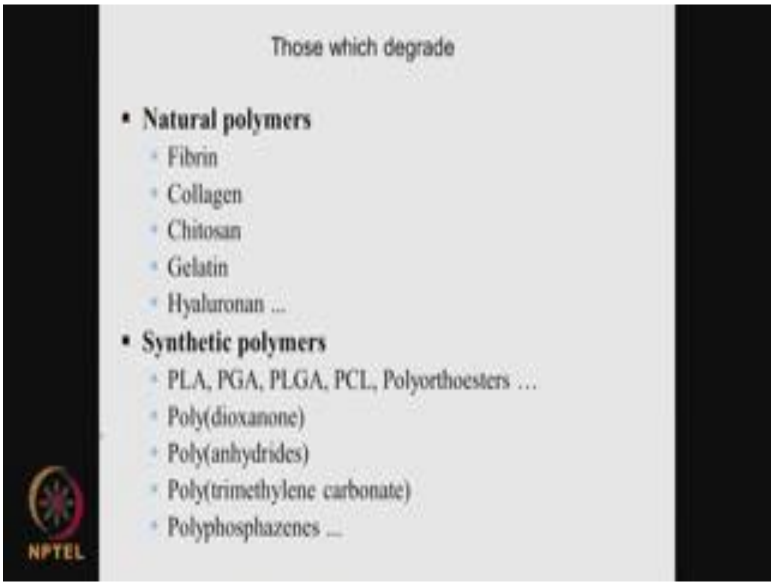

Those which degrade

- **Natural polymers**
  - Fibrin
  - Collagen
  - Chitosan
  - Gelatin
  - Hyaluronan ...
- **Synthetic polymers**
  - PLA, PGA, PLGA, PCL, Polyorthoesters ...
  - Poly(dioxanone)
  - Poly(anhydrides)
  - Poly(trimethylene carbonate)
  - Polyphosphazenes ...

So, polymers: natural polymers or synthetic polymers. Natural polymers like fibrin collagen chitosan gelatin hyaluronic acid cyclic glucones alpha cyclic glucones and beta cylclic glucones and so on. If you got to synthetic polymers, poly lactic poly PGA that is glycolic poly glycolic acid or combination of lactic and glycolic polycaprolactone polyorthoesters poly dioxanone poly anhydrides poly trimethylene carbonates polyphosphazenes. So, lot of synthetic polymer that can also degrade lot of natural polymers, lot of synthetic polymers that can be degrading. So, we can consider designing may be drug delivery systems or scaffolds or bone plates using these polymers. And of course, we need to match the other mechanical and physical chemical requirements and initially for the material to hold.

So, you can also have enzymatic degradation apart from the normal hydrolysis type of degradation.

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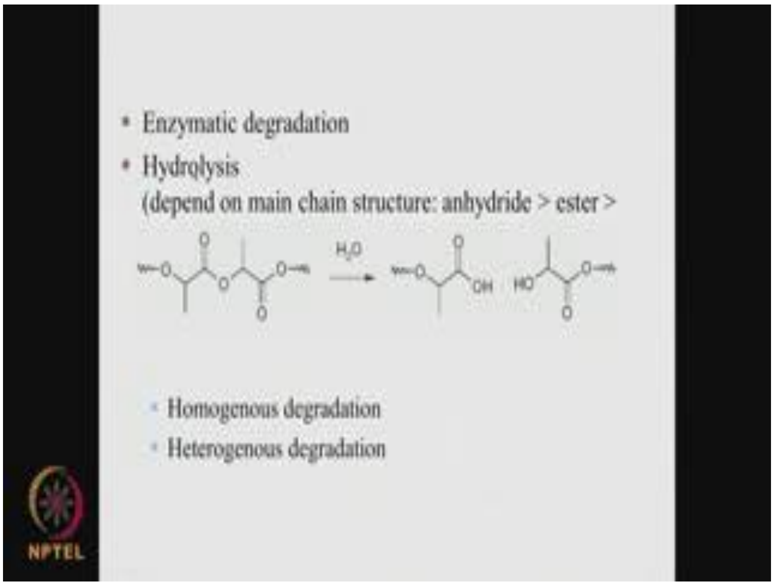

- Enzymatic degradation
- Hydrolysis
  (depend on main chain structure: anhydride > ester >
  - Homogenous degradation
  - Heterogenous degradation

So, hydrolysis like a it is anhydride or very easily degradable esters come next and so on. Of course, enzymatic you can have live phases we can esterases all these amides present in the in vivo system. They can also aid in the degradation. Some of the degradation is called homogenous degradation we can heterogeneous degradation. Homogenous means uniformly material the backbone gets degraded heterogeneous means indicates degradaded only at the specific location, where we have the sides favorable bonds for it to degrade and if the bond is not favorable for degradation then it will not degrade.

Bioresoption we can initiate by first solubilization like dextran polyvinyl alcohol polyethylene oxide.

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bioresorption can be initiated by

1. Solubilization (e.g., dextran, polyvinyl alcohol, and polyethylene oxide);
2. Ionization followed by solubilization (e.g., polyacrylic acid and polyvinyl acetate);
3. Enzymatically catalyzed hydrolysis (e.g., polysaccharides and polyamides);
4. Simple hydrolysis (e.g., aliphatic polyesters).

So, the it the polymer solubilizes and then later you can have a ionization, poly acrylic acid poly vinyl acetate. For example, some of the polymer poly lactic acid you can have ionization. You can have enzymatic reaction. Polysaccharides polyamides you have amides or you have esters or it could be simple hydrolysis like aliphatic polyesters and get simple hydrolyzed and completely get absorbed. So, these are various situations we can have solubilization which can lead to bioresorption solubilization followed by ionization, we can have enzymatic reaction after hydrolysis or simple hydrolysis without enzymes all these can lead to bioresorption.

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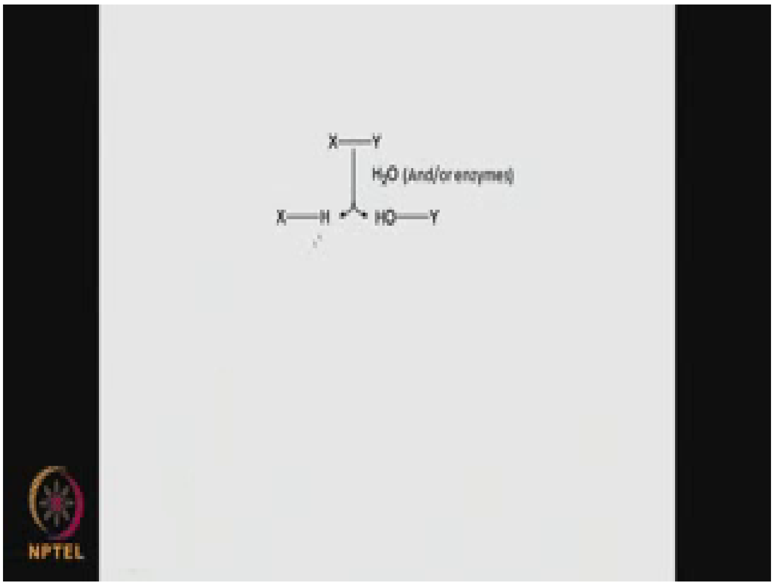

So we have a polymer and this bond is there. So, it can get hydrolyzed just plain hydrolysis or we can enzyme that is catalyzing the hydrolysis of this particular polymeric material.

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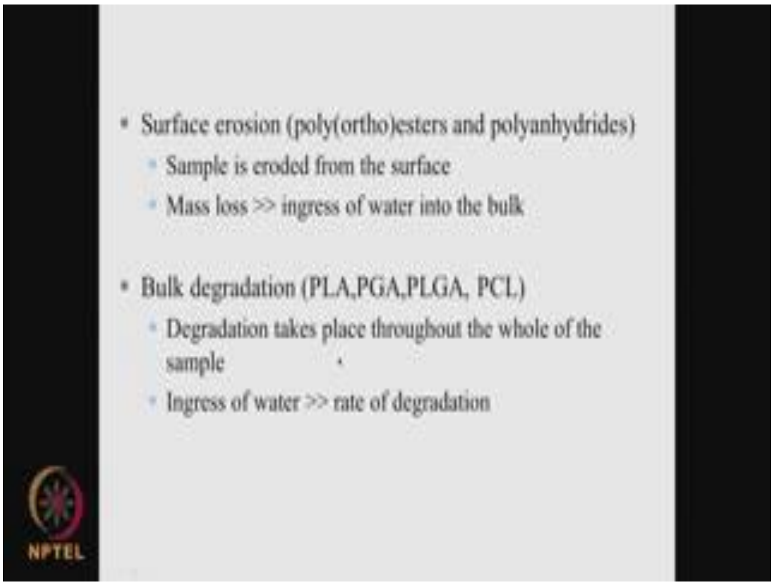

- Surface erosion (poly(ortho)esters and polyanhydrides)
  - Sample is eroded from the surface
  - Mass loss >> ingress of water into the bulk
- Bulk degradation (PLA,PGA,PLGA, PCL)
  - Degradation takes place throughout the whole of the sample
  - Ingress of water >> rate of degradation

We can have 2 situations surface erosion; that means, the surface slowly gets eroded or degraded or the bulk the entire polymer gets degraded and the polymer sort of dissolves or it is not dissolved. It is completely loses it is molecular mass. So, 2 situations surface erosion takes place; that means, the sample is eroded from the surface then mass loss is greater than ingress of water into the bulk, whereas if the water ingress is much more and degradation takes place and that is called bulk degradation. So, example of surface erosion poly ortho esters polyanhydrides; that means, if mass gets lost very fast and compared to water ingress into the polymer, bulk degradation like PLA, PGA, PLGA, PCL. So, the ingress of water is much faster than the rate of degradation. So, the water goes inside and the material starts degrading. That is called the bulk degradation. So, we have surface degradation.

So, in bulk degradation the degradation takes place throughout the material whereas, surface degradation mit degradation takes place at the surface because the water ingress is much lower than the mass loss, whereas in bulk ingress of water is much faster than rate of degradation.

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So, if we have a surface erosion situation may be like this, material may be becoming thinner. It is time whereas, in bulk erosion material may be getting lost, inside it may be start forming pores inside, material may be crumbling material may be breaking into pieces. So, all these can happen in bulk erosion. Whereas, surface erosion material will be uniformly getting thinner bulk erosion material may break into pieces’ mil material may form pores inside material may break at various places getting chipped because of bulk erosion. So, situations depending upon the type of situations even depending upon the thickness of the material it could have surface erosion or bulk erosion.

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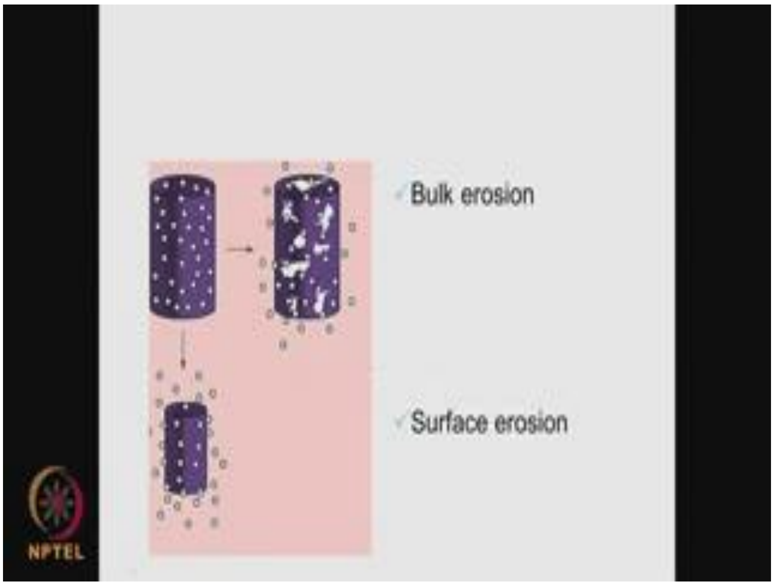

- Bulk erosion
- Surface erosion

So, pictorially we can show it like that surface only and the surface material gets degraded. So, it is very nice to have if you are talking about slow drug release whereas, bulk erosion as the water starts growing in an suddenly there could be degradation taking place at various places inside the material also.

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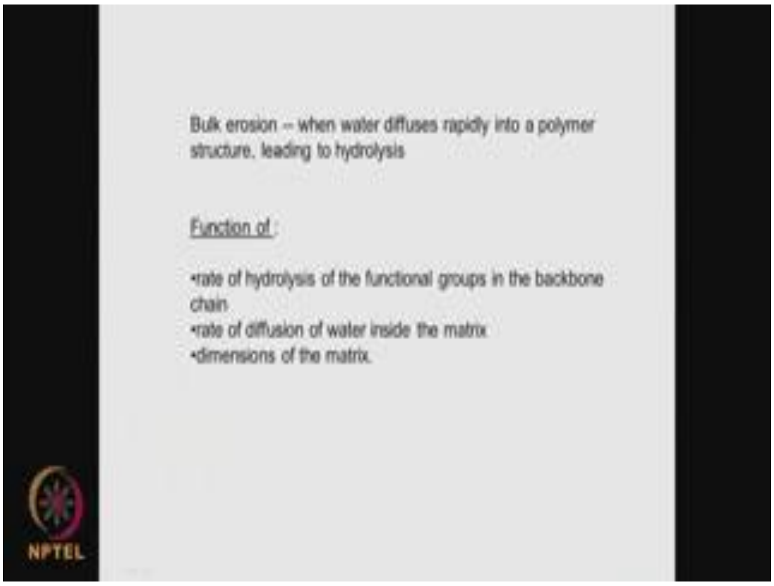

Bulk erosion – when water diffuses rapidly into a polymer structure, leading to hydrolysis

Function of :

- rate of hydrolysis of the functional groups in the backbone chain
- rate of diffusion of water inside the matrix
- dimensions of the matrix.

So, bulk erosion when water diffuses rapidly into polymer leading to hydrolysis. So, this is the function of rate of hydrolysis of the functional groups. Rate of diffusion inside the matrix dimensions of the matrix all these play very important role in deciding the material is bulk or surface degradation

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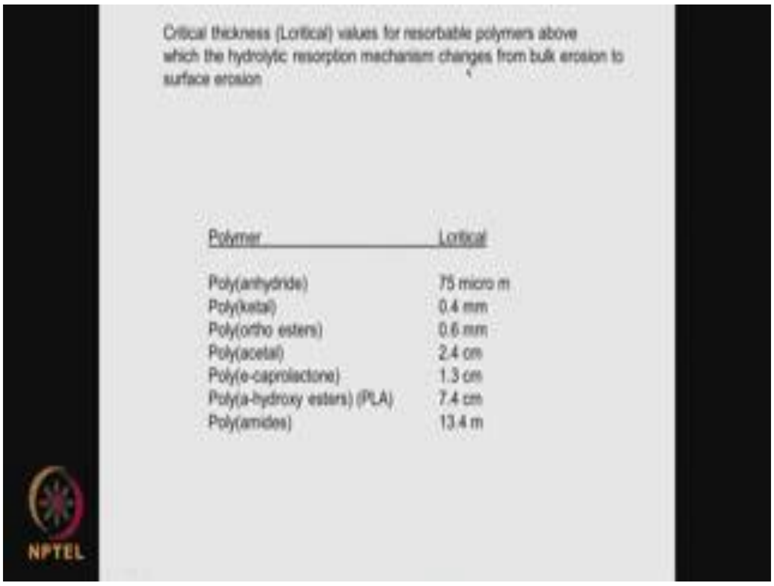

Critical thickness (Lcritical) values for resorbable polymers above which the hydrolytic resorption mechanism changes from bulk erosion to surface erosion

Polymer	Lcritical
Poly(anhydride)	75 micro m
Poly(ketal)	0.4 mm
Poly(ortho esters)	0.6 mm
Poly(acetal)	2.4 cm
Poly(e-caprolactone)	1.3 cm
Poly(a-hydroxy esters) (PLA)	7.4 cm
Poly(amides)	13.4 m

So, what is the critical thickness for resorbable polymers above which it is bulk or surface? So, if for these polymers if thickness is less than this, it will be bulk degradation. So, what it means is water has to ingress with the water can ingress inside then you can have very good bulk degradation. If the water cannot ingress into it then degradation is faster, then it will be a surface degradation.

So, if the material is very thin then obviously you are going to have a surface degradation. If the merity sorry; obviously, you are going to have bulk degradation if the material is very thick water is not able to ingress inside then you are going to have a surface degradation. And this dimension tells you whether it is going to be surface degradation or bulk degradation.

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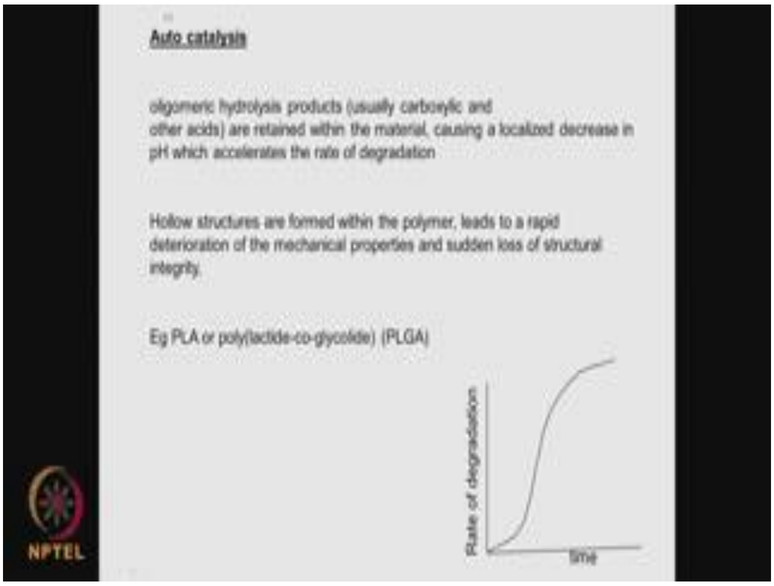

Auto catalysis

oligomeric hydrolysis products (usually carboxylic and
other acids) are retained within the material, causing a localized decrease in
pH which accelerates the rate of degradation

Hollow structures are formed within the polymer, leads to a rapid
deterioration of the mechanical properties and sudden loss of structural
integrity.

Eg PLA or poly(lactide-co-glycolide) (PLGA)

We can also have autocatalysis. Because for example, if you take poly lactic acid. When it degrades it releases lactic acid, which is acidic and which may enhance the degradation further and further. For example, if you look at this particular picture the rate of degradation was time initially the degradation is slow. So, may be acids are produced or may be some functional groups are produced in degradation, which enhances the degradation very fast. So, the degradation can sudden shoot up like this this is called autocatalysis.

So, oligomeric hydrolysis products like carboxylic acids or other acids which may aid the degradation much faster. And these material is retained inside they are not thrown out. So, it is get retained inside. So, it crosses localized decrease in pH; that means, material becomes acidic pH at different places which can accelerate the rate of degradation. So, we may form hollow structures within the polymer and because of these acids then this leads to rapid deterioration of the mechanical properties and sudden loss of structural integrity like PLGA or PLA autocatalysis takes place because the acids that are produced in various places can enhance the degradation further and further. So, there could be these are sides where degradation are going to be much faster called autocatalysis based degradation

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Type Ia = cleaving the cross-links (results in fragments which have to be further degraded)... covalently or ionically cross-linked monomers. After digestion of unstable linkages, water soluble fragments are released. Their molecular weight depends on the density of cleavable bonds. Cross-linked collagen or gelatin

Type 1b = digestion of the polymer backbone (have relatively low molecular Weight)... Polymers with unstable linkages are water insoluble. After either chemical or enzymatic cleavage, the resulting fragments are water soluble and have a lower molecular weight.

Type II initially water insoluble. Hydrolysis, ionization or protonation of a pendant group is necessary before these polymers become water soluble

Type III additional cleavage in the backbone

Type Ia with type III

initial cleavage of cross-links and subsequent backbone digestion.
eg. aliphatic poly(esters), poly(amides), poly(cyanoacrylates), poly(anhydrides), poly(acetals) and poly(orthoesters)

Now, we can have different types of degradation, if you look at type 1a. So, we have polymers they are connected by certain cross linkers. So, the polymer is stable it is not soluble in water. The cross linkers could be covalently ironically cross linked monomers. So, what happens after digestion of these linkages, suppose these linkages degrade then the fragments which are formed could be water soluble the. So, if I have say for example, collagen or gelatins which are cross linked collagen and gelatin may be water soluble, but the linkages prevent them from degrading or water solubilizing.

So, once the linkages disappear then the remaining portions could be soluble. So, that it is called a type one degradation if you have 1b the digestion of the polymer backbone some portions could be degrading; that means, they have a relatively low molecular weight because of either chemical or enzymatic cleavage then the resulting fragments are water soluble and have a lower molecular weight. So, some portions of the back bone could be degrading because of presence of low molecular weight. Once they disappear because of degradation through enzymatic or chemical the resulting fragments are water soluble because they have lower molecular weight that is type 1b.

Type 2 initially water insoluble. The may has some pendant group which may get ionized or hydrolysis degrader. Once these pendent group degrade because of hydrolysis then the remaining polymer could be water soluble that is type 2, type 3 we have addition cleavage in the backbone. So, the backbone some portions can get degraded. So, you can have combinations of type 1a with type 3. So, initial cleavage of the cross linkers and then remaining backbone could be degrading later actually. For example; aliphatic poly esters poly amides poly cyanoacrylates poly anhydrides poly acetyls poly orthoesters, so they have cross linkers which may initially get cleaved. Then the remaining polymer could be degrading in that. So, you can have combinations.

So, these are various situations by which we can create biodegradable polymers which may degrade with different mechanisms at different time periods. So, we have lot of flexibility in designing polymeric systems with that biodegradable property.

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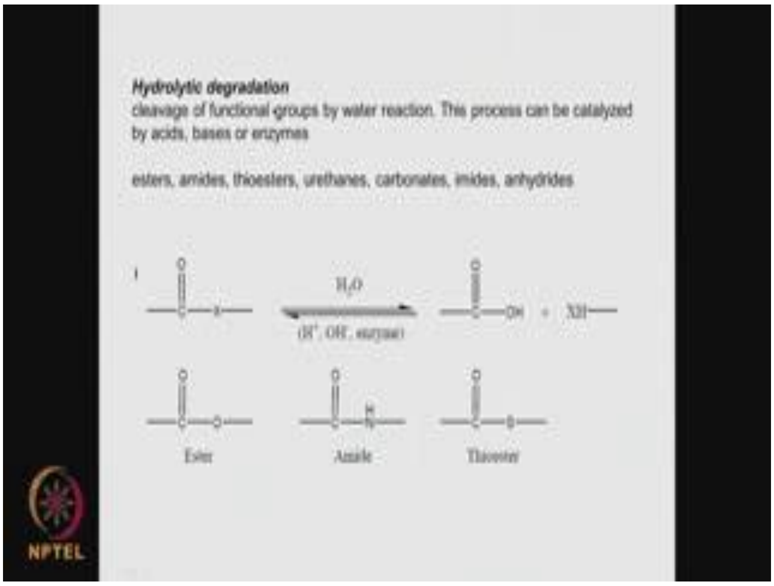

Hydrolytic degradation

cleavage of functional groups by water reaction. This process can be catalyzed by acids, bases or enzymes

esters, amides, thioesters, urethanes, carbonates, imides, anhydrides

So, when we talk about hydrolytic degradation we, so water is reacting with some functional groups. So, we can have acids catalyzing these bases catalyzing these enzymes. So, as I mentioned before. So, these are the situations where can have enzymes also catalyzing or even bases may be catalyzing this type of reactions.

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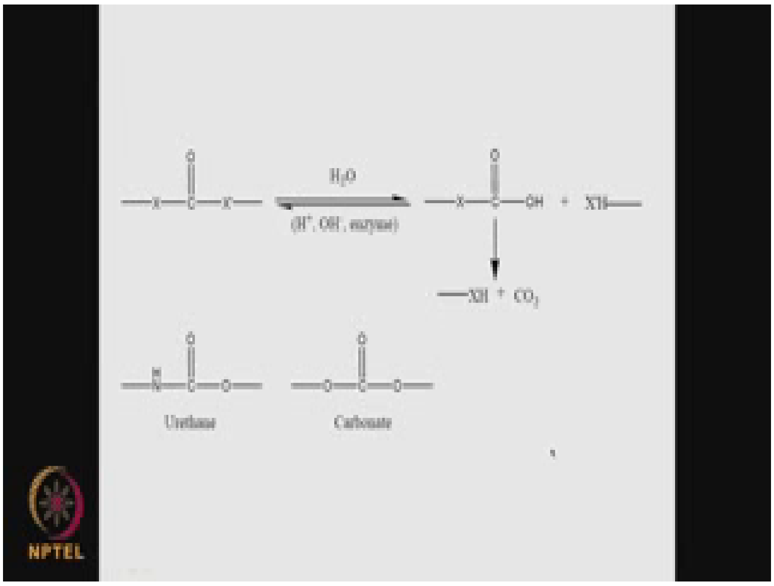

So, lot of these again what as I showed again before the catalysis could be taking place because of enzyme or acids or bases we I showed you before also.

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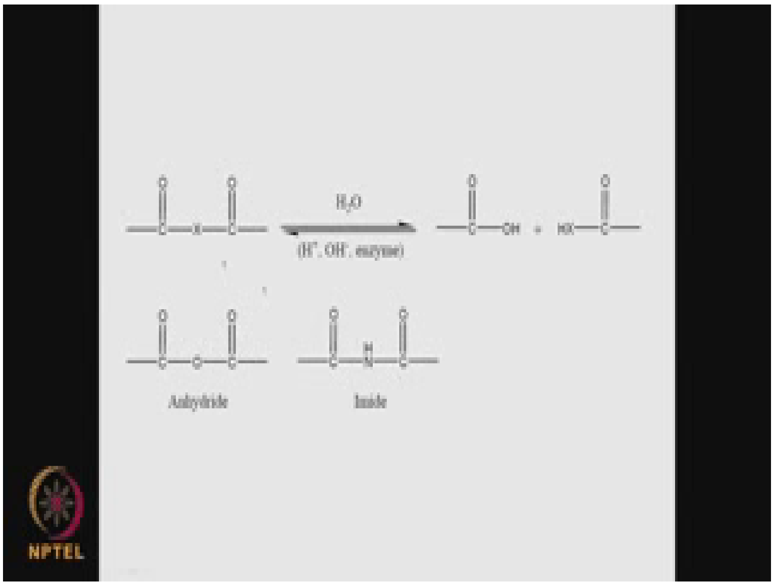

So, all these situations; so we can have a acids for a water to react or bases or even enzymes which are catalyzing this reaction.

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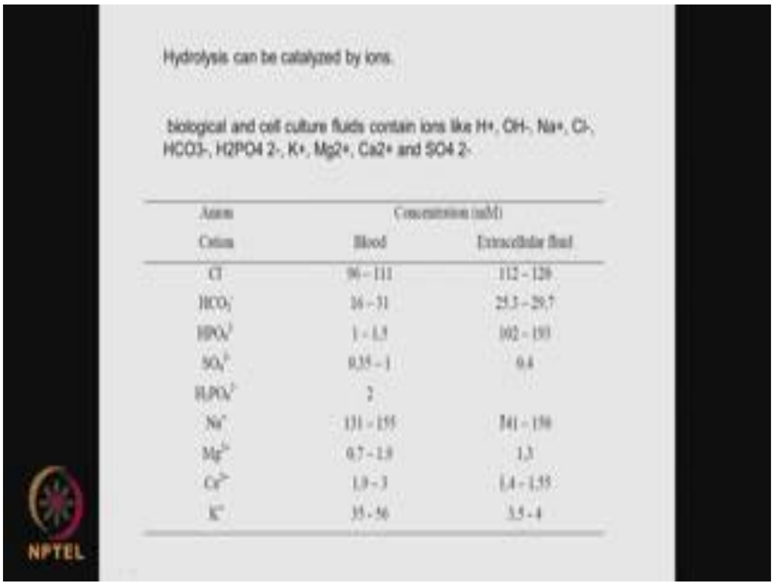

Hydrolysis can be catalyzed by ions.

biological and cell culture fluids contain ions like H+, OH-, Na+, Cl-, HCO3-, H2PO4 2-, K+, Mg2+, Ca2+ and SO4 2-

Anion	Concentration (mM)	
Cation	Blood	Extracellular fluid
Cl^-	96 – 111	112 – 120
HCO_3^-	16 – 31	25.3 – 29.7
HPO_4^{2-}	1 – 1.5	102 – 193
SO_4^{2-}	0.35 – 1	0.4
$H_2PO_4^-$	2	
Na^+	131 – 155	141 – 150
Mg^{2+}	0.7 – 1.9	1.3
Ca^{2+}	1.9 – 3	1.4 – 1.55
K^+	35 – 56	3.5 – 4

Sometimes even ions could be catalyzing you may wonder where are they ions in the body, but biological and cell cultured fluids contained lot of ions H plus O H minus sodium plus chlorine minus phosphate grooves potassium magnesium calcium sulphate 2 minus and so on. For example, if you look at a blood or extracellular fluid you can see C l minus it contains lot of C l minus carbonates, phosphates, sulphates hydro phosphates, sodium, magnesium, calcium, potassium.

So, all you can see blood contains all this as well as extracellular fluid contains all these. So, these could be catalyzing hydrolysis reaction. These could be breaking esters amides or and these could be breaking orthoesters carbonates. So, these could be catalyzing some of these reactions, acid be acid catalyzed base catalyzed or metal catalyzed reactions hydrolysis type of reaction.

So, body contains so many mate metal irons both in the blood as well as in the extracellular fluid. So, they could be catalyzing many of the degradation process. So, even if you do not want degradation sometimes you may be surprised the material is degrading because they are catalyzed by acids bases and ions.

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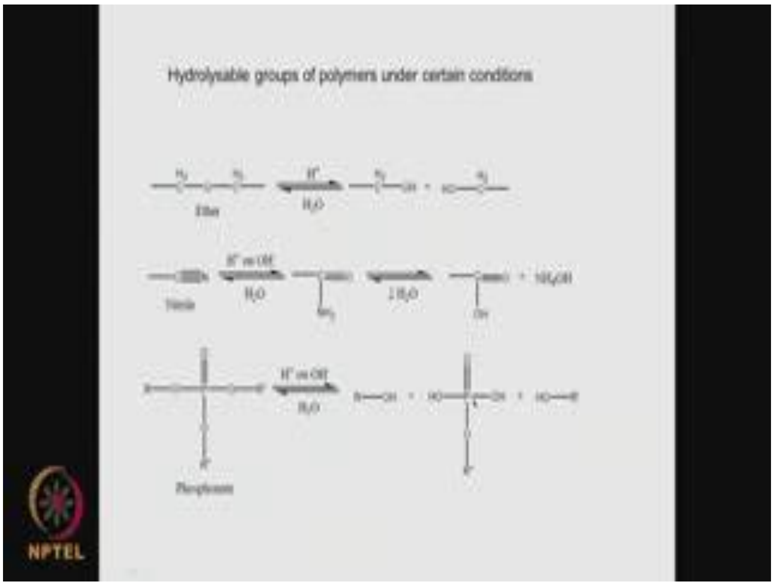

Hydrolysable groups of polymers under certain conditions

So, lot of these materials nitriles, ethers, phosphates, and phosphonates. So, all these are getting degraded because of presence of a acid acidic ions or basic ions and so on actually.

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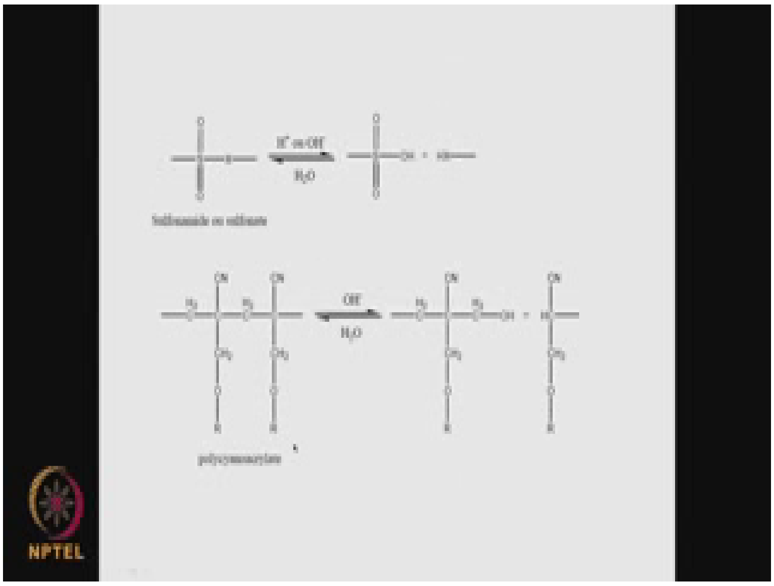

So, quiet a lot of situations, where you can have sulfonamide. For example, produces acidic functions polycyanoacrylate we have the cyan group. So, C triple bond N and C triple bond N and they are getting again hydrolyzed in the presence of base sulfonamides, they are getting hydrolyzed in the presence of acidic or basic functional.

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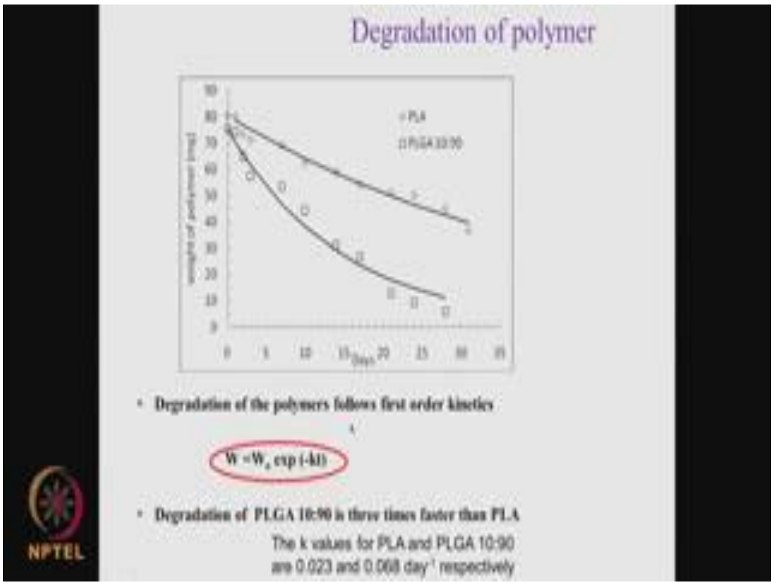

Degradation of polymer

- Degradation of the polymers follows first order kinetics

$W = W_0 \exp(-kt)$

- Degradation of PLGA 10:90 is three times faster than PLA

The k values for PLA and PLGA 10:90 are 0.023 and 0.068 day^{-1} respectively

Now, if you look degradation of a polymer, this is an example picture I am showing. PLA starting from 80 milligrams going down to 50 milligrams in 30 days PLGA starting from 75 milligrams going down to 25 milligrams in 30 days, Gallic acid is more biodegradable than lactic acid as you can see in these 2 pictures. So, by modifying the amount of glycolic acid in poly lactic system, I can modify the weight loss, as you can see and we can assume a first order type of degradation like this, you know weight loss is equal to weight loss at times 0 exponent minus k t k value for PLA poly lactic acid is 0.023 k value for PLGA is 0.068. So, I am having different by having different amounts of glycolic acid. I can achieve different degradation rate which means I can have different k values here.

And the degradation generally we can assume it as a first order as you can see in this nice fit this is a experimental and data is the squares and diamonds on the model fit is given by this straight line.

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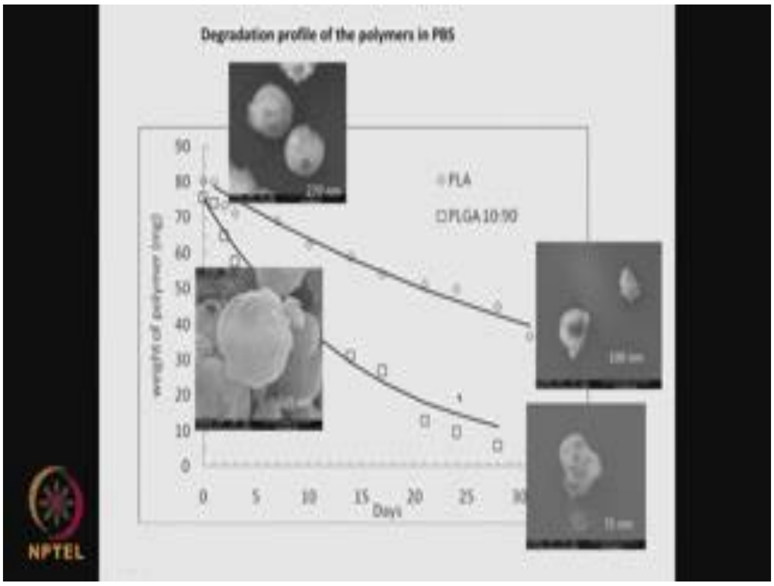

Degradation profile of the polymers in PBS

This ultra-shows you as a scanning electron pictures of the degradation of both ply lactic acid and poly lactic glycolic acids system. Nice polymeric spheres here as you can see and with time it goes down you can see nice degradation and the polymers of certain diameters 270 nanometers becomes almost 100 nanometers in 30 days. PLGA is starting from 325 nanometers coming down to 75 nanometers. Nice degradation profiles you can see and changes in the size of these polymers also you can see.

So, if I am using this system for drug delivery; obviously, if I have drug incorporated into this as the polymers degrade losing it is sized diameter, it may be liberating the drug may be antibiotic or anti-inflammatory drug. So, we can use PLA or PLGA both PLA and PLGA are FDA approved drugs. So, we have very nice situation where we can have a drug loaded polymers. And as you can see within 30 days we achieve almost 2 times reduction in the size PLA and almost 4 times reduction in in the size of PLGA.

So, we will continue in the next class more on the biodegradation as well as bio resorption of polymeric material.

Thank you very much for your time.