Basics in Inorganic Chemistry
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Lecture - 19
Oxygen Transportation Mechanism

What is cooperativity? Lot of slides are there it is written form I will explain very briefly fast here ok. The moment one of the oxygen binds like this ok, how it binds? It binds like this.

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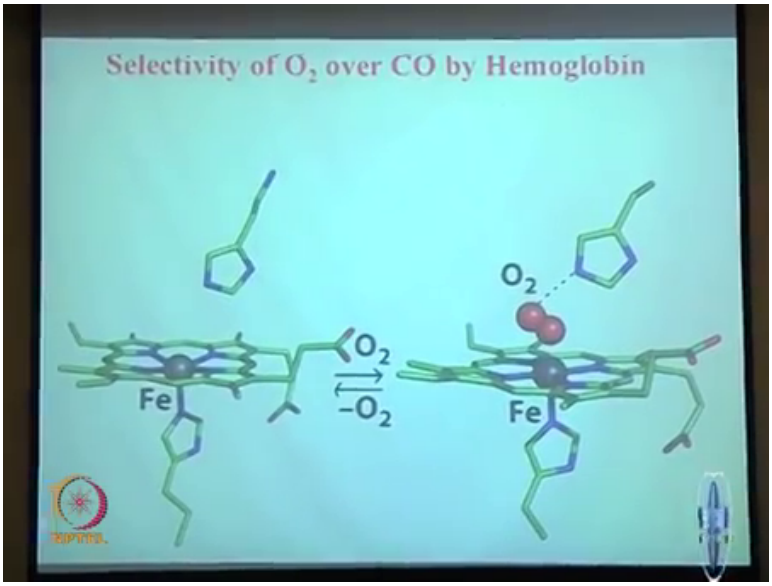

Iron porphyrin site iron sorry iron porphyrin site, this is imidazole that is that deoxy hemoglobin, no oxygen is there. This is the other histidine that I am talking over here, which is far ok. This is the reduced form oxygen binds with it and what happens this is the oxy form oxyhemoglobin and there is a hydrogen bonding ok.

Now, the moment it binds, this is definitely going to come one from the other in exam. What happens? This iron in the deoxy form is in reduced form ok. Both the structure we are discussing only iron 2 plus, no iron 3 plus, iron 2 plus. Iron 2 plus see this is not a very good ligand it is too far, it is not going to bind. You have a porphyrin ring and a imidazole, this is the iron 2 plus high spin, it is a high spin configuration. And, this iron is not really in the plane. So, if the porphyrin plane is here I mean sitting half in half out it is not into that cavity perfectly.

So, as you can see you can see the iron on top, it is of course, little bit in the cavity, but it is on the little top ok. It is not really inside the porphyrin cavity, what in the porphyrin cavity we were say showing?

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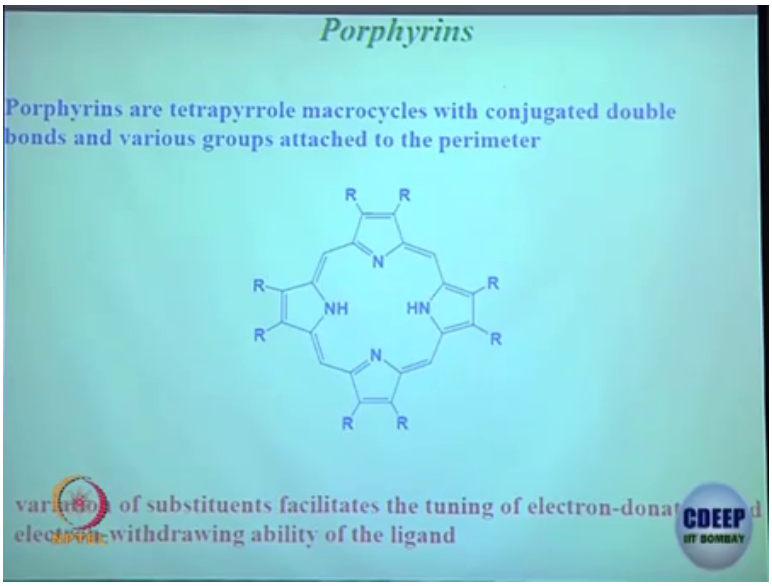

Here this is the cavity right.

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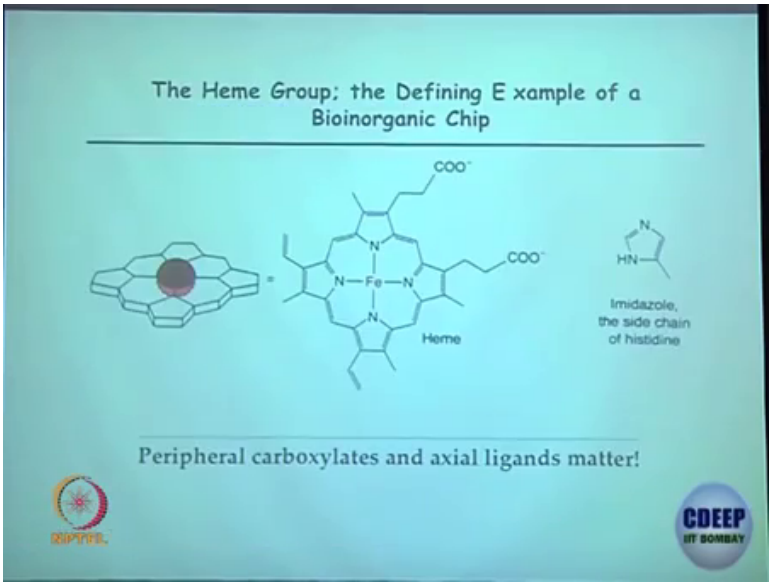

Now, this is iron 2 plus in the high spin form, the moment oxygen binds ok, the moment oxygen binds over here it goes to low spin form. So, it is now an octahedral complex perfect or not perfect, it is a very good octahedral complex right. And, you know that iron 2 plus high spin means, what D 4 sorry t 2 g 4 e g 2, upon the oxygen binding it goes to t 2 g 6, e g 0, t to g 4 e g 2 this is t 2 g 6 high spin to low spin configuration change.

The moment high spin to low spin configuration change is there. So, there is t 2 g e g all of a sudden, there is no electron in e g. And, therefore, what happens is the repulsion of the ligand becomes less and the size of the iron decreases. So, in this case iron 2 high spin is larger in

size, low spin is little bit shorter in size, little bit shorter that is good enough; that means, it will go into the cavity in the porphyrin and thereby then that pull that is a structural change.

So, this imidazole you can see it was bind or it is bind with the iron center and it is like big iron center is big, the moment it gets shortened it just. So, it is over here iron is here, if you use make it little shorter and then you pull in that change it is over here, it goes down that change that change will trigger the cooperativity.

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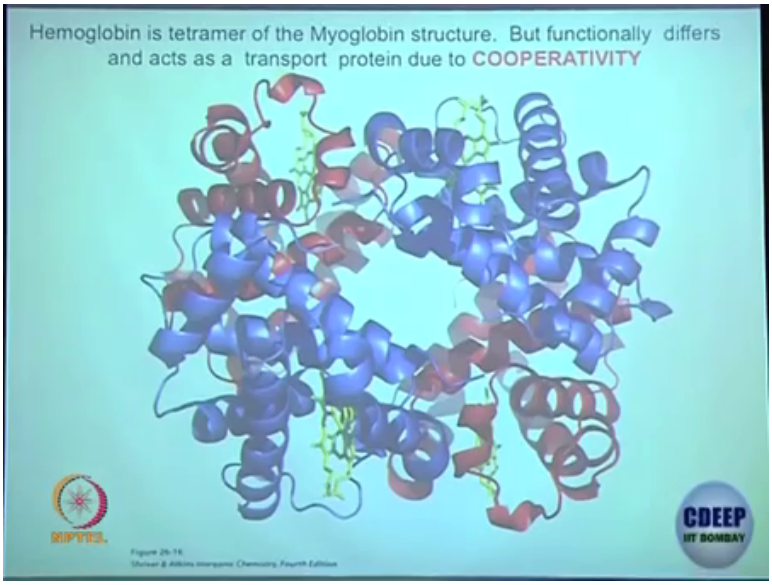

What will happen? The moment it gets pulled in the cavity, that change in configuration or confirmation will be relayed all over. That will send the message the moment one oxygen binds in here, it pulls in or it passes the information and this guy knows that oxygen is available and it almost again this guy undergoes high spin to low spin configuration change oxygen comes and sit down.

It happens to here, it pulls in again it related, it relate. So, the activation barrier or how much energy you need to put for the first oxygen is always going to be high. The moment you are able to bind the first oxygen, second, third, fourth, it is going to be less, less and less it is just a relay I mean you are having a 16 00 meter race let us say, it is it just gets relayed very fast.

If there is a message that oxygen is there the high spin to low spin change is happening, oxygen binds, oxygen binds high spin the iron 2 plus goes to low spin iron 2 plus it gets reduced inside. It gets pulled in the pocket of porphyrin that little change it is a very subtle change, it gets communicated with the next porphyrin center.

That next porphyrin center binds oxygen, it gets communicated next one, it gets communicated next one. So, that is cooperativity, they are cooperating, they are you know working in tandem, they are very good communicator, they are communicating with each other.

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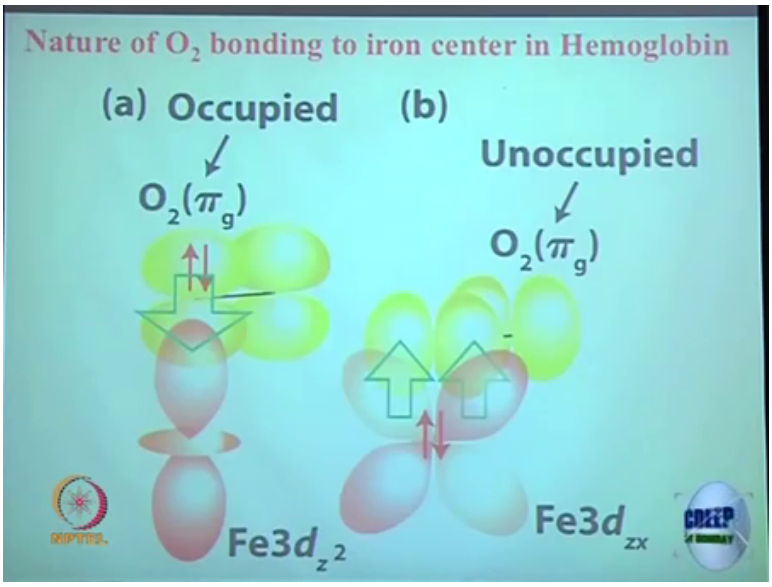

Ok. Now, that is cooperativity, it is very nicely also written in the slide from I will come, I will may not discuss way too much afterwards ok. Now, show how the binding happening? This is oxygen these are let us say this oxygen to electrons; it is metal sorry ligand to metal bonding is happening ok. It gives to that d z 2 orbital the axial position right, it give to d z 2 and from d z x orbital it donates back to the oxygen pi star orbital right.

So, it is a back bonding, it is it is forward bonding and then back bonding; that means, that the binding is going to be good. It is of course, you know it is not too tight, but it is good. Iron center will bind with the oxygen decent amount that is occupied means filled one will be donating and then there will be back donation ok, will not get into too much details of that.

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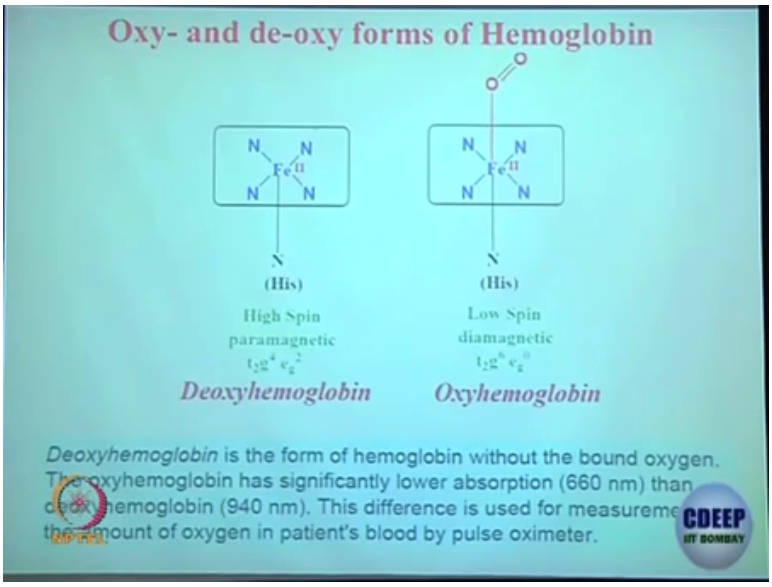

Now, this is what exactly, this is what exactly I tried to say, I will just briefly go through the slides, it will be provided to you in the Moodle. So, I will be going directly. Now, iron 2 plus this is the high spin paramagnetic. Of course, it is high spin paramagnetic right, because it is t 2 f 4 e g 2 high spin right iron 2 plus paramagnetic t 2 g 4 e g 2 the moment oxygen binds, it becomes low spin diamagnetic t 2 g 6 e g 0 no unpaired electron yeah.

Student: (Refer Time: 08:17) octahdral (Refer Time: 08:19).

No, it is not really octahedral, but it is you know it, but still there is a loose coordination as you are showing this histidine is there. The moment it is there it is of course, the sixth coordination side is almost vacant it is not hundred percent vacant almost vacant ok. Now, of course, you can see that these information iron 2 plus 2 these are iron 2 plus I mean not really deoxyhemoglobin to oxyhemoglobin changes, this will also have some effect in the

spectroscopic behavior ok. What we are not discussing here is a right after oxygen binding, iron oxidation state also changes.

Iron 2 2 2 goes to iron 3 plus oxygen becomes superoxo reduced by one electron, that we are not discussing you do not have to write in that exam; do not write in the exam. Oxygen gets reduced by one electron that is called superoxo. So, what we have discussed here is peroxo. An iron 2 plus gets oxidized to iron 3 plus that is a reversible process means it can go, but forward and then come back ward as well anyway.

Now, these due to these all these changes we will get a spectroscopic difference, the color or if you if you measure before oxygen binding and after oxygen binding, the spectra of the compound will be different. Based on that we can measure how much oxygen is bound let us say some people, you know suffer from you know this is a less oxygen delivery to certain part of body that is bad right. So, may be enough porphyrin center or not there ok.

So, how much let us say at a certain body part, how much oxygen is there that you can calculate, it is a very simple test you take the blood or you take some site specific reaction or site specific study a specific area you just see or in general you can figure out how much is there? So, oxygen how much oxygen content is there from this spectroscopic change, you can find out that is what you know pulse oximeter is ok; you can just read and understand nothing in there.

Now, what happens when the oxygen binds to hemoglobin, I think I have discussed already.

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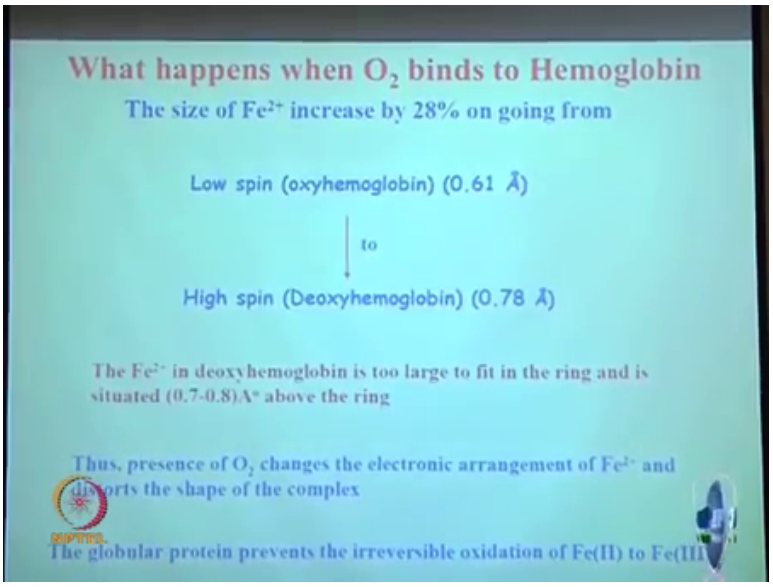

So, high spin goes to low spin all the informations is covered.

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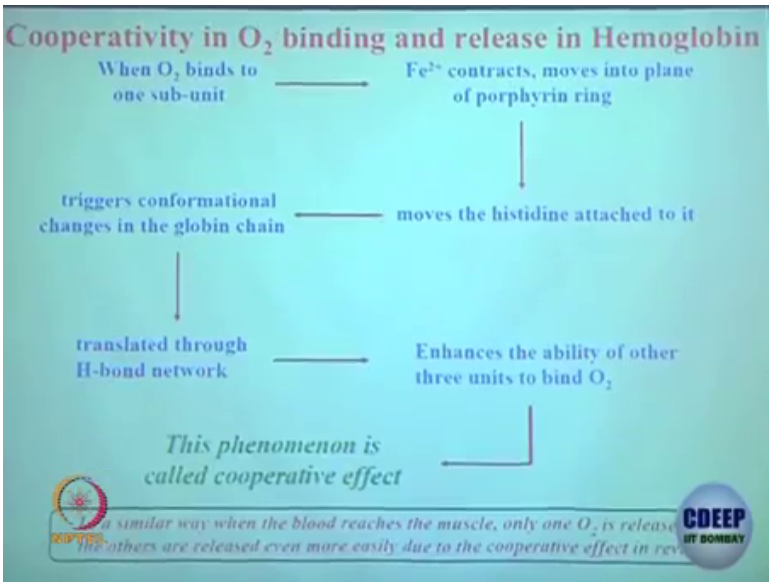

So, this phenomenon is called cooperativity. For your exam purpose these are the slides that exactly same thing what I have said without looking at this slide that those informations are there, you read it. Now, see there are some slides I will take 5 to 10 minutes to discuss; this is for your general understanding well the problem is let me in 1 minute let me discuss the problem. So, all other section whoever or that you know instructor, they have discussed it ok.

So, I have to discuss it simple, but I will give this slide in this form. So, you decide how much you want to read, how much you do not want to read. I have given it is for your information I am very clearly saying, I think we are not going to I mean most likely 90 percent guarantee maybe some information understanding may be tested, but not in deeper level ok. Let me get into that you will see it is not that boring alright.

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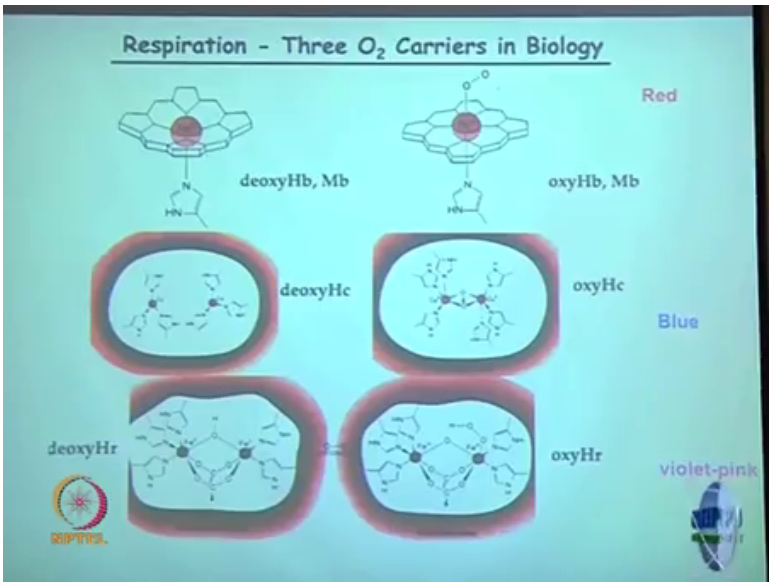

All well let me go to the, next slide it is interesting right, alright.

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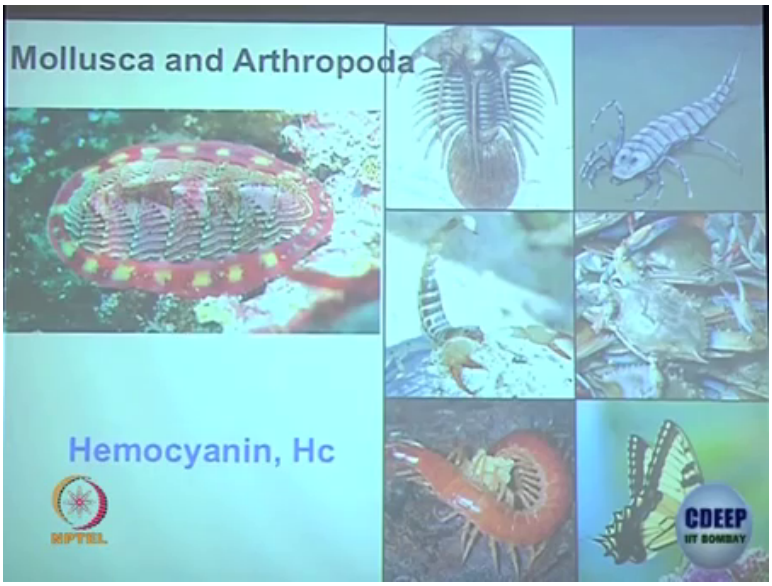

We do know that our blood is red, then there are some animals, some other species with red blue blood, they are not demons not in movies the blue blooded there are cold blooded people ok, but these are blue blooded animals ok.

So, the reason why I this is again not for example, I mean give me 5 minutes, I will finish it is important that you understand ok. Never you are going to look back perhaps ever again these things ok, it is important you just do understand little bit, I will discuss some little bit interesting thing ok, including the rule ok..

How it get digested? Ok. So, in our blood we have we have this porphyrin center right, iron center.

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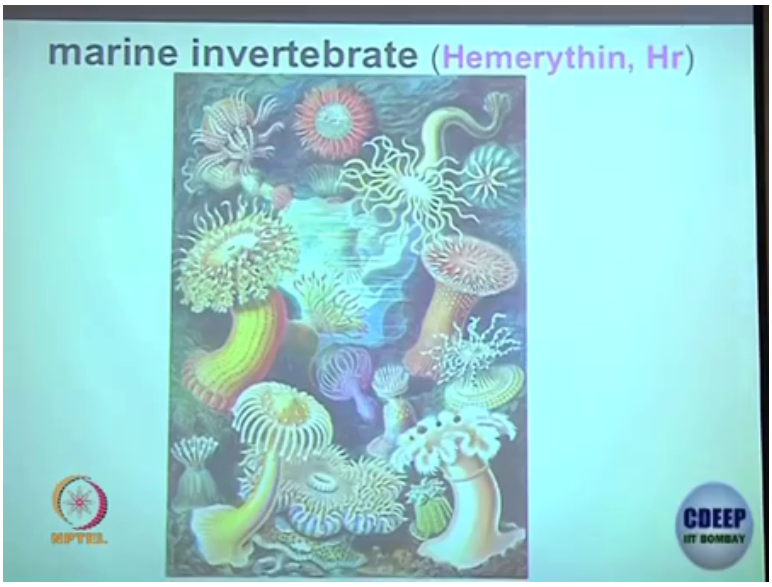

These other cases we a lot of other animals or some, some of this you know these marine invertebrates they do not have the blood or so, called blood as you see in red. Because, they have of course, they have to take oxygen; I mean all we are saying is these are the oxygen carrier protein. The way they carry the oxygen is little bit different instead of iron center there you have copper centers. Those are these porphyrin iron center instead of those you have copper centers, that gives it blue color.

So, there are some of this hemocyanin or some of the animals are there, some of the species are there, which have blue blood right. At the end of this class we will be discussing tutorial part. These are the one where we have again slide will be given I think I may not be allowed too much, but it is.

So, there you will be saying the blueblood ok. There you will be saying that seeing the violet ok, violet pink colors. Due to the fact that the ligand is different or the metal is different or both is different ok. Therefore, although oxygen binds mode of binding is different.

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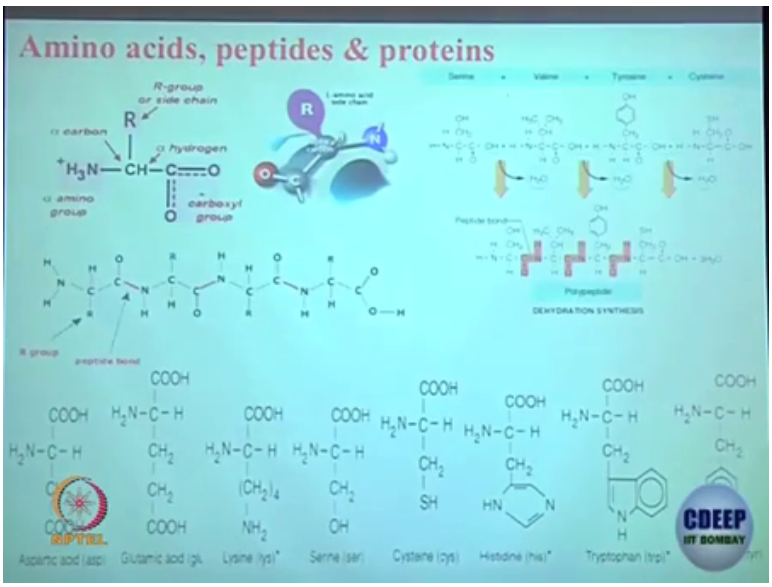

Now, these are the slide amino acid peptides and protein, you know it amino acids is something like this, acid and amine part amino acid put together is protein backbone right. And, these are different amino acid we are talking aspartic acid, glutamic acid, lysine serine cysteine lot of iron I am not asking you to memorize, but if I think 3 4 amino acid you must know, this is your responsibility, if someone is asking question I cannot help ok. So, pure amino acid you must know and you know the that is how the peptide backbone is formed?

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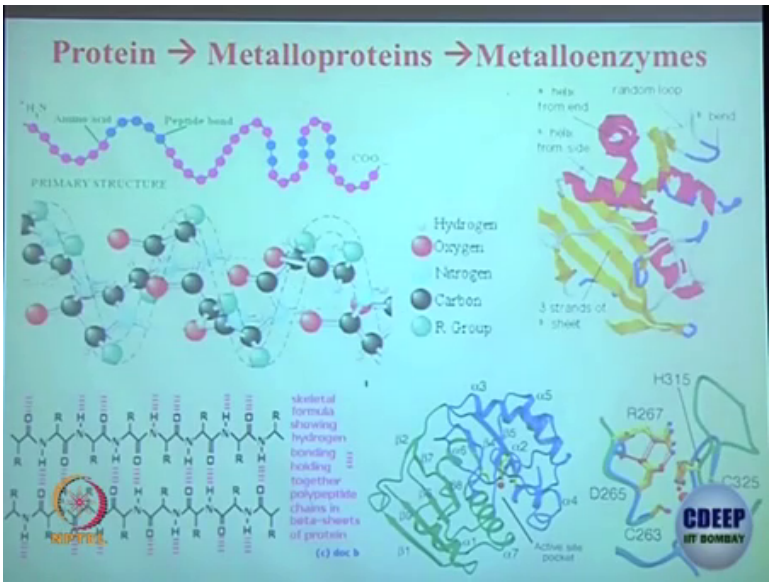

And, then those peptide backbone can have the hydrogen bonding or inter linked or cross linked and thereby they can form the you know 3 D structures ok. That is I think you have started in biology or somewhere or do you just essentially understand how it forms fine?

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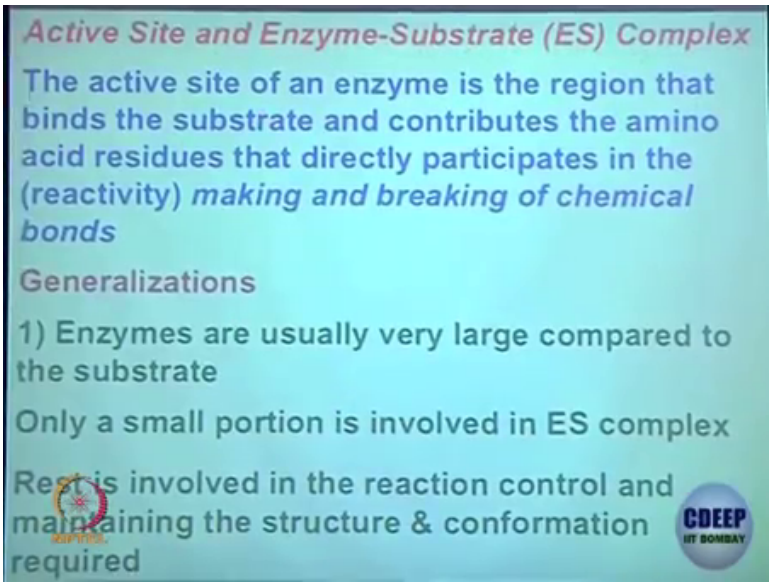

Next is enzyme substrate complex, I will take you here.

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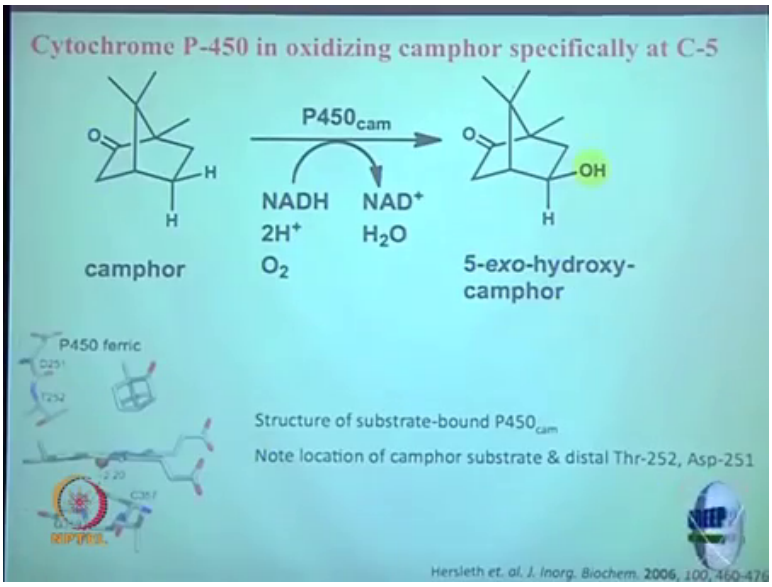

Enzyme substrate complex is what, you have an organic compound organic you have taken you see lot of carbon hydrogen bonds are there. And, if that organic compound is getting functionalized, let us say hydroxylated lot of possibilities are there right, only a particular carbon hydrogen bond gets functionalized.

How does that happen? That happens, because let us say you have a porphyrin center or a iron center in front of that whole organic molecule is there, it is not like that only a particular carbon hydrogen bond gets exposed or comes very close to the active site, that metal active site metallo enzyme.

And, therefore, even if you have all those carbon hydrogen bond or carbon hydrogen bond, covalent bond present, all those hydroxylation and products are possible only selectively one carbon hydrogen bond gets functionalized. Because, that is how it gets exposed not these are

getting functionalized only let us say this is getting functionalized hydroxylated you see only one particular CH is getting hydroxylated.

Now, that is called substrate binding pocket substrate comes in, there is metal binding pocket, there is substrate binding pocket. Substrate comes in and sits in there and the metal is there and the chemistry happens ok.

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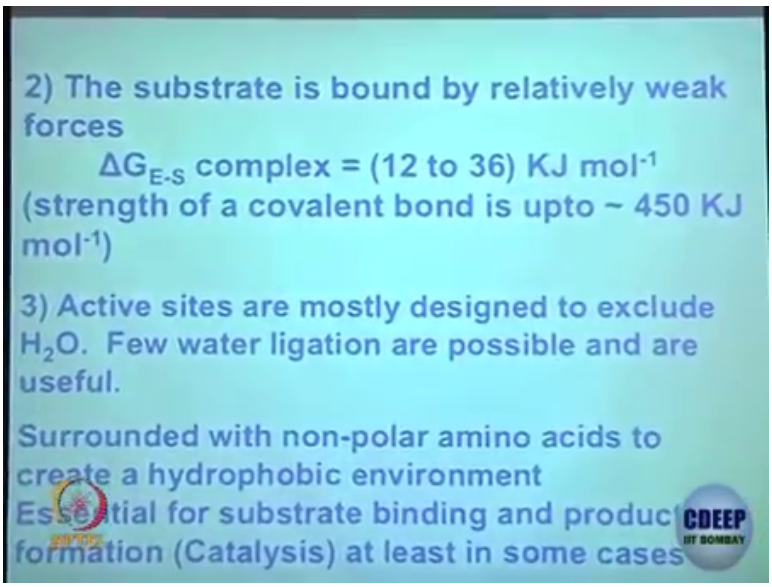

Now, so, enzyme and substrate interaction those E S complex we are saying this is where you know the substrate is bound by relatively weak forces; substrate is not going to bound that organic substrate, let us say is not going to be bound very strongly they forms weak complexes ok. Another important thing is to understand enzyme is huge not everywhere it is binding substrate, there is only a specific center where it binds right.

Now, rest of the things may not be involved in catalysis this is the reaction we are time to tell is catalysis right. It is a reaction happening rest of the protein backbone or peptide backbone, we are not seeing much of a role in the substrate binding. Only a particular site or particular place substrate comes in sits in there and the enzyme or let us say the metalloenzyme does the chemistry the or the catalysis part.

So, something about the enzyme substrate complex is given in the slide, it is a very easy to understand. I am once again, I do not expect you to memorize all these you know these things these are not of much of huge for the course purpose, but you try to flip through give yourself 10 15 20 minutes some idea wise, if some question is coming you should not be complaining, we are not going to ask you to draw a peptide bond ok, right anyway. Now, let us move on this is one of the thing what I was trying to tell you synthetically.

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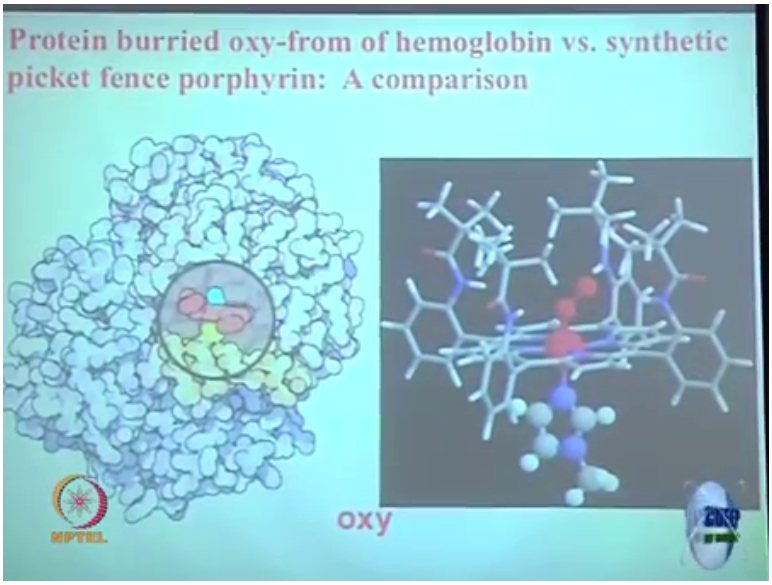

See, if this is the umbrella like structure you see the umbrella is forming over here ok. Now, oxygen is prevented in the synthetic system, oxygen is that is how prevented from reacting at the other center, that is a you know that is just a view you see that how people would make the porphyrin functionalized, porphyrin from porphyrin backbone, how people put the umbrella and put the oxygen in a protected manner, it is protecting. Ok.

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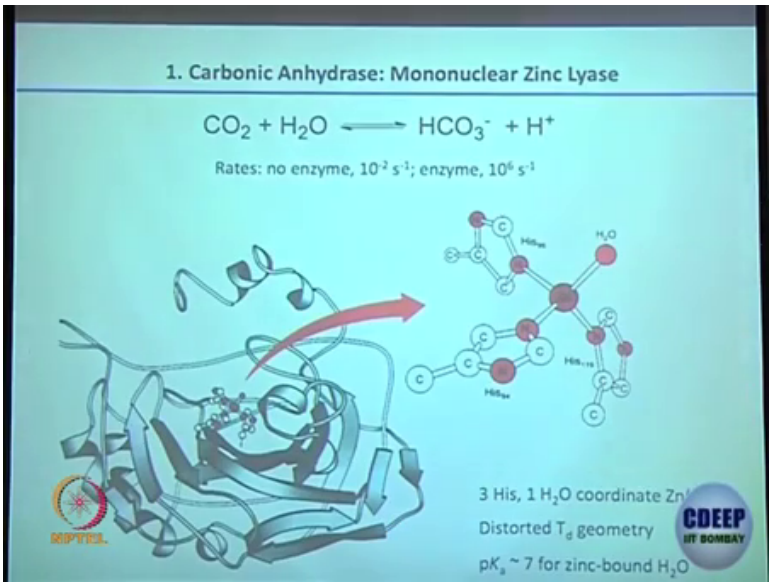

Whoever is not interested please be my guest leaving or do not be my guest. Now, carbonic anhydrase, there are certain enzyme ok, this is called one of the enzyme called carbonic anhydrase, that has zinc site at the middle. Now, it is coordinated with histidine, histidine, histidine and water, what it does it converts carbon dioxide into carbonate ok.

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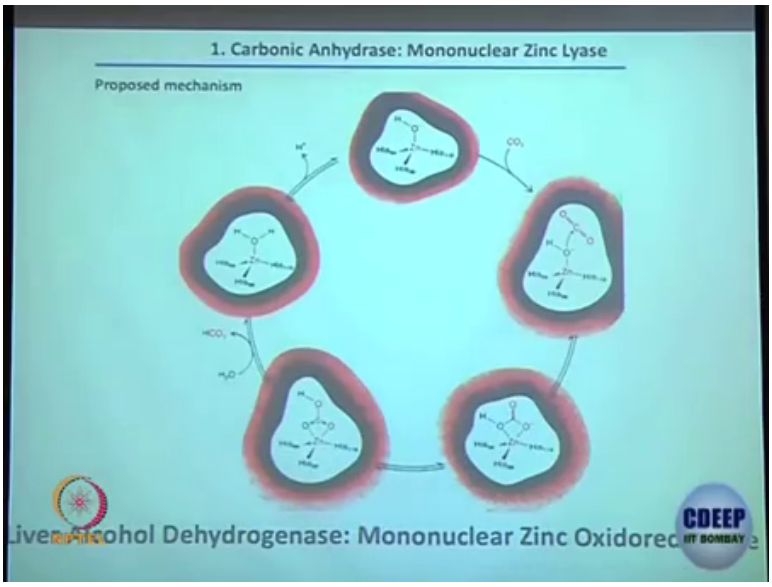

How it does, again you do not have to memorize you just see one time it is a very easy organic chemistry I am talking about. You have zinc hydroxo formation; zinc water to zinc water was there ok. And 3 histidine was there these are the ligand for zinc 2 plus zinc is redox inactive, zinc 2 plus stage zinc 2 plus water gets deprotonated. Water is elf deprotonation will not be easy, but the moment it binds with this Lewis acid, zinc 2 plus acts as a Lewis acid.

The acidity it becomes highly acidic this O H bond deprotonation become easier, water itself under the physiological condition it will not let us say undergo deprotonation. Now, the moment water binds with the zinc 2 plus zinc 2 plus is a Lewis acid and thereby you will have an opportunity to deprotonate. The moment the hydroxy forms, carbon dioxide can be attacked by this hydroxy and then you can form the carbonate. So, see sodium bicarbonate it is something like that so, carbon dioxide forming carbon bicarbonate or carbonate ok.

So, that is the carbonic anhydrase activity, if carbon dioxide reacts with the water it is a simple reaction, but it is not that very easy at all I mean you take carbon dioxide gas you put water how can you react, but simple zinc site can do the wonders, its catalysis very very good I mean these are all happening in our body man come on it is very important. Ok.

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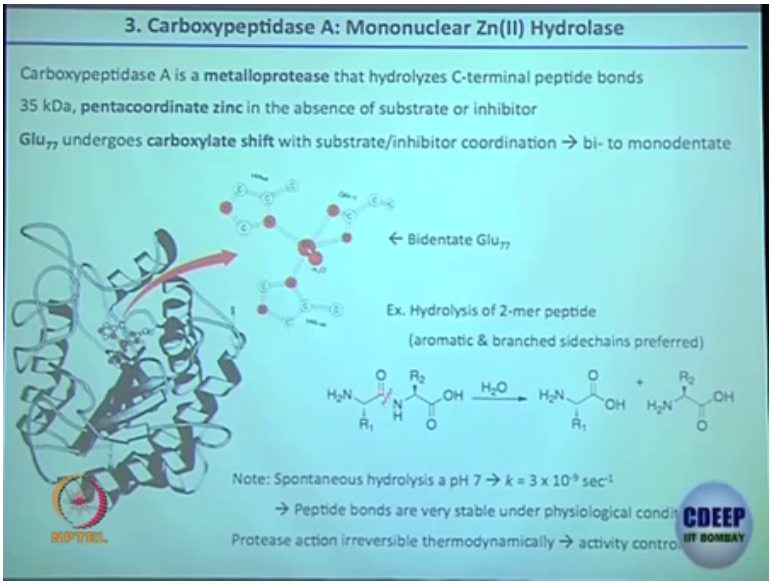

Now, then the peptide backbone cleavage of course, you know how to cleaves a amide peptide bond it is an amide linkage right hydrolysis you need to do, but these hydrolysis in organic chemistry what you will learn it may not be official may not be fast ok. It is slow enough, but the moment you have this zinc site, this cleavage becomes easy ok, it is it cleaves actually in a similar manner.

So, this hydroxo this zinc hydroxo that forms over there this zinc hydroxo attack over there of course, let us say base catalyzed hydrolysis of amide is possible, it is a amide bond is there

you put a base a nucleophile attack at that center and it gives you an acid, but from here and I mean from here. Like it is a hydrolysis ester hydrolysis you have studied it is a amide hydrolysis, but that amide hydrolysis is very slow under you know physiological condition.

But, the moment zinc site is there, zinc hydroxo formed due to zinc being the Lewis acid, deprotonation becomes easier, deprotonation of water becomes easier, that zinc hydroxy can do this wonder ok. If you drink, if you drink alcohol your liver will be damaged. Why? Its very simple reason right your liver is going to be damaged, that is mainly all first to remind you ethanol is the one which is used as a alcohol to drink not the methanol. The methanol you drink again I will see you ok.

Student: (Refer Time: 23:56).

Alright. So, why ethanol and then how our body digests it or breaks it is not good for our body, it is a foreign object we get high, but that is why we drink ok, but a not necessarily I do not promote just like movies any actor.

Student: (Refer Time: 24:15).

Does not promote any of these I do not promote anything, I am not promoting anything, and that is a very serious note it is an academic institution ok.

Now.

Student: (Refer Time: 24:27).

Now.

Student: (Refer Time: 24:30).

So, how although definitely people drink alcohol, that is a fact. How body digested? What happens alcohol ethanol C H 3 C H 2 O H ethanol is converted to acetaldehyde C H 3 C H O alcohol oxidation to aldehyde happens. And, then aldehyde gets chopped up to carbon dioxide and water and so on, that is another enzyme. The first step ethanol to aldehyde formation that happens in here, the enzyme called lad liver alcohol dehydrogenase.

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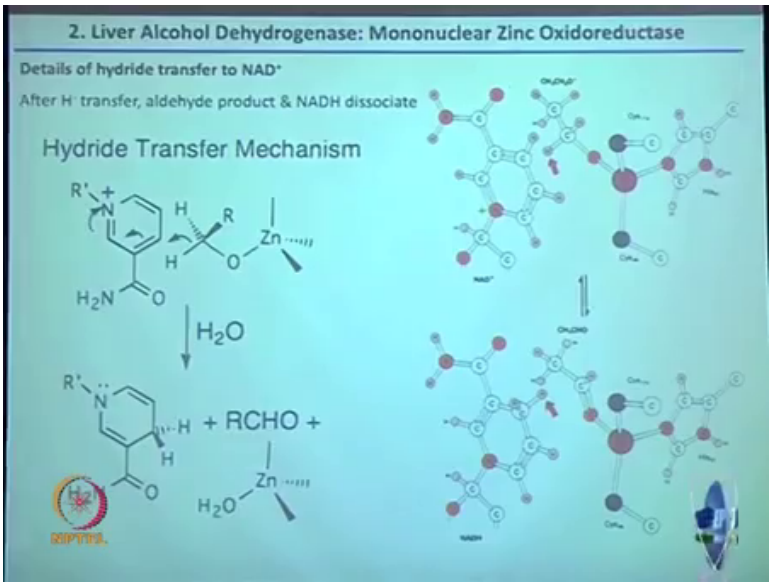

It is nothing, but once again it is a zinc engine ok. Alcohol, if that is why liver gets damaged, if that enzyme is not working, which is at the liver. That enzyme is not working of course; our body will not have the ability to dispel carbon I mean dispel the alcohol from our body right. If liver alcohol dehydrogenase is not working, that enzyme is not working alcohol becomes toxic for us I mean of course, it is toxic, but it becomes even more toxic right. It is it could be

deadly. I mean if someone has it is deadly yeah you do see the nude someone had liver which is damaged and keep on consuming alcohol of course, right.

So, this is how it happened it is a little bit different mechanism I will not you do not have to remember again, what happens over here is this is the pyridine ring, you are seeing it is called nicotine, as well something like similar moieties they are in your cigarette also nicotine ok. I will fine let us stop there. So, this hydride so, zinc center binds with the alcohol r in C H 3 methyl C H 2 O H. Now, gets deprotonated.

And, this hydride gets transferred to this pyridine ring. It is a this is the this is the center, which is helping and the enzyme is zinc again ok. Zinc center with 3 of them zinc center with all those coordinates and the alcohol binding here, and the way alcohol is converted to aldehyde is shown is there. It is a hydride transfer mechanism simple organic reaction, but without this enzyme you can understand this process will not happen and it does not happen.

That is also true for lot of these you know east Asian people like, Chinese people, Korean people, you see the moment they drink alcohol their whole body goes red not long all of them, some of them. Fortunately, for us we are most of us are a lot of us are not most of lot of us are brown.

So, we do not show up that much. So, all Chinese lot of Chinese people, lot of Korean people, South Korean people as for at least I have seen. Actually, they do not have this enzyme sufficient amount of course, how your you know if it goes back to your gene, it goes back to your evolution or the you know your generation how it has come? See you know that is that is how if the enzyme is not there in enough quantity?

What will happen is it if they are not able to digest or take much amount of alcohol, little bit is good enough for them their you know body gets you know swollen or red colored. It is just like almost like an allergic symptom it showed up of course, some of us can have the exactly same symptom, if your body or if your liver is not having this enzyme anyway enough for that.

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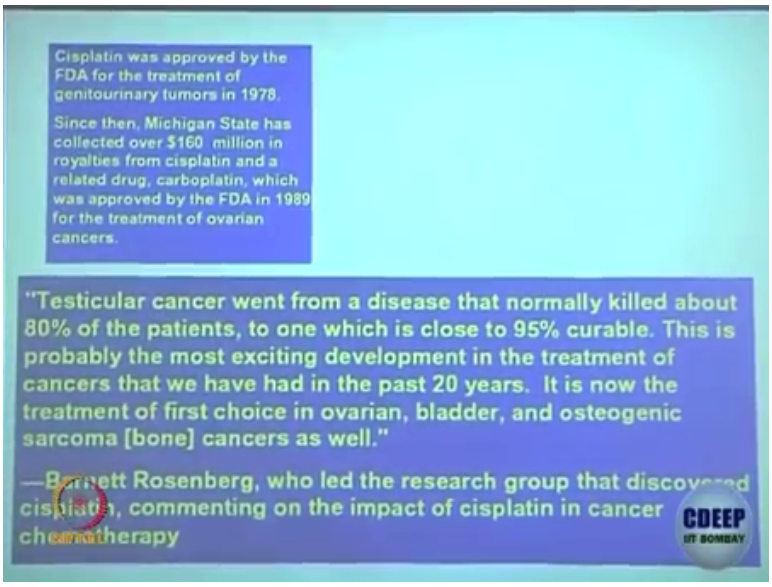

So, this is some information about the cisplatin how much money you can make, you can be a trillionaire, a billionaire dollars not rupees ok. You can be of course, rupees is good enough, you can be if you have discovered a good drug. If you have discovered a good catalytic reaction, simple thing I did not discuss let us say water to hydrogen production, that is the another enzyme since the class is only one we did not discuss that. There is an enzyme which can convert water to ox hydrogen right water splitting.

Now, if you happen to have a good catalyst for that, you know this is fuel right, fuel lots of fuel. Let us say, if you have an enzyme there is enzyme if you can convert let us say methane to methanol. That is a trillion dollar project, if you have a good catalyst enzyme does this thing routinely, enzyme is very good at doing this, methane to methanol, I am giving you target you pick up be bill trillionaire give me some money back ok.

These are these are ideas ok, methane to methanol you produce hydrogen ok. These lot of simple reaction, which nature does it could be in our body, it could be somewhere else, if you can do develop a good system, catalytic system for them I mean nothing can stop you from being rich ok. It has to be appreciated ok, it has to be industrially viable industry has to by your technique chemistry can be reordering to all right.

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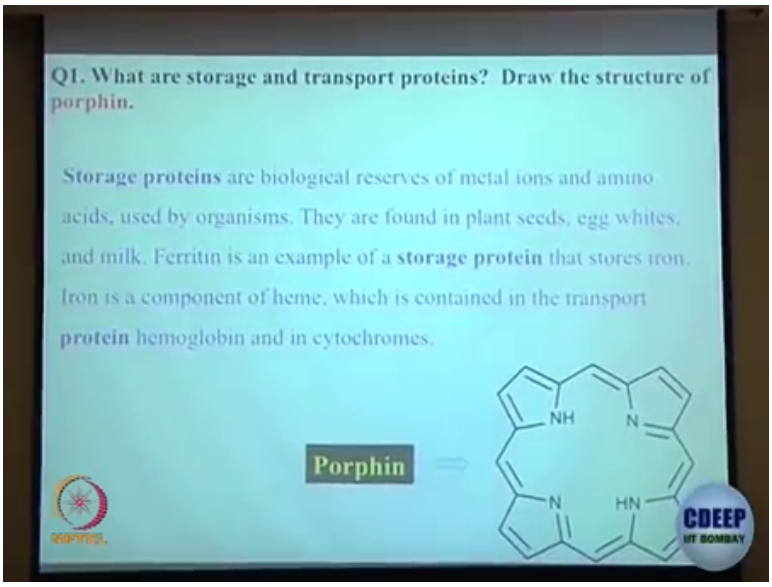

Tutorial, tutorial, what are storage and transport protein? We have discussed storage protein store things transport proteins transport things.

Student: (Refer Time: 30:56).

The answer is given over here answer is given in here. If, you give me an opportunity I will I will know it for you, why cyanide is toxic we have discussed again.

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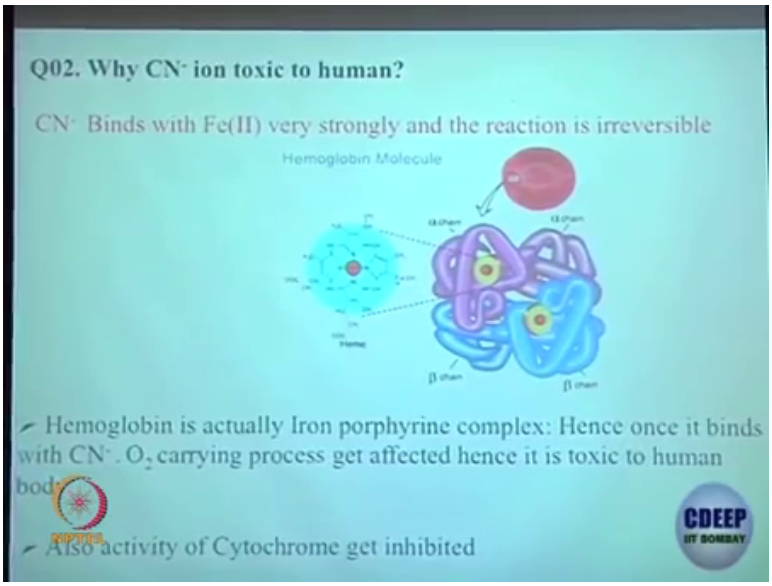

Student: (Refer Time: 31:16).

The binding site over here for oxygen.

Student: (Refer Time: 31:19).

Will be occupied by cyanide and thereby it is toxic and you cannot that is an irreversible process you cannot change it ok.

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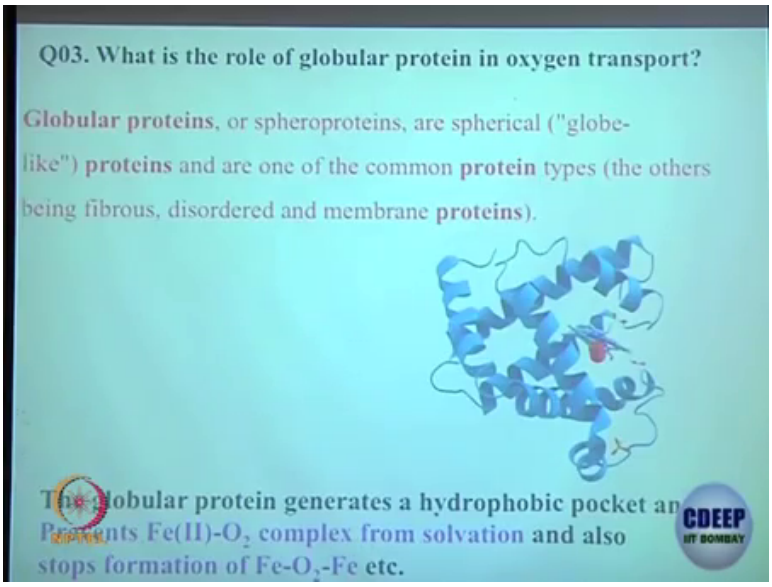

So, what is the role of globular protein in oxygen transport? It is nothing, it prevents the dimerization, it prevents, oxygen, you know iron center to get further oxidized and other site reaction it prevents ok. Lot of site reaction can happen that can be prevented by this globular protein.

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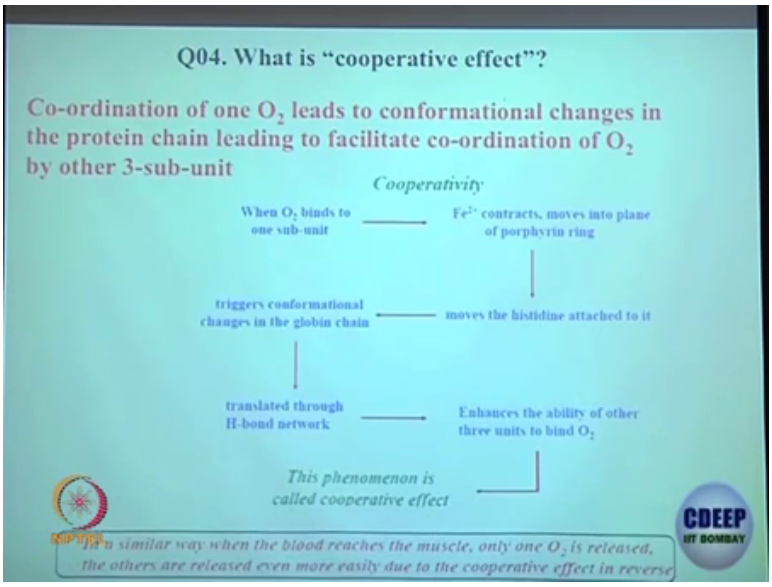

What is cooperativity? Everybody knows by now right; if you did not understand go through these step wise ok, it is fine.

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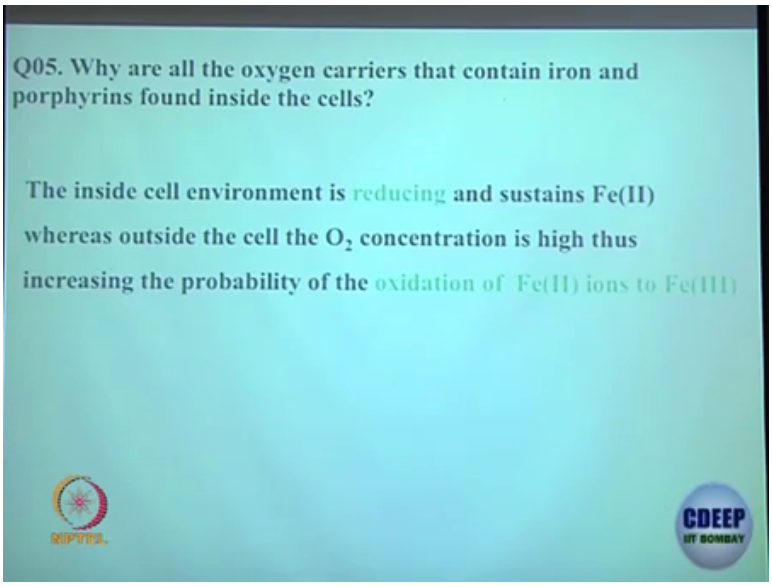

Now, why are all the oxygen carriers that contain iron and porphyrins found inside the cell.

Student: (Refer Time: 32:05).

Why inside the cell, outside the cell is very oxidative atmosphere? Iron can be oxidized irreversibly to iron 3 plus, then you cannot have them used for oxygen carrier right.

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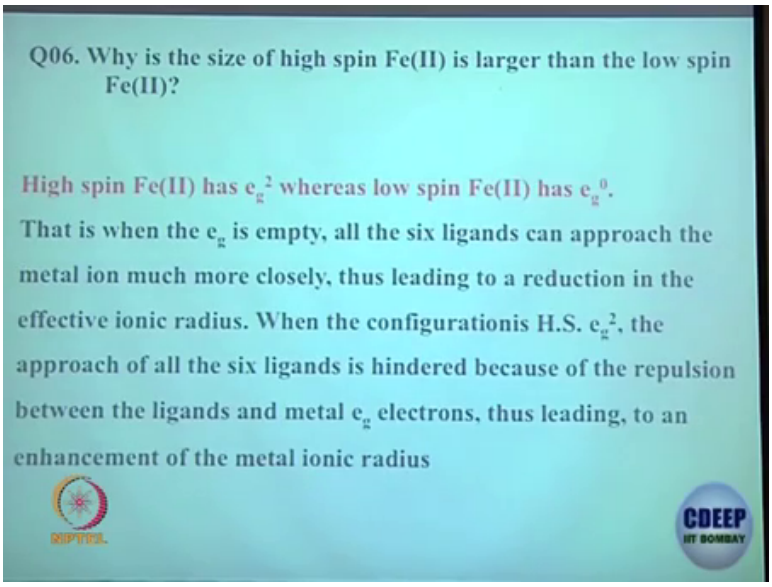

Why is the size of high spin iron 2 plus is larger than low spin iron 2? We say that high spin to low spin t 2 g 4 e g 2 to low spin you are going to t 2 g 6.

Student: (Refer Time: 32:33).

E g is the out e g out means lot of repulsion is out and the cell is becoming smaller or sorry not said iron center is becoming smaller high spin to low spin size varies size gets smaller it is written over there.

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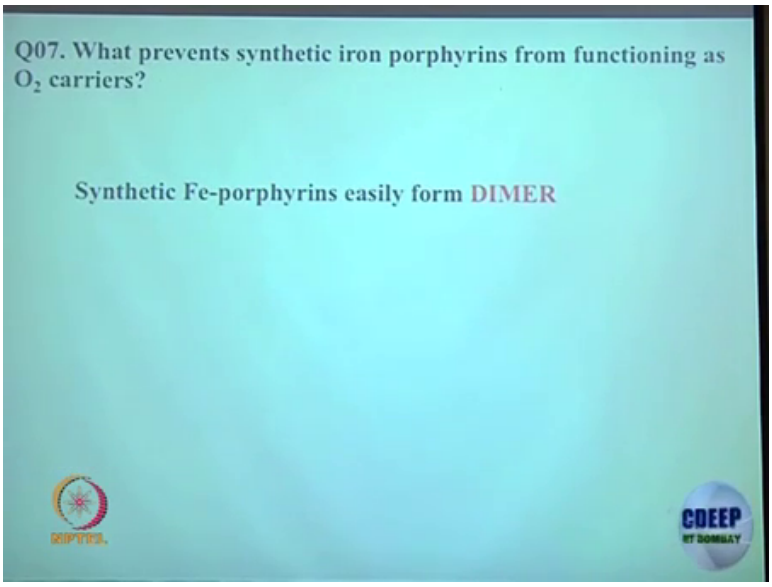


What prevents synthetic iron porphyrins from functioning as a oxygen carrier? We have discussed this umbrella thing we are talking.

Student: (Refer Time: 32:56).

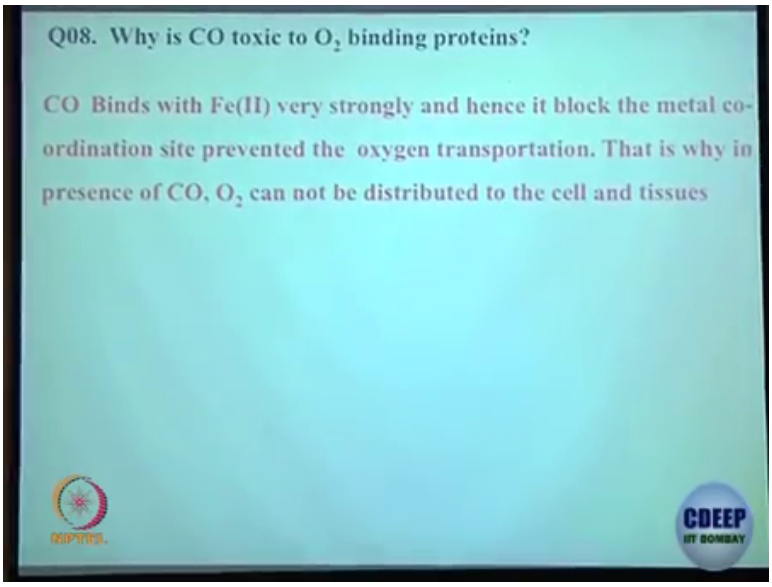
Do not write umbrella and this is just for explanation.

Student: (Refer Time: 33:00).

You can write if I am checking you can get marks if I am not you do not get marks. So, it prevents dimerization. Dimerization we have talk iron 2 plus and 2 iron center can give one electron to the oxygen, oxygen will be reduced to peroxide and it is dimer formation see some

of these term you must write, if you if this question is asked. The first thing you will be it will prevents dimerization. Even, if you explain a lot of thing you do not say that it prevents dimerization, you are not going to get the mark hopefully ok. Why CO is toxic?

(Refer Slide Time: 33:44)

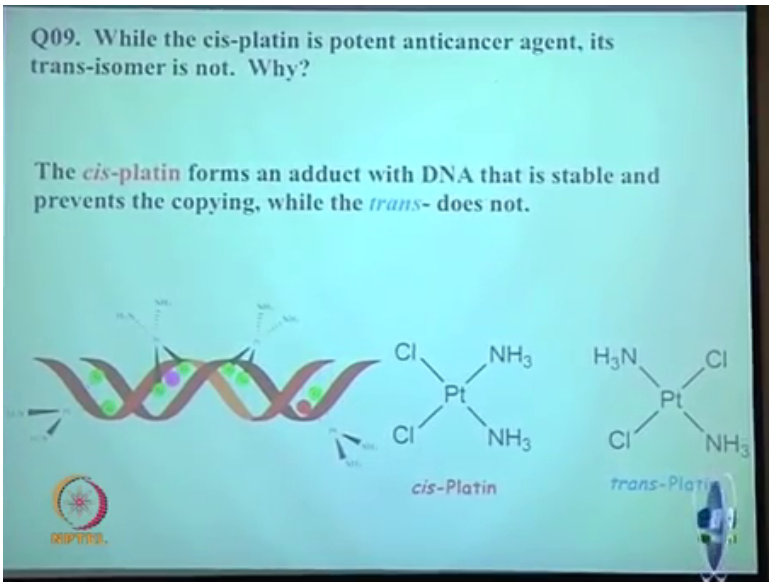


We have discussed.

Student: (Refer Time: 33:46).

Yes.

(Refer Slide Time: 33:48)



You know that while the cisplatin is potent anticancer agent it is trans isomer is not.

Student: (Refer Time: 33:55) transplatin.

Yes that is cisplatin that is transplatin transplatin and how it binds, who you are discussing? Right.

Student: (Refer Time: 34:04).

Show see the 2 guanine for example, are binding.

Student: (Refer Time: 34:07).

So, actually sorry the here actually chloride is going up going out all right.

Student: (Refer Time: 34:14).

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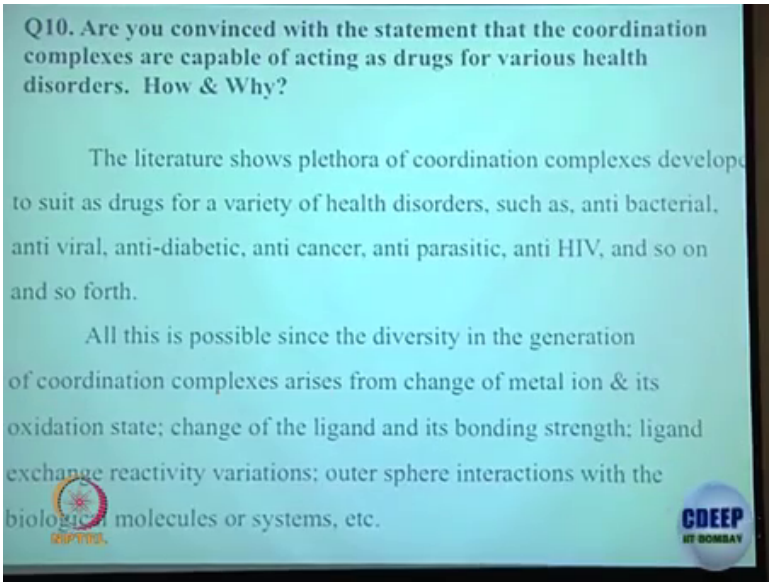
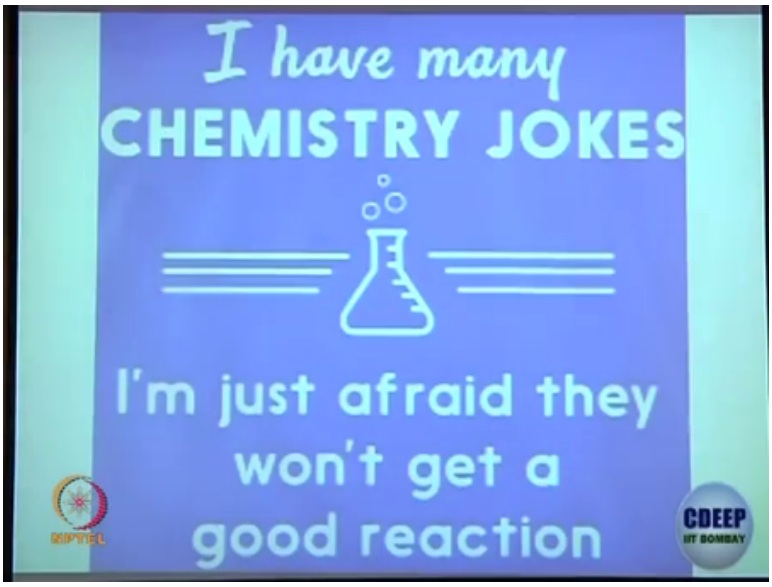


So, this is are you convinced are you convinced I do not think so.

Student: (Refer Time: 34:19).

Are you convinced with the statement that the coordination complexes are capable of acting as drugs, I think you better be come convinced ok. There are medicine I am sure some of you are taking or some of us are taking all of us are taking at some time of our life which has metal in it ok.

(Refer Slide Time: 34:38)



I think I forgot I do have jokes, but I cannot tell you now, but I will leave you with this.

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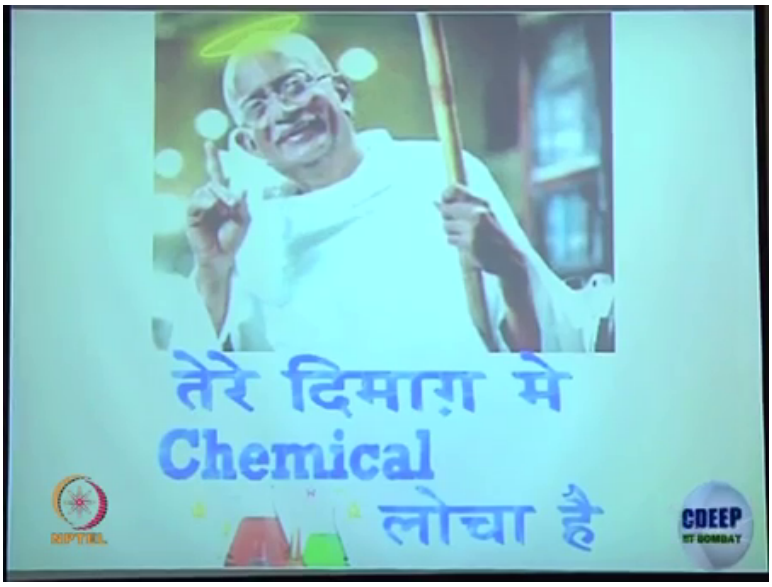

Student: (Refer Time: 34:47).

This is the last slide, a message from oh right.