Biological Inorganic Chemistry
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Lecture 31
Functions of Iron Ions and Iron Ions Proteins

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Welcome back to our class which we just start now to Module 7 and from sodium, potassium, calcium, magnesium all these things all main group metal ions are now finished. So, we have reached to the 7th week of class and where you can have the module 7 and will be talking now about the transition metal ions; so very important thing is the iron.

And when you talk about iron, we all know that we will be talking about the blood and all these things. So, iron ions in life processes how they are important; how they are particularly involving. So, in lecture number 31 today we will discuss about the functions of many of these types of iron ions and iron ion proteins.

So typically, we should know about what how much we should know about the corresponding chemistry as well as the coordination chemistry of iron ions and how we can consider all these when they are present in the different proteins.

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So, we will have many iron bearing biomolecules we will try to identify from a huge map of these biomolecules where the iron is present. So, iron when it is writing only we will write Fe is not the Fe, Fe ions are there. Then how we can bring another interesting molecule again from our very fascinating molecule what we learnt from our school days oxygen molecule. Doctors know, we also know even physicists know and everybody is knowing during this corona time also that how much important is your O2 molecule.

Then the reaction in the laboratory prepared molecules or the lab molecules, the synthetic molecule how the preparation of those synthetic molecules can let us to know that the different types of reactivities and the identification part whether your O2 is directly interacting with the metal ion center or not.

Then we will talk about little bit basically this is the introductory class definitely that we can have the corresponding understanding about the O2 transport and storage and then the Heme and Non-Heme iron ions. What does it mean and how it can be useful related to that of your hemoglobin and myoglobin.

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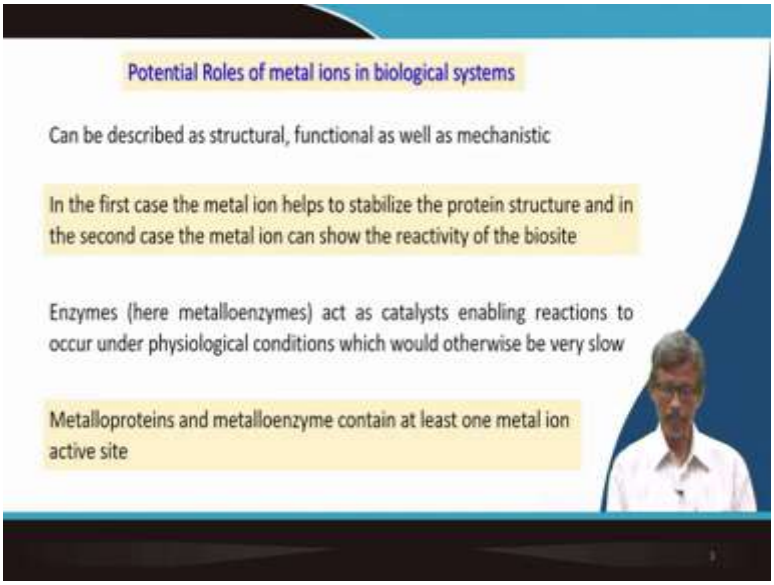

So, what are the different metal ions we can think of not only iron but the many number of metal ions already we know we have started our discussion from our sodium; potassium days now we have reached to the transition metal ions stage where now we have the most important thing what we are again starting from your college level that bio-inorganic chemistry part the first example we give as your iron example because we all know historically also it is important.

If you go to a geologist; if you go to a metallurgist, we know that we can have the corresponding stone age several thousand years back then we can have the bronze age then we can have the iron age. So, this iron age basically if you consider if you try to learn this iron age the iron pillar in Qutub Minar and everywhere.

So, this iron pillar if you now start thinking okay everything was there in the biological world but we are knowing only during the last 50, 60 or 70 years. So, how much important is all these apart from your typical iron as the elemental iron as Fe only but as the ionic form because once you go for these ions you will get the MIs always I abbreviate is m capital M and capital I and small s capital MIs in the different biological systems.

So, we can have the different functions so you can have the corresponding informations you can describe these in terms of the structural part. In our previous class what we have seen that the corresponding important structure; the bone formation, bone is our structure, bone is for anybody

structure all animal kingdom even other kingdom also you can have the corresponding solid structure of the bone.

How the bone is forming; so you can have not only that bone structure that is the material wise the material structure but when we talk in terms of the structures of the metal ions in biological systems we try to say about the structure of that particular metal ion environment, the protein structure, the coordination environment and the relative positioning of the corresponding amino acid residues.

Then their functions whether the structure is dependent on the functions as well as one the function is known will try to put the reaction mechanism, we should know the reactions and its mechanism and in mechanistic way will try to put that particular importance of that metal ion in this particular biological world. So, in the first case when you talk in terms of the structure you bring the metal ion, you try to stabilize the metal ion through coordination as well as the protein structure.

And in the second case when it is the corresponding functional one the metal ion can be present at the active side and can show some reactivity. Then if that metal ion is present in the other category of molecules will have now two categories of molecules will find within the protein environment; one will call as the metal of proteins and other will be calling as the metal enzymes. So, that under physiological conditions you can have some reaction but that if the reaction is slow, you need the corresponding biological catalyst.

So, the biological catalyst can enhance the rate of the reaction that is why we get the enzymes. So, both these two categories the metal enzymes and the metal of proteins at least they must have some metal ion active site otherwise we cannot consider them as the catalyst or we cannot consider as the important role to play by the protein molecule.

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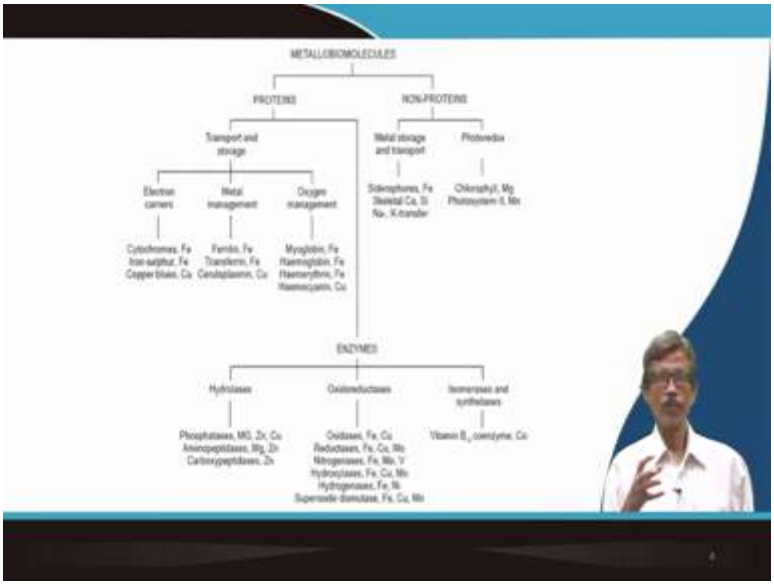

So, you have now a very big list do not worry about this big list. So, many all the common books you can have all these things, but this is the classification this is the family tree we call; the ancestral family tree of the metal biomolecules. So, from the top basically what you see this is your metal of biomolecule. So, if you start from reading it metal biomolecules to at the end basically either vitamin B12 coenzyme or superoxide dismutase. You have the all these arrangements basically in your hand.

But try to read this in such a way that you should be able to explain or define what is superoxide dismutase? If the table is given to you is something like that of your table or the family tree you should be able to tell under which category your super oxide dismutase is falling from the top. Definitely it is the metal of bio molecule then you come under two heads that means you can have the protein part and the non-protein part.

So, it is under the category of the protein and then you come at the enzyme. So, definitely super oxide dismutase is a metal enzyme; of what category? You can have broadly we will talk about 3 categories but nowadays is many categories are opening up, discovering we are day by day we are discovering many more activities due to that metal ions and its present within the enzymes which I know as your biological catalyst.

So, they are functioning as a oxido-reductase family, so your superoxide dismutase it can have the metal ions always try to remember if these are not metal atoms these are metal ions, MIs; so

you have the iron site, you have the copper site, you have the manganese sites in different oxidation states. If I say okay I know superoxide dismutase but the next question immediately will come to you which oxidation state you know.

If you do not know the most stable oxidation state only if you know the okay I know manganese in the oxidation state of plus 7 in potassium permanganate so you cannot say is a wrong answer. If you say that manganese is in plus 7 oxidation state which is highly oxidizing you cannot put manganese in plus 7 oxidation state within superoxide dismutase molecule.

So right now where we are focusing our attention if time permits definitely our 3 next weeks will be devoted in that way 3-4 weeks basically will go like that. Iron then copper then zinc and then all other like cobalt, nickel and manganese little bit all. So, next 4 weeks basically will go in these all these ways but it is not possible for me to cover the entire gamut of all these metalobiomolecules.

But whenever I find occasionally I will refer back this particular table you keep this with you like your periodic table or log table, another table or another family tree I am giving it to you, you keep it with you put where you are studying in your table in front of your table and you put it because the way I am will be talking next is that if I next go for your hemoglobin and myoglobin molecule that also you are studying from your college days.

But if I ask you to define in this particular in terms of this particular family tree so if you find out you try to locate where you have the myoglobin and hemoglobin. So, the positioning of this myoglobin and hemoglobin is important then you go back from there earlier I am coming from the top to the bottom, then you can go back from this particular point. So, your hemoglobin and myoglobin those are iron bearing biomolecules are showing can show the oxygen management. And they are of transport and storage category.

Transport and storage another categories also you see side by side for the metal ion management not metal management metal ion. So, wherever you sign people are writing metal try to correct yourself that whether it is truly metal or metal iron. So, it is basically we write it as metal ion also we write it as the metal but it should be definitely the correct version of it would be the metal ion.

So, metal ion management there are also some groups; then electron carriers then the electron management or the transfer management we can also see. So, the oxygen transport and storage molecules, so what it can store? It can store oxygen, it can transport oxygen and they are of protein category.

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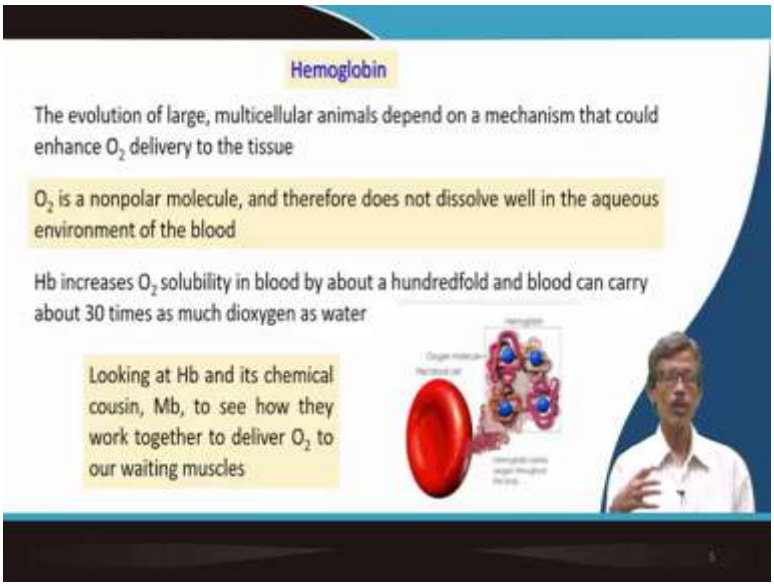

So, we now move to the hemoglobin; so is very clear is the two parts it has the another is the heme part another is the globin part and you know the definitions from your school days or even the college days that how it goes like the way we try to think. So, the evolution from your iron age if you consider so after stone age or the bronze age you have the iron age.

So, from the iron age to this point to up to this day basically you have the evolutionary processes and you have different multicellular animals but they all depend on the corresponding assimilation of oxygen, processing of oxygen and all these things they are also very much dependent in all these cases. But what we should know here very quickly that we know that the oxygen is a non-polar molecule, it does not have any charge and is basically no polarity is also and it can have no permanent dipole also like carbon monoxide.

So, it does not dissolve well in the aqueous environment of the blood. So, because the water molecule is a polar molecules that will try to attract only the polar molecules. But Hb the abbreviated version of hemoglobin is basically try to increase the O2 solubility in blood. So,

basically, we are comparing the solubility of O2 in water in one hand and solubility of O2 in blood in another hand.

So, this is the thing where we can go for the corresponding oxygen molecule then red blood cell the big disc is your red blood cell and you can have the hemoglobin and that hemoglobin basically as the oxygen transporting material throughout your blood and everywhere it can go and show something where you can have this thing. So, not only your hemoglobin but its chemical cousin that one monomeric part.

So, one you are showing four these units the four these units, so is not the iron we do not designate as blue but sometime for your color contrast people are tempted to show you in the blue color. So, because the crystallographic is not the recommended color for blue for the iron center. So, because it is visible in the red or yellow or orange background is easily visible to you for the metal ion center so definitely is a tetrameric unit.

So, hemoglobin is nothing but a tetramer of the monomeric part and those monomeric part is basically building you the myoglobin that is why your myoglobin is your cousin, chemical cousin of hemoglobin and they are responsible for delivering O2 to our muscles and our waiting muscle. The muscle is waiting to get that oxygen such that it can also consume ATB molecules and get the energy.

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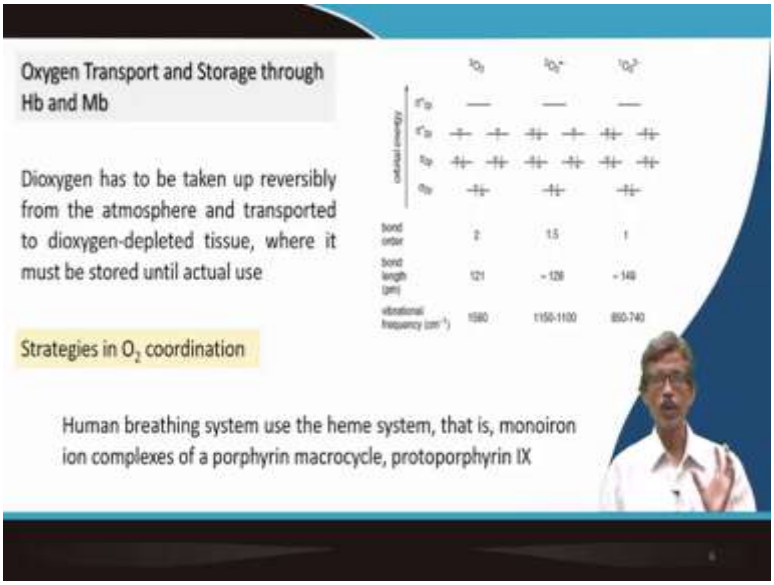

So, it is not the metal ion transport and storage do not confuse in this particular point again you go back to that family tree page and you can compare it what we are talking about so for this Hb and Mb molecule it is the oxygen transport and storage. So, O2 molecule we can have, the dioxygen molecule we can have in our hand and which can reversibly take up those molecules of oxygen, the metal ions can take up those molecules of oxygen and can be transported to the tissues.

Basically, in the lung will be taking oxygen and those oxygen hemoglobin can be taking up and that oxygen will be carried to your tissues and to the muscles and then ultimately to the cells. So, you can have the corresponding abstraction mechanism where you can take up and you can have the storing mechanism. So, some molecules will be responsible for the oxygen transport or O2 transport and some other molecule can be useful for your O2 storage.

So, if you look at the corresponding basic feature, the chemical feature of the different O2 bearing species. So, we know the molecular oxygen what we have in the environment the O2 molecule, simple O2 molecule the non-polar O2 molecule so you can have the orbital energies a little bit you recall back all you have studied in your chemical bonding classes so I am just taking the help of that chemical bonding class also that you have the triplet oxygen which is 3 O2; triplet is the state.

You have two unpaired electron, so 2 S plus 1; 2 capital S plus 1, 2 into half plus 1. So, basically, that way you get the corresponding value that means 2S capital S will be half plus half is 1 so for two unpaired electrons so 2 into 1 plus 2 plus 1 is equal to 3 is the triplet state. So, similarly, what would be the state for your another species which is O2 minus or 1 dot is the extra electron we are showing on 8 O2 and another one is your peroxide which is O2 2 minus we are not showing that extra electron.

So, if you have unpaired electron a big dot will sometime will show but it does not matter you may not show it. So, you can have the triplet state, you can have a doublet state and you can have a singlet state. So, will not only find all this thing but the bond order, bond length and the vibrational stretching frequency the O-O bond stretching frequency which is the quantity which you have to compare when O2 is binding to your metal ion center.

So, that will see afterwards also will take back the help the where your value will be coming whether it will be coming in the 1500 centimeter inverse or it will be coming at the 850 or to 740 centimeter inverse in resonance Raman technique. The resonance Raman stretching frequency so strategies for O2 coordination what you can think of for this O2 coordination?

You have to grab this or you have to take up the O2 molecule by some mechanism or by some species or by some material or by some biomolecule. So, when we breathe basically the human breathing system what does it mean basically it uses the heme system; what does it mean? What is heme then? We know iron so something associated with iron will be calling that as your heme species.

So, we can have when iron is present we can have now the designation that you can have heme iron and in another case we can have the non-heme iron species. So, is a single iron species a one iron species; iron ion either ferric or the ferrous and you have a macrocyclic ligand already we know from our very beginning of the ligand classifications and the nomenclature and all these one type of ligand we call is the protoporphyrin 9, So that protoporphyrin 9 is basically category.

So, many types of porphyrin molecules are there depending upon the substitutions on the pyrol carbon the two positions of the two, the outside positions of the payroll unit you can have the substitutions that will see in detail; how it binding the iron center? What sort of coordination you expect? So, what is the structure then? If I give you the ligand you know the ligand structure then you put the metal ion; what should be the structure of that particular species; that means what would be the structure of your heme iron. And what heme iron will do next?

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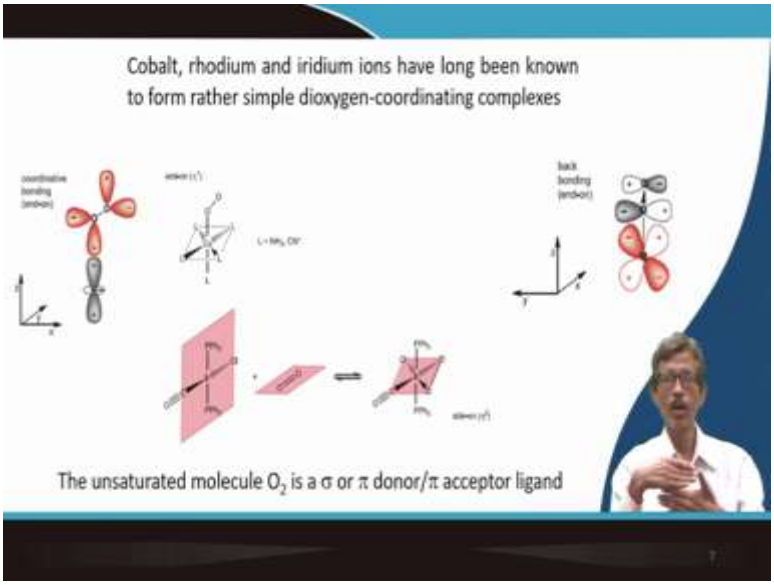

So, before going into detail of all these thing because we are talking here only the iron coordination chemistry, iron binding to the porphyrin on any other ligand and as well as the oxygen coordination. So, if you talk not iron but other synthetically available or the naturally available but processed synthetically in the laboratory the metal ions like cobalt in the same group the rhodium as well as the iridium can have some affinity for O2 coordination that we all know.

From our typical coordination chemistry classes, we know that if you have a cobalt center and the cobalt we know that the hexamine complexes are very easy to make the cobalt hexamine complexes but also the pentaammine complexes aqua pentaammine. So, if you have a aqua pentaammine type of complex or aqua pentasano type because L is giving here as the example as ammonia the nh3 or cn minus. So, aqua penta amine amines are all neutral ligands.

So, you can you do not have any charge consideration on the cobalt center but if you put more number of cyanides you have enough number of negatively charged species on this but your property will definitely be changed because you can have the donation and back donation that the bonding parameters and the bonding conditions and the bonding character will be changing between that cobalt and the oxygen.

The terminal oxygen of that particular dioxygen molecule when it is binding in the end on fashion which is known as eta with a superscript 1, eta 1 coordination so this eta 1 coordination

of this O2 is giving that way and the bottom also we see another variety but when you have this eta 1 coordination for this unsaturated molecule, we know why it is unsaturated molecule because you have only partially occupied those pi star levels.

So, you can have one extra electron over there so it can have the corresponding affinity for taking of oxygen next electrons. So, it can be a pi or sigma donor or it can be a pi acceptor ligand what sort of ligand it is? So, you should know by the typical nomenclature or definition of the O2 molecule.

So, in the 3 directions; 3 x y z directions you can have the corresponding bonding from the end on. So, end on bonding is basically the corresponding sigma donation because you have the head on coordination or head on binding from the corresponding matching orbitals of your O2 to that of your orbital which is available on cobalt.

So, that gives you the corresponding donation and you can have also in another direction so that you can have the corresponding you can have the bent bond basically so it is basically going in that direction but you can have this corresponding lobes of these orbitals, atomic orbitals we are talking about and the corresponding d orbital on the cobalt center.

So, you can have the side on overlap which is the pi interactions and this is the acceptance basically. One is the donation and then it is returning back the corresponding electron density from the field level of the metal ion center to function as a pi accepting ligand.

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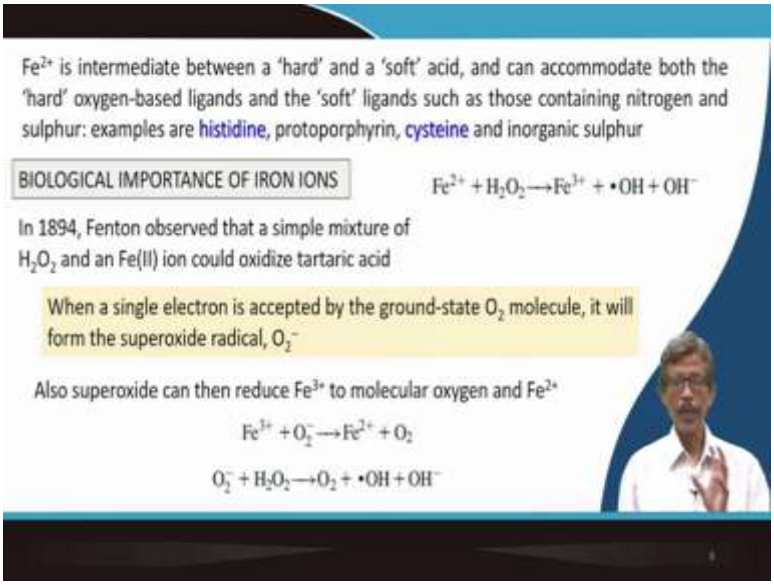

Then what we see here is that your Fe 2 plus is intermediate type is neither hard in true sense and a soft center, so it is the borderline. So, the borderline case is basically try to accept all the 3 different types of donor centers what we can think of that means O N S; oxygen, nitrogen and sulfur. Origins are for oxygen you have the carboxylatin, nitrogen you have the histidine side chain and for also the protoporphyrin which is a tetradentate micro cyclic ligand and the cysteines is the sulphur one and inorganic sulphur what will be talking in case of iron sulphur proteins.

Then you bring that particular iron little bit of that chemistry what you know from the laboratory world or the synthetic world then you bring it to the biological world and you now try to find what biological effect you can see if your iron center is present in there. So, two things are there; one is your coordination chemistry and second is your redox chemistry or the redox thermodynamics.

So, long back you see in 1894 professor Fenton he was working at that particular time and he was thinking and getting some informations that a simple mixture of hydrogen peroxide because hydrogen peroxide was well known to us even ozone was also well known to us, so at that particular point when we do not know much about all these basic properties of these molecules or the atoms and all these things that we that observation is very simple that only if you the corresponding Fe 2 plus that iron in the lower oxidation state the ferrous state if H2 O2 is there it

can basically oxidize that hydrogen peroxide is functioning as the oxidizing agent to oxidize the tartaric acid.

So, basically, is oxidizing and giving you a dihydrogen fumeric acid. So, one double bond is forming due to that oxidation. So, if you write immediately that Fe 2 plus then H2 O2 what is happening Fe 3 plus then hydroxide ion and the hydroxyl radical. So, that basically is a very important reaction we call these added phantoms reagent because you are able to produce not only hydroxide ions H O minus but also the hydroxide radical.

So, when a single electron is accepted by the ground state of the O2 molecule so if that sort of change is possible that means single electron transfer reactions can take place then what we can see here that you can have the hydroxide ion and that particular hydroxide ion and you can have the O H minus as well as the hydroxide radical.

Then if the single electron transfer can take place on the O2 molecule it can give you the super oxide anion that means O2 minus dot also. So, that this super oxide can reduce Fe 2 plus again to molecular oxygen so super oxide can function as oxidizing agent. Hydrogen peroxide is oxidizing agent oxidizing your Fe 2 plus similarly super oxide can also be a corresponding that particular super oxide basically can reduce the thing.

So, that can function as a reducing agent then so this is basically to and fro movement one which direction you can move for the oxidation and which direction you can go for the reduction producing Fe 2 plus and O2. So, now if you add up this first two reactions or the first two equations this top one and this second one will end up with this equation that are super oxide can react with hydrogen peroxide producing O2 back. Then O2 plus the hydroxide ion and the hydroxide radical, so these are the basis of your phantom chemistry.

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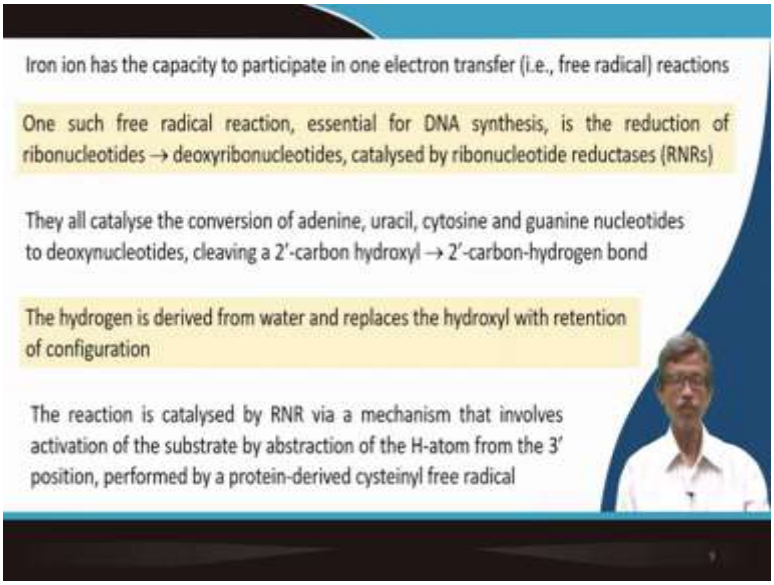

And iron-iron has the capacity to participate in one electron transfer that means the free radical formation. So, free radical reactions are there and that those radical reactions are very important and very interesting also that since iron is responsible for giving us the free radical thing we are able to produce a free radicals.

Out of that iron center and obviously your hydrogen peroxide is there how you get the hydrogen peroxide we know that the reduction of O2 molecule by two electron reduction of O2 molecule can give you hydrogen peroxide. So, initially if your O2 can be reduced to hydrogen peroxide you will have the hydrogen peroxide and you bring now iron and you will be able to produce the radicals.

So, one such very important reaction is the fundamental reaction for your DNA synthesis is your that particular mechanism will see for ribonucleotide reductases RNR. It is the reduction of ribonucleotides to deoxyribonucleotides O H will be converted to H then Co H will be converted to Co H system. So, in all these cases for all these nucleotides based on adenine, uracil, cytosine or guanine in all these cases we will just basically talking or handling that particular sugar part.

So, sugar part you have the two prime carbon molecule hydroxyl molecule will be craving to 2 prime carbon hydrogen bond that mean 2 prime Co H will be converted 2 prime CH bond that is the very fundamental reaction you can write it down in that way. And basically, will be doing

that hydrogen is derived from water and replaces the hydroxyl form with the (reduction) retention of the configuration.

So, how the configuration will be changing for the sugar molecule that will see and is catalyzed by different RNR molecules. So, RNR molecules are there which involves the activation of the substrate by abstraction of the hydrogen atom. If your free radical is available so your HO dot is available it can immediately take up one hydrogen forming water molecule and the 3 prime position basically if you use that and basically can perform by a protein derive cysteine free radicals is not that a radical which is coming from other groups.

So, there are the little bit complicated at that particular point but since we are talking about the phantom chemistry, we are talking about the iron coordination chemistry or the reaction chemistry one is your coordination another is your redox chemistry. So, this is iron based redox chemistry, phenton is a very beautiful and typical example of iron based redox chemistry then that redox chemistry can be transferred to other iron biomolecule which is your ribonucleotide reductant but it can be a complex one when you have the cysteine free radical.

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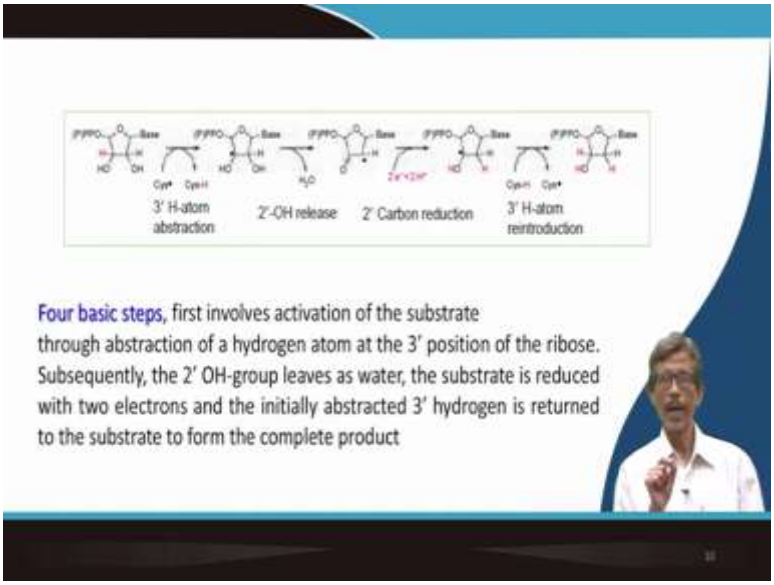

So, that cysteine will free radical if you bring and that basically happening for many steps of all these reactions. So, 3 prime hydrogen atom abstractions so 3 prime hydrogen atom reintroduction so that basically gives us all these things such that your OH-OH can be converted to your H form CH form only. So, it can have 4 basic steps; you can see that the top figure you

can have four arrows. So, these four arrows basically your four steps and they are leveled nicely also you see all these things nicely.

Try to understand nicely what are the different steps are happening from the corresponding hydrogen atom abstraction to hydrogen atom reintroduction and all these steps are written in detail do not worry for learning all these things what I am telling but you should read it again and again and you will find stepwise also basically that is why these things have been taken from the textbook and given it to you as your study material also this part also.

That you can see and you can read and you just work it out and you practice it and write it all this thing otherwise it not be possible to find where your free radical is forming so carbon dot you see many places you write dot on the carbon. So, how to find out how to determine the carbon dot or any other dot what is forming the radical what is forming; how to detect it in the solution also when the reaction is going on.

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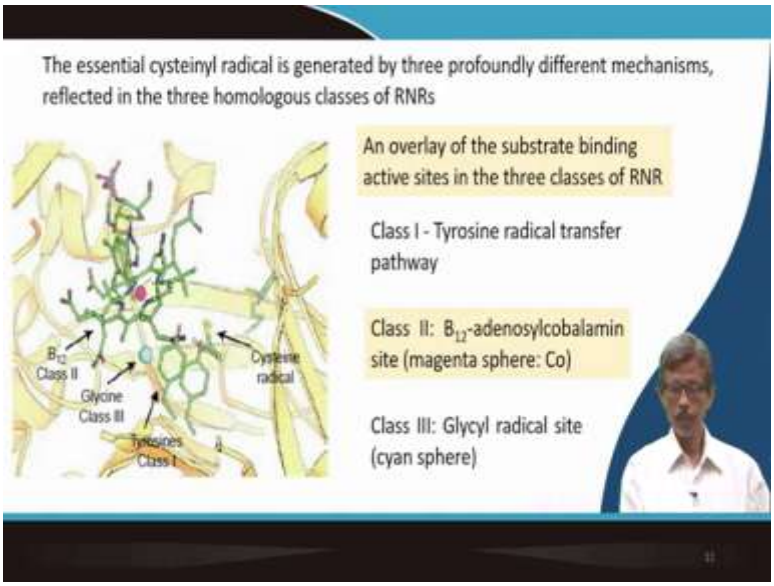

So, the cysteine radicals are forming there directly and in the big environment and all these things but what we see the position basically. The cysteine radicals we require, the system radical, the sulphur radical, the file radical SH is there, S minus is there then S dot. And along with three other supporting points or supporting phases are there which are class 1, class 2 and class 3.

So, basically, the substrate binding active site for the different classes of RNR; class 1 is the tyrosine radical, for the first one is the phenol bearing tyrosine radical then O is O minus then O dot then the vitamin B12 we all know that the B12 adenosylcobalamin can also give you a radical formation and also the third category which is the glycine base.

So, not only the removal of the proton as H plus give you the charge but also you can take out the another electron from there making that particular one as the radical, so in essence what you can take out? Proton you take out first then the electron you take out, you are basically abstracting hydrogen atom. So, abstraction of hydrogen atom will leave behind you the corresponding radical.

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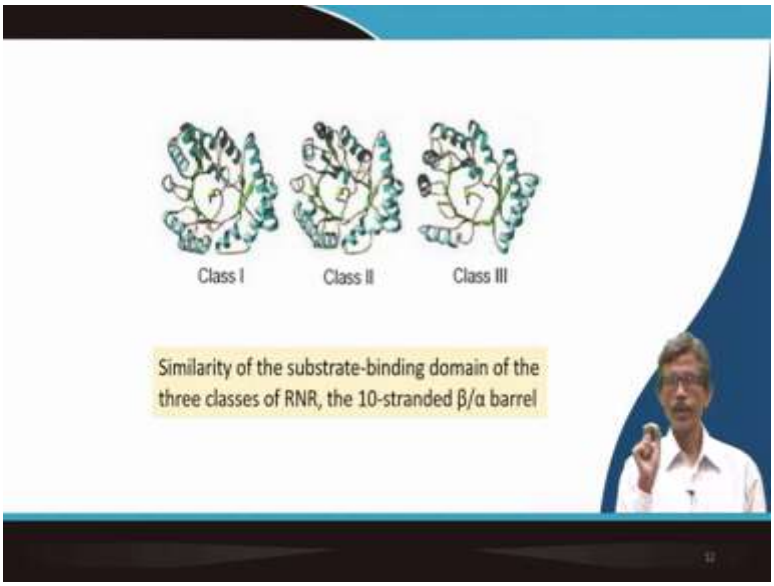

So, we will have class 1, class 2, class 3 and the different conformations basically ut to see the 10 stranded beta alpha barrel; how you see the look, look wise they are different. So, your critical eyes should also be able to identify which one is class 1 and which one is class 3 and you should be mastered enough train yourself in such a way that three figures are given to you, you should be able to tell which one is for class 1, class 2 and class 3 ribonucleotide reductases, okay.

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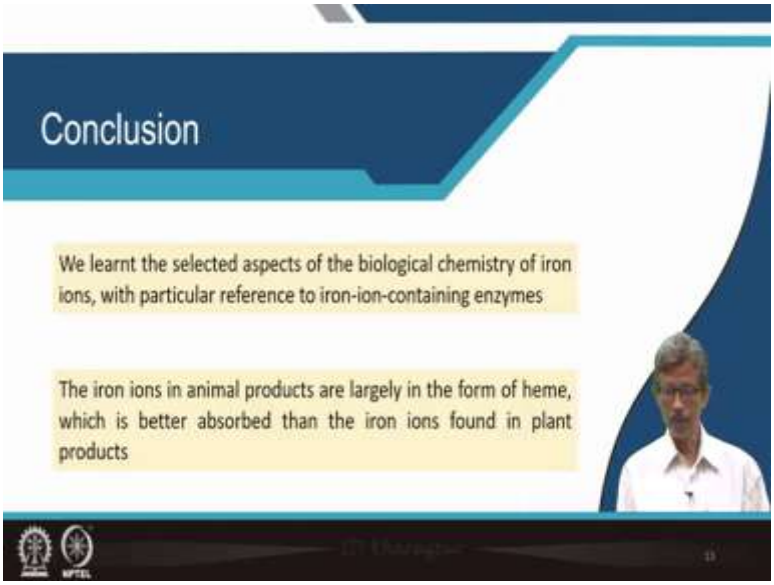

So, now we have reached to the conclusion page where we have seen that what are the aspects we have seen for the biological chemistry or the biochemistry or bioinorganic chemistry of iron with particular reference to the enzymes where iron ion is present. And these iron ions in the different animal products basically we know these are all heme iron. They are largely in the form of heme iron which is better absorbed than the iron ions what we can available from the plant products. So, in future we will discuss all these things what we should take whether we should take mutton we can should the meat or we can only the leafy vegetables wherefrom we get these iron.

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So, page on human iron metabolism page which is very important to start with the starting point of your reading in the Wikipedia page and the book, okay. So, thank you very much for your kind attention.