Biological Inorganic Chemistry
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Lecture No. 08
Potential ligands of different type

Hello everybody, so we are still continuing with the ligand system. So, where we are in lecture 8 of Module 2 that the different biological ligands we are giving examples and how the biological ligands can have available the availability of the corresponding donor groups as well as it is available to bind the metal ions. So, we can have the different potential ligands potential ligands in the term that you can have the different ligands.

Which are available to bind or grab the available the bioavailable metal ions in the living system. So, what are those different types of ligands we can have.

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So, the concepts what we will be covering we will try to cover in this particular. So, if we can have a donor atom. Which can be charged on neutral which is very important. Now that so far we have discussed about the water molecule. But we have not brought any charge on it but we all know that water molecule itself is a weak acid. So, it can go for the protonation it can produce hydroxide ions, it can produce oxide ions also.

So, that particular aspect is also valid for any other donor groups within the ligand say the carboxy end of the glycine molecule. So, the carboxyl end of the di glycine molecule falling deprotonation it can have a charge. So, your ligand which is the bidentate one in our last class we have discussed it that you can have a donor groups from nitrogen and the oxygen. And

now it can be charged by dented ligand which is not true for ethylene diamine, ethylene diamine is a neutral molecule.

So, not only the donor atoms but also the chelating ligands can be charged can be neutral or some groups say phosphate groups, the carbonate groups or the nitrate groups can also be a donor atom can supply or provide the oxygen sub carbonica carbonate ion, the oxygens of the nitrate ion and the entire molecule will see small molecules will consider also. Then low molecular weight inorganic ligands like just now, I told you that you can have the corresponding chloride anion, bromide, fluoride, phosphate and so on.

Then hard and soft acid based theory can be applicable. So, that particular principle or rule of HSAB can basically dictate the nature of the metal ion binding or coordination. Then how the different types of Lewis acids which are available which are typically available in the biological world can be discriminated by the available ligand system. Similarly, how we can modify the ligands? That ligand modification is also possible inside our body inside our system that means the C2 ligand modification.

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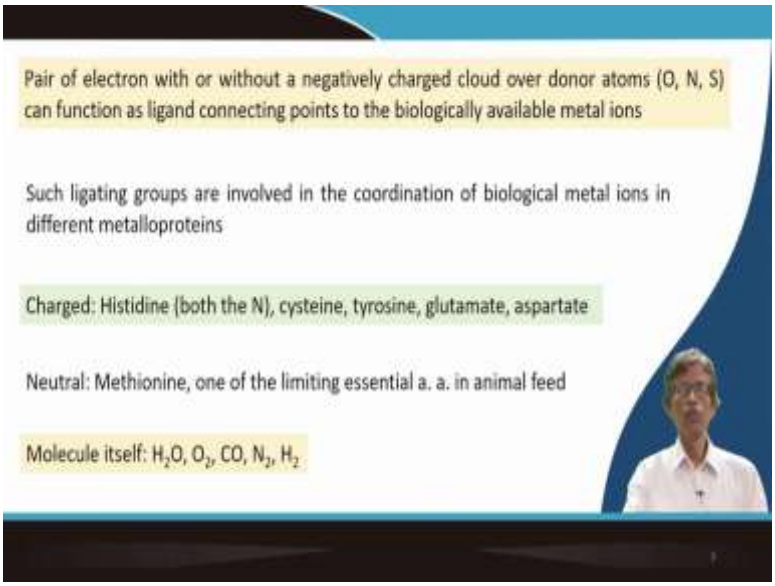

So, as we have seen that pair of electrons are important. Which are there on the water molecule itself the water molecule itself has two pairs of electrons and those two pairs of electrons when they are available for coordination. We at least get two coordinate bonds from the simple water molecule that we have not discussed yet. We are talking about the formation of a single mono dented coordination of the water molecule.

But if we are able to utilize both the lone pairs of electrons on the water molecule. It can be a very good bridging ligand. And we call as a symbol as mu, mu is the bridging function which is denoted by the bridging function as mu. So, mu H2O is the bridging water molecule when both the two electron pairs are utilized for bridging two metal ion centers. That means if we can have one iron at the left and another iron on the right.

You can have a water molecule in between such that you can have two coordinate bonds to Fe1 on the left and Fe2 on the right. So, you can have also the negatively charged cloud over donor atoms. If your oxygen is now charged through deprotonation there is hydroxide ion formation or the nitrogen also. The amide function say the CONH functions we are discussing at some point the CONH of the amide backbone.

And we all know that the deprotonation of CONH is also possible. So, when you take out that hydrogen from the NH function like water molecule. But the pKa values are different. So, we get like that of your hydroxide ion. We also get the amide as the N minus the charged nitrogen center on the amide backbone. Similarly, other pendant groups which will be available to us we will see also certain good examples can also be charged.

The thiol, yes is very simple to that of your oxygen. So, the thiol function we all know the corresponding thiol function of water molecule is H2S only the hydrogen sulfide. So, if it goes for deprotonation like water molecule it can also give you HS minus or S2 minus finally. So, these are very good connecting ligands or the clips or the connectors between the metal ions centers for those metal ions centers which are available in our body in the biological world.

So, what we now see that such ligating groups when they are involved in the coordination of biologically available metal ions in different metalloproteins. So, we have to find out only that particular part, that particular part which can supply the donor groups or the donor atoms to grab or to collect the metal ions in the system such that you are able to form the corresponding metal ion complex.

So, if we take only some examples that histidine we all know the backbone is the corresponding immediate jewel as the r function on the glycine backbone. And the histidine is having a imidazole hetero cyclic ring and that imidazole hetero cyclic ring all we should know. When you read these you should have in your mind that how you know these that what is histidine.

And whether that part of the histidine of the amino acid residue can function as the ligand. So, if it is a ligand but it is not a simple hetero cycling ring. Imidazole has two nitrogen within the 5 membered ring; 2 of them are nitrogen and 3 of them are carbon within the 5 membered ring. So, within that 5 membered ring whether both the nitrogen centers are available for coordination to the metal ion center or not is important.

Similarly, cysteine what is cysteine is a sulfur bearing amino acid residue. What is tyrosine? What is glutamate? And what is aspartate? So, we will have a list of 20 amino acid residues. In one of our previous class I told you that at least you try to a little bit understand. Because these are our ligand building blocks without these amino acid residues or without the knowledge of these amino acid residue the chemical structure of these amino acid residues will not be able to understand even the formation of the protein chain.

And the function of that particular protein chain as a big macro ligand around a particular metal ion center. So, this is a very important thing that you should know it about these amino acid residues. So, if you have 20 21 amino acid residues in your hand. So, these are nothing but your alpha weights basically. So, only this particular information is useful to understand this particular part of chemistry.

Which is mostly dominated by the biological world. Then once we have the charged one we can have also the neutral one where there is no possibility of deprotonation. And which is a very good essential amino acid example of methionine. And it is available in our food and in animal feed also. Then the whole molecule itself summer we are talking about that whole molecule.

So, if you talk about the water the water coordination we can talk about.Similarly, the oxygen coordination so that is important thing that we will consider at some point that you have the myoglobin molecule in our blood. So, that myoglobin molecule can coordinate then your the entire molecule of oxygen. So, your oxygen can function as a very good ligand. Similarly, at what point we can have the carbon monoxide, nitrogen, and hydrogen.

So, this molecular thing can also be a very good ligand, small molecule can function as a ligand to the metal ion center.

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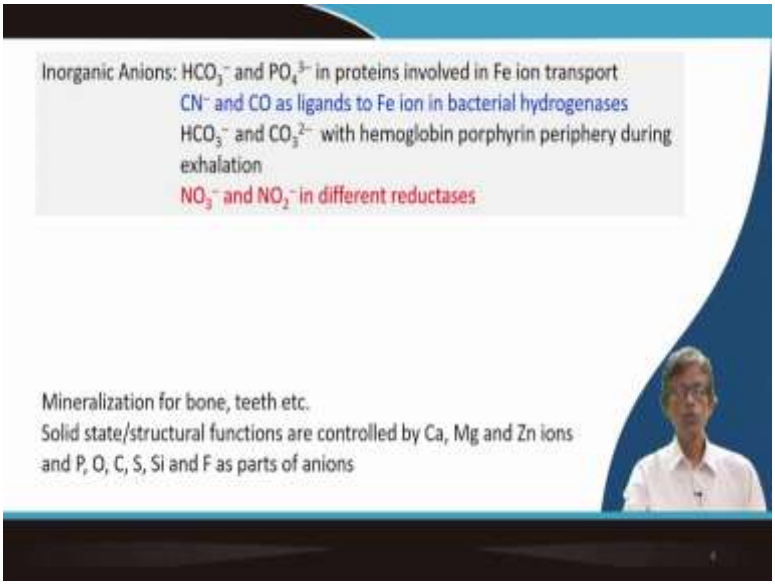

Then we talk or think about the corresponding inorganic anions. So, one simple example is the corresponding an anionic form or the free acid form of carbon dioxide. When you consume oxygen by our blood hemoglobin or myoglobin molecule. We all know that oxygen can be utilized for burning of our food material to produce certain amount of ATP molecules. Which is our nothing but your energy currency in our system.

We need to run our system our bodies also is a machine. So, what is your fuel to run this machine it is your ATP molecules. So, your energy currency can be produced if you have in your hand the burning of certain amount of food material. So, while doing so we basically can produce carbon dioxide. So, we are burning carbon, carbon is the ultimate fuel basically like our fossil fuel. So, burning up carbon with oxygen give you the corresponding carbon dioxide.

Then the hydration of that carbon dioxide. The hydration of that carbon dioxide is also involved the corresponding participants of some metal O enzymes like carbonic anhydrase. Which will convert the carbon dioxide molecule to free carbonic acid H2 CO3. And that H2 CO3 falling deprotonation can produce the anion. So, you will get a very good anion which can be there or try to be there close to that of your iron center which is positively charged or any other catatonic matal ion center.

Similarly, phosphate another very important inorganic anion the bioinorganic anion. Because we will not have enough time to talk about the bioinorganic chemistry of all these anion basically. Because we will restrict our attention or focus mainly on the metal ions. But while we will talking all these things I will give you the typical examples the role of these things

the formation of this phosphate, phosphate also we can have is a very important micronutrient for our survival also.

So, those phosphates our bone formation, our teeth formation is required. And these basically are involved for iron ion transport. Why we write is this is also important to understand over here that Fe ion transport we are writing it not showing the charges two plus or three plus that means both ferrous ion and ferric ion are important. Then at one point we will find that how the cyanides can be formed biologically. And see also as the ligands to iron iron in bacterial hydrogenases these are very good ligands basically. We will find in hydrogenases the CN minus as well as the carbon monoxides are good ligands to your iron center.

So, while we make these oily produce the carbon dioxide it can protonate or it can hydrate to give you the carbonic acid. And in other way it can go for deprotonation forming HCO3 minus which is your bicarbonate anion or CO32 minus which is carbonate anion. So, when we go for exhalation so during our exhalation we just removed the carbon dioxide from our body in these two forms.

And your hemoglobin molecule again is responsible to carry those molecules or anions from our lung to outside our body. And in some other cases also the nitrogen fixation we all know the nitrates and nitrites are important for the different reductases and the redox and reactions. So, this phosphate as well as the calcium ion is important for mineralization of bone and teeth etcetera.

So, not only the solution chemistry but also the solid state chemistry is important. So, the biological world is further dominated by the formation of many such solid products. The formation of our bond the formation of our teeth which has a very direct correlation to that of our study we go for that particular study in geology. So, in the geological world we know about the mineralization process.

Similarly, from the elemental constituents that means Fe3 plus in aqueous medium in your biological fluid. How this can be stored in our body for future use also. So, that process the formation of bone, the formation of teeth, all are involving your mineralization process. And in many cases we will find that the cations are important not that your phosphates or hydroxides or oxides are important.

But also your cations are there that is why we get a huge structure. Which is neutralized by your oxides, hydroxides, and carbonates, phosphates, silicates and all. So, those anions

basically of phosphorus, of oxygen, of carbon, of sulfur, of silicon, and fluoride bearing anions are important to grab or to trap these metal ions centers like calcium etcetera.

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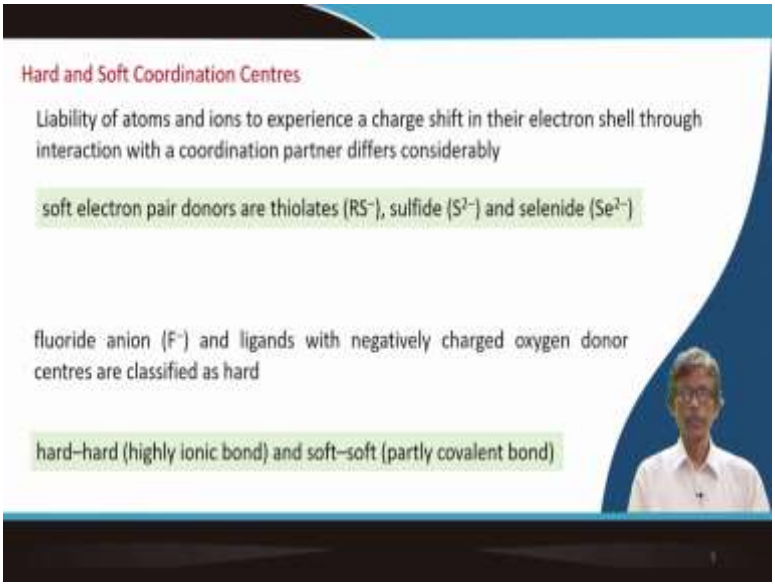

So, we will then again we will follow the HSAB principle. So, we will have two types of coordination centers. Either the soft center or the hard center that means soft Lewis acid center or the hard Lewis acid centers which are your metal ion centers. So, those hard and soft metals ions centers can have some important thing to follow.

So, the liability of the atoms or ions to experience a charge shift in their electrons shell, how much electrons are there surrounding a particular metal ion center or a donor group. Say nitrogen center or the oxygen center when the corresponding bond is forming that means the coordination partners are coming to each other. That means you have Fe3 plus ion and you have the water molecule. So, you bring that water molecule to that of your Fe3 plus ion and you have the interaction, we consider those interactions are typically ionic interactions.

But the distribution of the electron density that means the electron cell will be part out such that there will be some movement of the charge density in between these two groups of atoms. That means the iron center as well as the oxygen center and will be localized in between. That is why the availability or the probability of finding the electron density along that particular bond will be maximum.

So, how that soft center will be polarized or the hard centered should be polarized during the formation of these sort of coordination bonds. So, this interaction is important. And if you have a soft center and the soft electron pair we now considering the electron pair on that

particular big anion like your Sulphur center. So, that big iron, sulphur center we will considering at the soft center. Because it is possible to polarize that particular electron density which is not tightly held on the sulphur center and the sulphur size is also big.

So, it is true for ties let it is true for your sulfide and it is true also for the selenite. Because these three are there for your organic part of your amino acids. Then as typical inorganic part is the fluoride anion our teeth formation and all these. That is why you use the fluoride toothpaste. And the other ligands with negatively charged oxygen donor centers are classified as hard because they are small and it is very difficult to deform the electron density around these centers.

So, is basically a hard donor. So, hard donor centers will try to stabilize or form bond to the hard metal ion centers. So, you have the corresponding interactions will be considering these the hard interactions having a maximum amount of ionic interactions. Or the charge charge interactions. As we consider in terms of the crystal field.

The crystal field you have like your sodium chloride cation is a in a crystalline form there is a cation. And anion the chloride is also in the crystalline form. So, when you treat this particular thing as the crystal field theory we can have also the harder thing. But when you go for the soft, soft, we allow some covalency. That means we will be deviating from the typical assumption of hard hard interaction in the crystal field.

Or the interaction which are typically ionic in nature. So, that also gives us some good informations when the interaction is soft soft instead.

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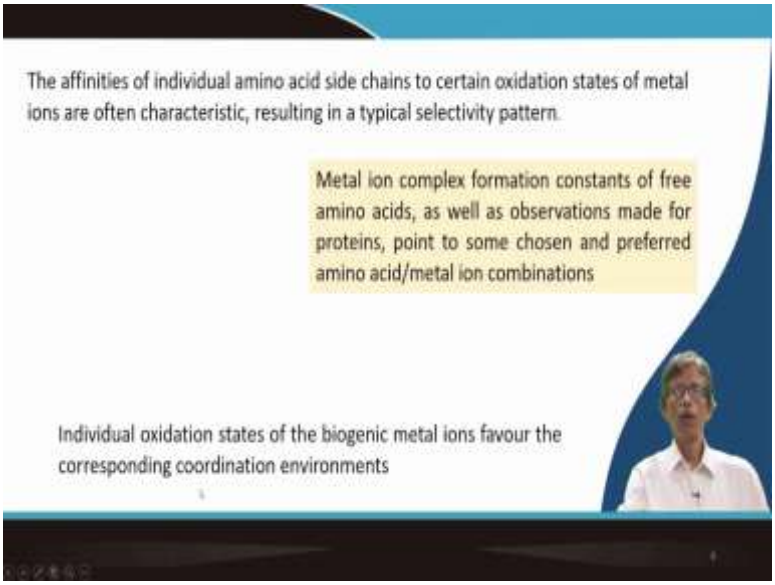

So, the affinities of these amino acid residues if we go back to those amino acid residues. How these amino acid residues can stabilize the different oxidation states. Suppose two oxidation states we are talking from our previous class also or the from the very beginning also. That the ferrous center as well as the ferric center. So, if you have the ferrous center or if you have the ferric center so what are the donor groups or what are the amino acid residues will be suitable to stabilize that particular oxidation state.

Not very high or not very low oxidation state it is only one unit difference. So, you will have a typical selectivity pattern for these groups to stabilize the different metal ion complex fragments or metal ion complex species. So, during the formation of this metal ion complex says the free amino acid residues. We will find that as well as the different observations made for proteins. Point to some chosen and favored amino acid on metal and combinations.

So, as we find a metal ion is the hard one say Fe3 plus. So, definitely the oxygen donors centers will be your preferred donor centers. Which can come to bind to your metal ion center. So, these particular combinations what we get there is that individual oxidation states of the different biogenic metal ions basically favored the corresponding coordination environments.

So, if we have a metal ion in class two or class three oxidation state. And our challenge is that how you can stabilize that particular oxidation state. So, you have to give a an appropriate coordination environment. Suppose, we want to stabilize the ferric center. What you should give? The ferric center as per of our discussion we have already considered it as a hard center.

So, if we find that harder interaction is the most stable interaction. And the most stable arrangement we can get. So, we will try to bring more and more hard donor centers around that ferric ion. So, the oxygen or sometimes the borderline nitrogen donor can be useful. To stabilize this particular ferric iron center. But if we try to stabilize the ferrous center sometime we will find that during reduction also that electron transfer can take place between these two centers the ferric center and the ferrous center.

And during that particular process, one of this oxidation state will be definitely destabilized compared to the other. So, it is the ligand environment, the donor atom environment will dictate us that which particular donor atom environment can stabilize that particular oxidation state. And that also give us the corresponding potential value, the thermodynamic potential

value that is E0 value. How quickly we can oxidize a particular center or we can reduce a particular center that we can also see there.

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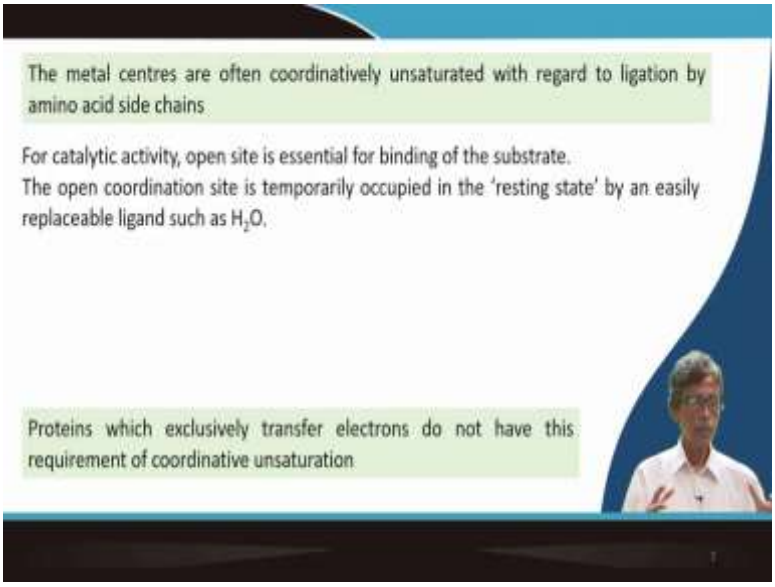

So, when these metal ion centers quite often we have already seen that they are coordinatively unsaturated. In terms of your amino acid side chain coordination. Suppose you have one bidentate ligand say like your ethylene diamine. So, NH2 CH2 CH2 NH2 is coming. And that ethylene diamine backbone is only one of them. One of the ethylene diamine backbone is coordinating to a particular metal ion center say again Fe3 plus.

So, other positions as I told you that can be occupied by water molecules. But now if you bring in amino acid residue for the protein chain. Say histidine residue so the histidine nitrogen any one of the nitrogen of these two of the heterocycles ring can come. And bind to that coordinatively unsaturated center of iron or that echo bound what the corresponding Fe3 plus center.

Because it will try to kick out those water molecules surrounding these iron 3 plus site. And also for our catalytic activity this open side is important some vacancies is important. Because your substrate will come and occupy those positions. So, if you have your iron center occupied by two other oxygens, one good example of oxygen bearing bi dentate ligand is acetyl acetone.

So, if you have some site which are occupied still by water molecules so, the open coordination site is temporarily occupied in the resting state by easily replaceable ligand such as water. If water molecules are available those water molecules will come and bind to that

particular metal ion center. But when substrate is available the substrate will come and basically replace those water molecules. So, these proteins which are exclusively responsible or transferable electrons do not have this requirement of coordinative unsaturation.

That this particular tie line will basically explain in detail afterwards that when you want to have the catalytic activity you need coordinatively unsaturated metal ion site. But when we look only for electron transfer because there are many number of proteins we know that those are known as electron transport proteins. And having a iron center also. But we do not need any coordinated vacant site for that particular electron transfer reactions.

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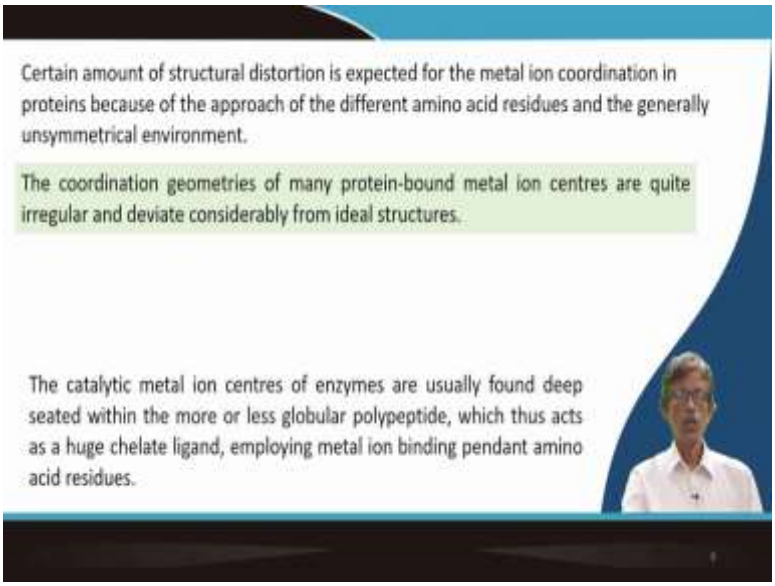

So, certain amount of the structural distortion is expected then and the metal ion coordination in all these proteins basically approach the different amino acid residues. And generally we get an unsymmetrical environment because now it is connected to the huge or large protein envelope. So, definitely we will have a distorted situation and the coordination geometries of these protein bound metal ion centers are irregular in structure and deviate considerably from the ideal structure.

So, ideally when you have a hexagonal iron center which is ideally octahedral in nature. But then protein will come and bind replacing all 6 water molecules or 4 or 5 water molecules we will get a situation where it is highly distorted. But if you have a catalytic metal ion center of enzymes the different metal O enzymes.

We have classified these basically earlier what are metal O proteins and what are metal O enzymes. And those are deep seated within more or less globular polypeptide which is

nothing but your protein chain which does acts as a huge chelating ligand like your EDTA like your desferrioxamine as we just seen. So, those basically employ the metal ion binding by the pendant amino acid residue.

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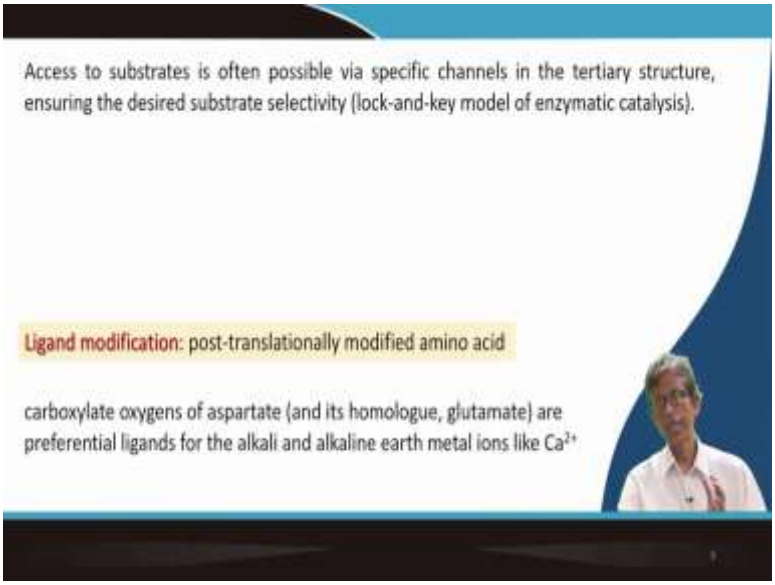

So, the pendant amino acid residues are therefore crucial are important to have the coordination and sides. Now, to bring the substrate around that metal ion site. We have to access of these substrates via some specific channels in the tertiary structure. The protein structure we have seen earlier also that you have the primary structure, you have the secondary structure and ultimately the tertiary structure which is a three dimensional structure a globular structure.

But if we have the channel then only you will be able to reach at the core of this tertiary structure where the metal ion is present. So, the substrate suit had some channels. And through that channel the substrate can swim basically in the aqueous medium or the water medium. So, we will also think about the lock and key model during the enzymatic catalysis on the metal ion center.

And we will go for the ligand modification which is a very simple one for post translationally modified amino acid residues. If we can have carboxylate oxygen sub aspartate. And its homolog such as glutamate they are very useful ligands for binding alkali and alkaline earth metal ions like calcium, magnesium, etcetera.

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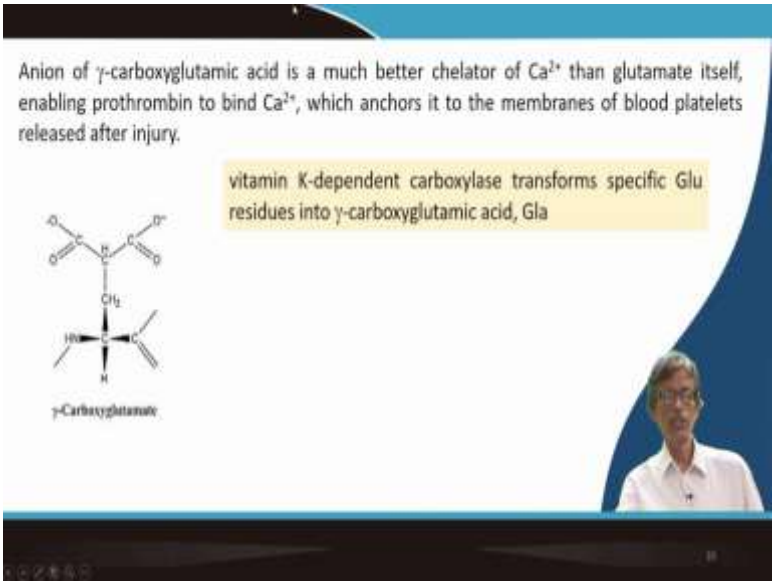

So, one example we will find for a system where we find that we can have that alpha keto glutamic acid so what is that? So, the gamma carboxy glutamine acid GLA. So, it is nothing but an anion of gamma carboxy glutamic acid. And which is a better chelator of calcium than the glutamate itself. So, through modification the post translational modification as just now we seen we have seen that through that modification we are getting a stronger ligand.

And when we find that in the biological world the pro thrombin is used. Which is responsible for our blood clotting when we have an injury the blood is coming out from our body. But we know we have to have the corresponding clotting system. And more and more prothrombin will be released which can bind the calcium available over there. But that binding should be stronger enough if we just modify the ligand.

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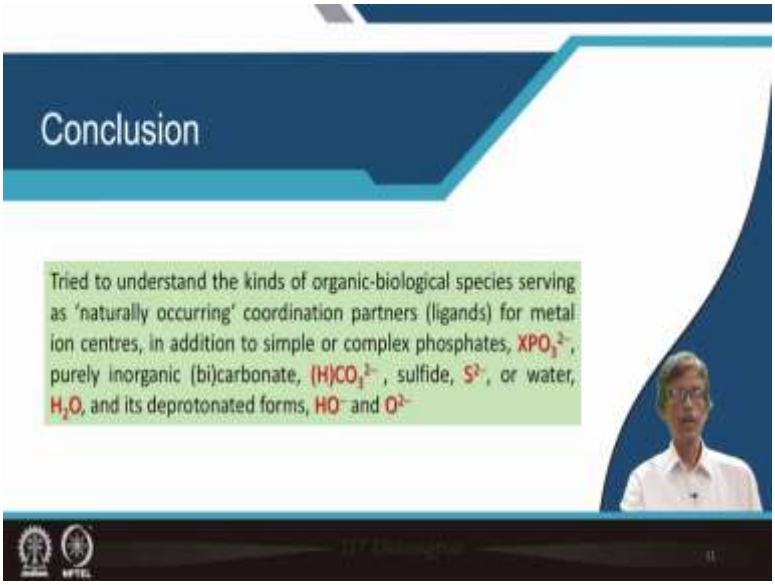

So, in C2 we are lucky enough to have the modified ligand system over there to bind the calcium. So, that modification on the ligand system is also important to have good understanding about the corresponding chords in chemistry not only for iron but also for calcium. So, now we can conclude over here by seeing what we have learned so far during this half an hour time.

So, what are we basically seeing that different kinds of organic and biological species are there which are definitely naturally occurring. So, small biological molecule and small organic molecules are there. And in a plethora of different metal ion centers. So, the naturally occurring coordination partners that means the ligands for metal ions are important. But along with that like what we have discussed in case of our bone formation and teeth formation.

The different complex phosphates one connectivity you can have or one x is also there as one of the oxygen bicarbonates sulfides water and it is different deprotonated forms. So, not only the metal ion but also the ligand residue whether it is a neutral one or the charged one is important. At the same time the institute form that means whatever we are forming inside our body due to the consumption of carbon dioxide due to having water molecules in our hand or some sulfur residues coming out from the sulfur bearing amino acids.

These anions are there so these anions are Lewis basis. So, they are very good ligands itself to the metal ions centers. All we know that if you have sulfide ion is present. And if your iron is present say ferrous iron is present it will immediately form ferrous sulfide. And which we call as the corresponding mineralization process. In the biological world how this simple understanding of the interaction between the metal ion and the anion.

The metal ion and the ligand can give us many meaningful information's and the explanations of the thing what we do not know much.

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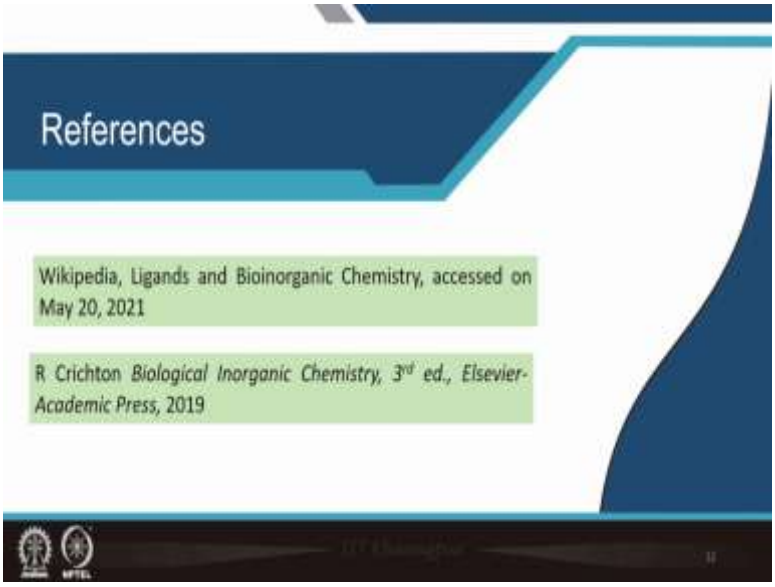

So, again we have the references now we have to access the Wikipedia page for ligands. And they are corresponding bioinorganic chemistry that we can see and the same book the Crichton's book, the Robert Crichton's book on biological inorganic chemistry. So, thank you very much all.