Inorganic Chemistry of Life Principles & Properties

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Lecture – 05
Coordination in enzymes

Good morning and welcome you all to these next lecture on the Inorganic Chemistry of Life Perspectives Principles. In the previous class we have been looking at a few aspects I will bring recapitulation of those, one of that is we looked at absorption of elements by intestine and this we have looked at as an example for the iron case.

Then later on we also looked at the inter element absorptions will have interactions either antagonistically or synergistically. So, antagonistically is that when the concentration of the one of the element goes up the concentration of the other element would get hampered.

Synergistic is exactly reverse to this where the absorption of one of the element will favour the absorption of the other element as well. This all we have seen; further we have looked in to another aspect, how these metal ions are bound in biological systems in particular to proteins.

In that we have a look at it is the side chains of the amino acids, and we have looked at that there are certain side chains like carboxylic, like amine, like thione function, such as aspartic, glutamic, histidine, cysteine, serine, thionine all these kinds of amino acids having side chain ligating centers which are capable of binding to the metalll center, I have also talk to you there are some special you know factors like heme, heme is nothing, but a porphyrin containing iron centre.

So, this entire heme is again embedded into the protein, so therefore, the metal ions are directly connected to the side chains of the amino acids of the protein or they are present in heme like systems or porphyrin like systems. And porphyrin like systems can also have additionally coordinated to the protein, where fifth and sixth coordination's are still available because the heme provided only four coordination and most of the transition metal ions particularly the ion nickel, these kind of cobalt ions can extend their coordination's to five and six as well.

So, therefore, therefore, the metal ions are bound either to the amino acids side chains or to special compartment or a combination of these and this is what we have learned in the previous class. Now, let us look at the same with the example being given over here.

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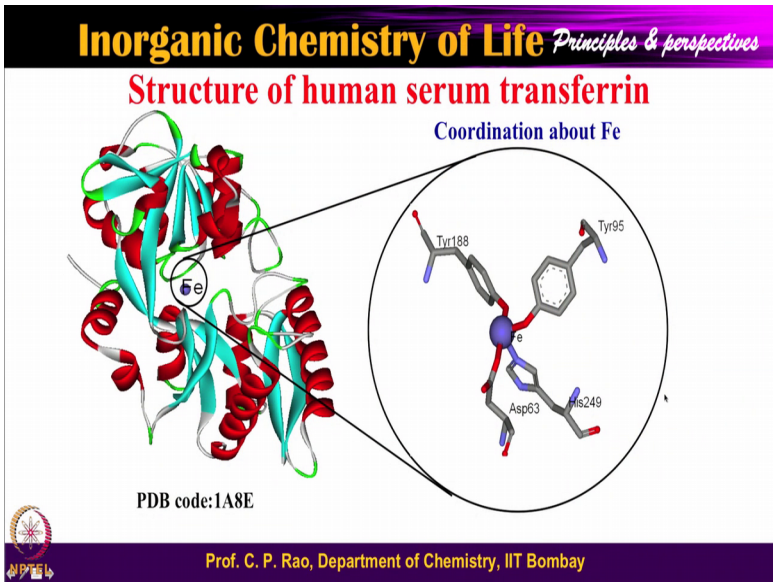

So, this is a protein is which is nothing that I which I explained to you called transferrin, a transferrin as I said earlier transports the iron ions across the blood, from one organ to the body that to the other organ via the blood now; you see that. So, you have an ion centre and ion center is covered by the protein and if you expand this region you could see the whole thing here.

So, what are you able to see you have a metal ion centre which is the ion which is connected to this which is the which is the phenolic oxygen another phenolic oxygen. So, where it is the phenolic oxygen come in kind of a amino acids structures it is the tyrosine. So, the tyrosine gives you the phenolic phenol phenolic group and the phenolic group upon deprotonation becomes phenolate and this phenolate will bind over there.

So, you have two of them are tyrosine groups tyrosine tyrosine's and then one of them is nothing, but the nitrogen of the imidazole moiety which is coming from the histidine. So, therefore, it is a histdine binding the fourth one is a oxygen or the carboxylic it is c o and there is another o and this is coming from the aspartic. So, you could see here there are three different types of amino acid residues totally four such reduces are binding to give a four coordinated spaces, and we know in cases of iron with a four coordinated they are

very likely to be of the tetrahedral type, but I will come to the geometry aspects bit later stage.

So, you can see therefore, the iron ion in enzyme like the transferrin has a coordination sphere and if you take this just this portion alone it is a primary coordination. So, it is a like iron is suspended in to protein in the form of a complex, where the ligands or the side chains of the protein; I hope you understand this.

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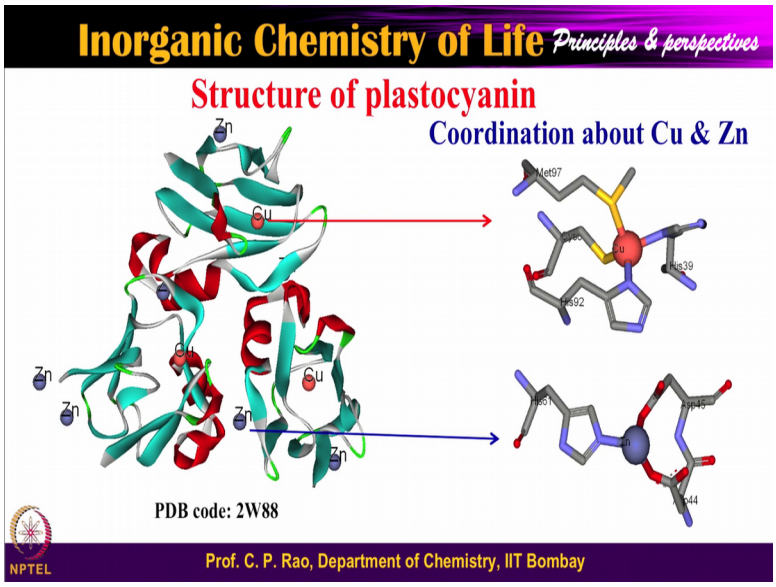

So to make your understanding for the better, I will show you one more example this is an example of an enzyme where we have a plastocyanin.

So, right now you do not need to worry what is enzyme is what its function is, though its function is electron transfer. It has two types of metallo centers one is the copper center other is the zinc centre ok. So, zinc center copper centre, so you have a copper center or zinc center. So, these are different subunits, so do not bother about all that.

So, if you look at the corresponding case of a this particular a metallo centre which is a copper. So, now, you can see that the copper is surrounded by four ligands one of it is cystenine, this one is cysteine sulfur and this is cystenine sulfur, but it is not cystenine it is modified cystenine modified cystenine is sme. So, sme is called the methionine ok, so therefore, is a methionine.

So, methionine sulfur which is a ether thio ether and then this is a cystenine sulfur which is s minus. So, this is a s minus this is sme and then you have a histidine which is you see from their perpendicular view. So, therefore, you are not seeing the total plane and you can see another histidine here which is you can see that the nitrogen. So, in this case there are three types of amino acid residues one is histidine, other is cystenine, other is methionine ok.

So, but there are totally four the four amino acid residues are bound to this; now what you can call this as a this is a coordination complex, now and these amino acids are connected to the protein therefore, it is suspended it is a protein. So, therefore, the metal ion copper here is suspended in protein through the bindings of these.

On the other hand if you come to zinc center you can see here zinc has got in this particular case, the three bindings two of these are from a carboxylate, you can see it is the carboxylic group, it is the carboxylic group, and one of it is the imidazole which is histidine is a tri coordinated zinc centre that you have, an a tetra coordinated copper center you have. Later on you will learn that the copper center is the, actually the one which is reaction centre and the centre of the zinc is basically the one which stabilizes the structure.

So, stabilizing the structure, so it is not involved in the function. So, therefore, this is structure ion and this is the catalytic ion. I will bring this distinction bit later much more clear right now you can say non-functional zinc a functional copper. So, the copper is involved in the redox process of you know the transferring the electron back and forth ok.

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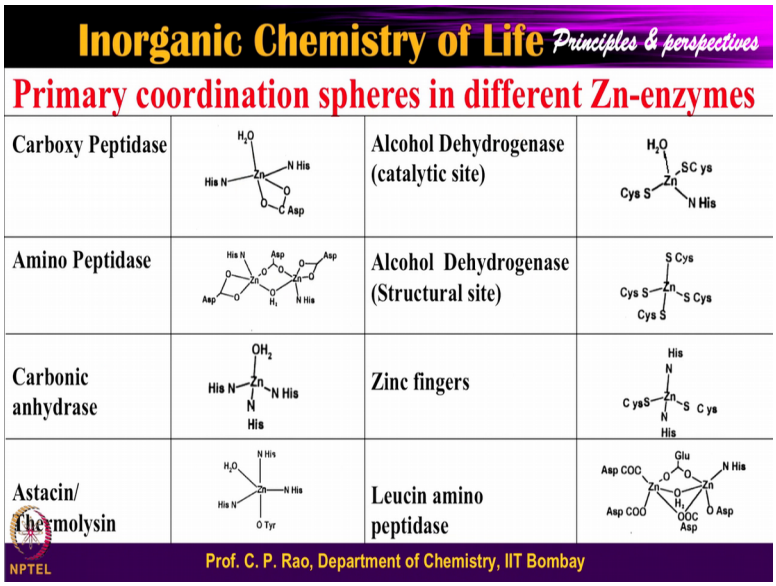

So therefore, redox enzymes; having seen these two examples let us have a bit of survey, survey among the large number of proteins of which I have picked up a few which are zinc containing and maybe the ion may be the copper. Let us first look at this particular table shows different enzymes based on the zinc ok. So, it may be useful for you if I take you through this even in a later stage, because you can study better in future when you look at the books etcetera. This enzyme may be carboxy peptidase and it has a lot of protein which is not shown here.

But what is shown here is a zinc centre zinc center has in one histidine another histidine another aspartic and is a water and so, and in this case the aspartic having a carboxylic group it binds like a bidentate. So, therefore, two coordination from this one coordination from this histidine, one coordination from this histidine totally four and one more is the water.

So, I will explain you why water is there what water does everything when we come to this enzyme I think. So, right now your idea is to see take that in this particular carboxy peptidase the zinc center has got the binding from these different amino acids coming from the protein and forming a five coordinated structure over here. And there is another example just below this has got lot one zinc center, but this has got two zinc centres, you can see that zinc center zinc one and zinc two.

And similarly this is also bound by a histidine and aspartic also by histidine aspartic and there is a bridging ligand, the two metal ions are bridged by another aspartic carboxylic group and there is one more bridging which is coming from the water ok. So, therefore, the two metal ions are not separated, but bound together or bridged together by an aspartic and a water molecule and each of this is a coordination sphere.

Now; that means, this di zinc center is suspended in a protein called amine peptidase and it functions, we will see functional aspects at a later stage may not be for this enzyme, but some, some other enzymed. Another example you take the enzymes name is carbonic anhydrase; carbonic anhydrase you have one histidine, another histidine, another histidine and a water.

So, there are three histidine residuals bound through the nitrogen and the which is nothing, but from the imidazole moiety. So, you know the imidazole moiety is a five membered ring having a nitrogen which has loan pair which will bind to the metallo center, and that is what and then you have one water role of water etcetera will be seeing later.

So, now what you can see this zinc this four coordinated zinc is a coordination complex which is suspended in a protein. Then you have another example over here astacin and thermolysin again zinc having a five coordinated structure here, as you can see and similarly you have on this side on the top alcohol dehydrogenase, we will be studying more details about this enzyme about their functional etcetera to much later stage when we come to the story of zinc enzymes.

This has a different kind of amino acid residues what are those residues you have a cysteine, you have a cysteine, what is cysteine, cysteine has a CH 2, SH and the CH 2, SH the proton is last the S minus. So, it is a thia thiolatto, so it is a thiolotto bond zinc thai lotto it is a zinc with the a s cystiene zinc with a s cysteine and zinc with a histidine.

So, there are three amino acid residues and the fourth one is a water ok. So, therefore, a zinc coordination complex is suspended in a enzyme is called alcohol dehydrogenase and does its function. So, come to another example alcohol dehydrogenase also has this is the same example, but it has two metallocenters; one metallocenter explain to you here this is a catalytic centre; that means, reaction occurs here and these another zinc center which is structural means no function occurs at this place, but it is required.

It is required because it has to hold a particular kind of a confirmation structure, so you called this is the structural rigidity. So, the structural rigidity for the protein is obtained when the zinc this kind of a zinc is present, and what is this zinc this zinc is bound to four cysteine (Refer Time: 13:37), things different from the zinc that is here. So, you have a two distinct zinc centers; one is the zinc catalytic centre and the zinc structural centre both of these are there ok, both are a part of the same protein, but two different centers.

So, more details will come when I explain to you the alcohol dehydrogenase its function etcetera and there is some proteins called zinc fingers. So, in the zinc fingers you have two histidines and two cysteins, and leucin there is another example leucin amino peptidase ok. This has got two again leucin centers and each of these is bounded by aspartic, aspartic. Again one histidine, one aspartic and these are bridged by the glutamic and aspartic carboxylates and with one water are hydroxo species.

So, these are the kinds of things, so what will learn what do we learn out of these entire table of things is that there are variety of zinc enzymes are there each of the zinc enzyme has a different function which we have not learned right now, it will be learn in later stage, but we know that they have a different enzyme different functions, but they have a different coordination's sphere.

And the common feature is in all the cases zinc iron is suspended in the protein and bonded through amino acid residues side chains of amino acid residues and in some cases water molecule and in some other cases not one zinc it will be two zinc dizing centre and both of these zinc centers maybe bonded together or bridged together, and this is what we understand from this particular table.

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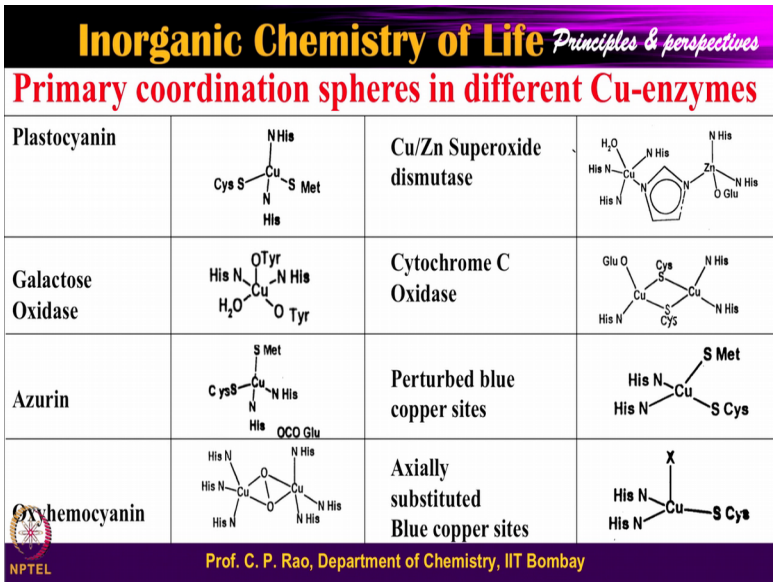

It is nothing to special with the zinc proteins let us look a different kind of a proteins proteins based on the copper. So, let us look at the copper based enzymes. So, again I have given a table of this, so I will not go as detailed as I have gone in the previous slide I will go bit more quickly here.

So, what do we have here is one protein called plastocyanin there is another protein called galactose oxidase there is another protein called azurin there is another protein called oxyhemocyanin, there is another protein called copper zinc superoxide dismutase and cytochrome c oxidase and blue copper site which are perturbed I will explain you at a very later stage.

What why the meaning of perturbed is coming into, but give you a small hint right now and then we have other kinds of axially substituted blue sites etcetera. In fact, the plastocyanin this one the azurin the second and the perturbed blue copper sites third and they axially substitute blue copper site, these are all coming from one particular class of copper enzymes and these particular class of copper enzymes are known as the electron transfer blue copper proteins.

So, they are blue in colour therefore, they are called the blue copper proteins ok. So, all of these four have the same function which is electron transfer, but other enzymes have a different function. So, for example, galactose oxidase it will oxidize the galactose primary hydroxylamine galactose ok. And oxo hemocyanin this is involved in

transporting the oxygen not in human in molsacus, I will explain little later when we come to the story of oxygen transport.

And copper zinc superoxide dismutase in this case these super oxide radicals are dismuted, o 2 minus are dismuted this also I have already mentioned earlier nothing new, but details will come later on and this is a cytochrome C this supports the heme centre. So, therefore, that much we will see at this stage in the electron transfer process and this again I told you this electron transfer protein this also electron transfer protein. So, now, have what have studied from all these this entire table.

We have variety of copper containing enzymes in each other case that the bound residues are different , different geometries also there four coordinated five coordinated. So, many things are there and they all do different functions; that means, a copper ions are suspended in the corresponding protein bonded with the different residues of the protein and making in to a copper enzyme.

And if this much information is understood, this much information is assimilated by you are forgotten this one it has absolutely more than sufficient at this stage regarding the metalloproteins and metal enzymes. I will show one another table which is which is pertain into the ion enzymes.

So, first of all I have to tell you when it, when it comes to the ion enzymes, I have to tell you there are two types of ion enzymes there; one is the ion enzymes where iron ions are directly bonded to the side chains of the amino acid residues.

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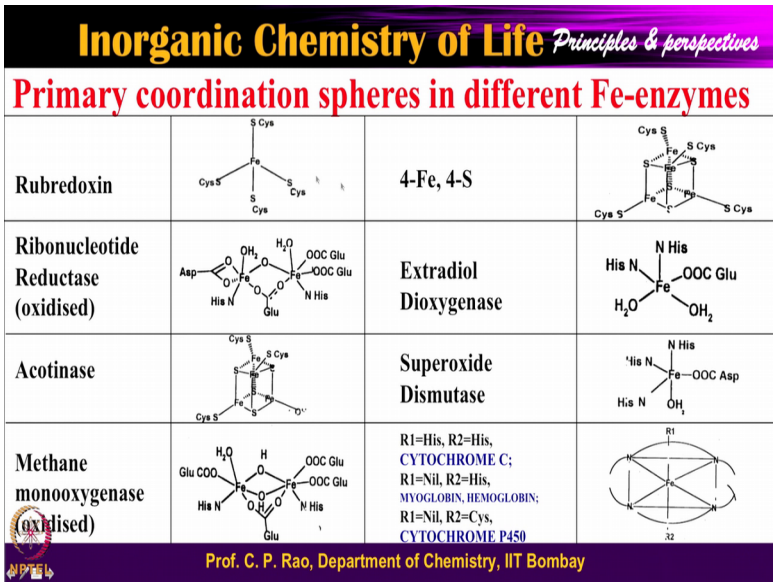

The second kinds of iron enzymes where the iron is bonded to a unit which I have already introduced to you it is called the heme. So, there are these four nitrogens or the porphyrin are bonded to the ion. So, therefore, these are ion nitrogen bonds and this in turn is bonded to the protein I remember there in this the ion in this hemes has got only four coordination and the four coordination in more or less in a square planar fashion.

So, iron is capable of showing fifth and sixth also; that means, six coordination therefore, the fifth and the top sixth on the bottom these are vacant. So, either both of these or one of these can be bonded by the side chain residue two. So, therefore, there a huge range of heme proteins are there. So, the in this case what I am telling you in case of iron there are two major classes of enzymes; one class of enzyme is called the heme enzymes and other class of enzyme is called the non heme enzymes.

In case of non heme enzymes the iron is directly bonded to the to the amino acid residues ok. Side chains of the amino acid residues you can see here rubredoxin and you can see rib nucleotide reductase, you can see aconitase, you can see methane monooxygenase you can say four iron, four sulfur cluster and a extradiol dioxygenase and you can see superoxide dismutase. So, many things in all these cases many more are there.

But I am giving only few selected examples just to give a feel in all these things the iron ion is suspended in the protein and where the ion centre is bounded by all these side chains of the amino acid residues. In this case it is a cysteine oil in this case for example,

aspartic carboxylate this is glutamic carboxylate this is histidine ok. And this is briding carbo glutamic and these are waters, the role of water we will see at a bit later stage there is a lot of important issue with the water presence there because they are involved in the catalysis effect or they are involved in allowing the substrate to be bound to this ok.

So, I have been telling you about the different types of iron enzymes; heme and non heme having different residues bounded to that. And in case of heme four coordination's are filled by the porphyrin and two other coordination's are in one of these coordination is bounded by the protein. When only fifth coordination is bounded by the protein, sixth will have more most of the times as a water and this can provide the substrate binding as well.

So, as I said the water position have got two kinds of roles one it will be sort of a ligand where can we exchange by the substrate, the second case is where the water is involved in the reactivity. So, these are two possible ways that we can see, so what all we have seen till now in the metalloproteins and metalloenzymes.

The metalloproteins and metalloenzymes the metal ion is suspended in the protein not just like that, but it is bonded to the side chains of the amino acid residue or it is bonded to a special group like a heme so, therefore, heme bond things. When the heme is bond there is a possibility the fifth and sixth co-ordinations can be bonded by the protein or even fifth co-ordination can be bound by the protein and then in such kind of a thing will basically function. So, now what do we understand from a metalloprotein or metalloenzyme.

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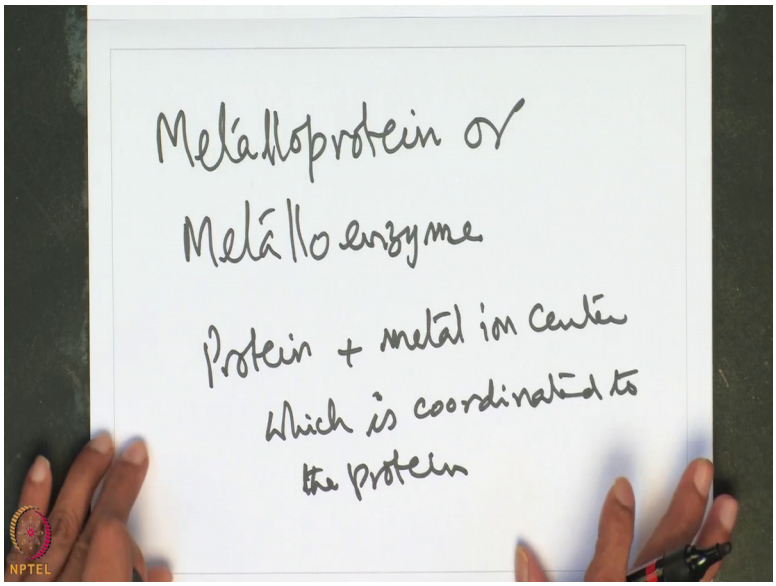

So, metallo protein or metallo enzyme is a metalloprotein or metalloenzyme is you have protein plus metal ion centre which is coordinated to the protein. So, therefore, one can basically see this as.

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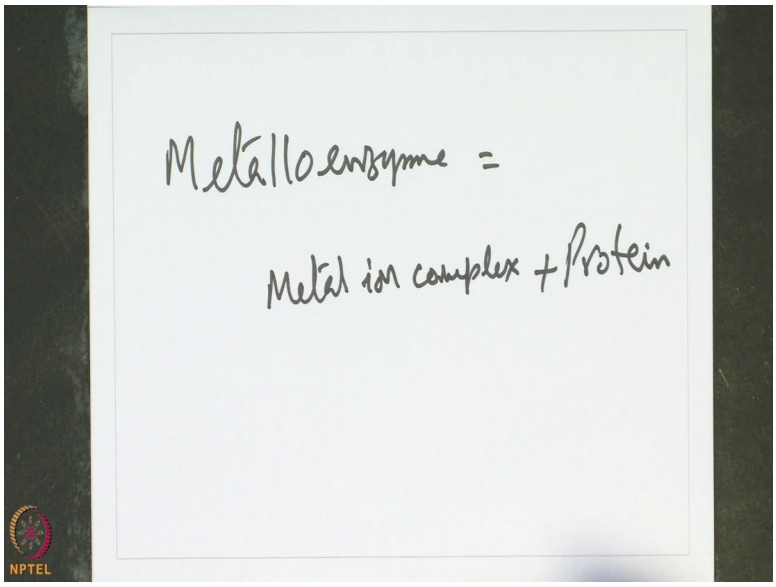

So, the metalloenzyme is you have a metal ion complex plus the protein. So, in other words we can say the any other metalloprotein or metalloenzyme, where you have a metal ion bonded to the protein as like a any other coordination complex and this

coordination complex is held by the protein, so what do you think such a kind of a complex can do.

Let us at this stage itself let me bring to you a simple case of let us say I have a an ion salt ok.

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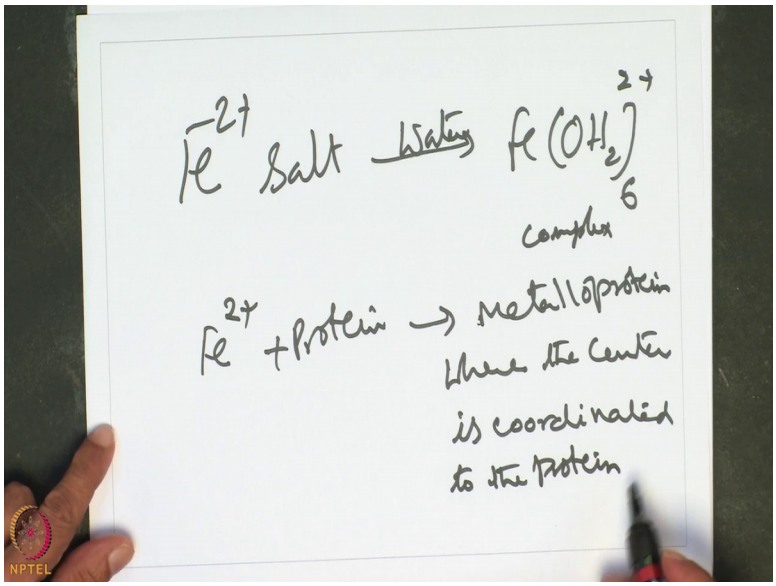

So, I have a ion solid let us ion 2 plus salt and let put in water. So, therefore, I get a Fe OH 2 6 2 plus complex. So now, if I put this ion in the protein and 2 plus plus protein; So, I will have metalloprotein, where the metal centre is coordinated to the protein.

There are two things are there, so one is that drug binding; binding on the protein resulting in a coordination complex. So, this complex is not a simple innocent kind of a complex like what you have in water. So, in water you will have just simple iron water aqua complex. In case of the metalloproteins the iron 2 plus bonded to the protein and the protein structure and the protein conformation; all this will influence the property is the iron centre.

Therefore, what I want to convey to you is that they are the properties of the iron ion in acqua in ion aqua complex is absolutely different from the same iron ion when is bonded to a protein and when is bonded to different kinds of proteins. So, therefore, diverse functions, diverse properties are possible by the same iron ion, but in different media. So,

therefore, in case of test tube reaction the water is the medium in case the metalloprotein and metalloenzyme it is the proteins which is the medium.

So, therefore, medium played role on the metallocenter is very influential. So, in one case it is water in the other case it is the protein. So, the protein binds to this and proteins alters the functions and protein takes care of the modifying the functions of all of this. So, that is very a absolutely interesting, you know why it is interesting, it is interesting because you have seen there are 100 of different types of metalloproteins and metallo enzymes where even for iron.

If each protein does not change bring such a change then all protein should have behaved the same way, but they are not true each of the enzyme for one different function, whether it is a zinc enzyme there are 100 different zinc enzymes. So, they are impact more than 200 are there and there are several 100 of ion enzymes are there and several dozens of 200 copper enzymes are there.

In each of this the coordination is different in some cases coordination very close by, but the protein is different. So, it is because the protein is different the property is important to the metal centre do de far. So, therefore, protein plays a very important role simple copper aqueous solution or copper amine complex and a copper in the protein, so protein will also have nitrogen ligands.

So, therefore, we cannot say that the copper present in a protein will have the same properties of the copper ammonia complex. Similarly, iron so iron aqua complex, so we should not think the simple iron aqua complex which is present in test tube is properties are going to be the same as the properties of the iron 2 plus in a protein it is absolutely different, in each of this protein and enzyme we have a different kinds of properties are there. So, therefore, the proteins modify the properties of the iron or zinc or copper thereby we have in nature has evolved with a huge number of different kinds of enzymes that is the take home lesson that one should see.

And just before we close this particular part of the thing I would like to tell you that these are already I have talked to you that they are bonded and this table will give you that different bindings binding.

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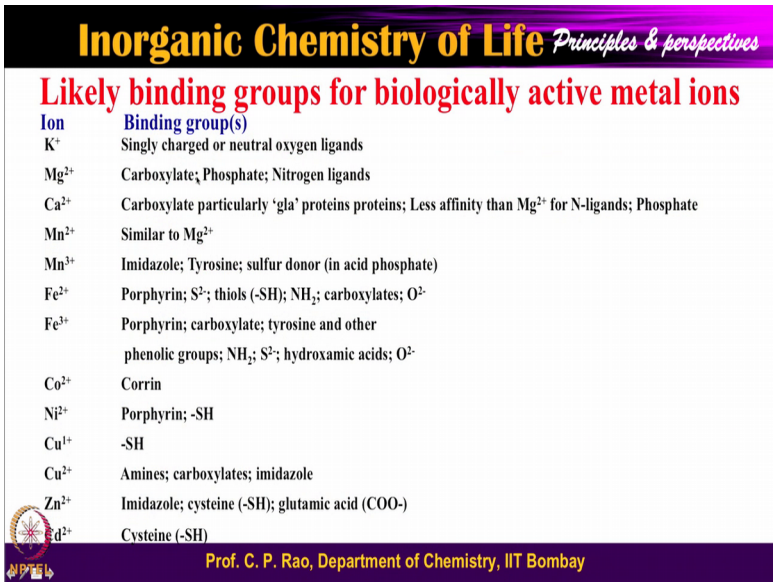

In case of potassium magnesium calcium etcetera manganese, iron 2, iron 3, copper, cobalt, nickel copper to copper 1, all these kinds of things. So, you have a different kinds of the binding and the reasons for this binding, I will explain you later which is can be explained based on the stability and also based on HS AB, hard soft acid base concept at bit later stage.

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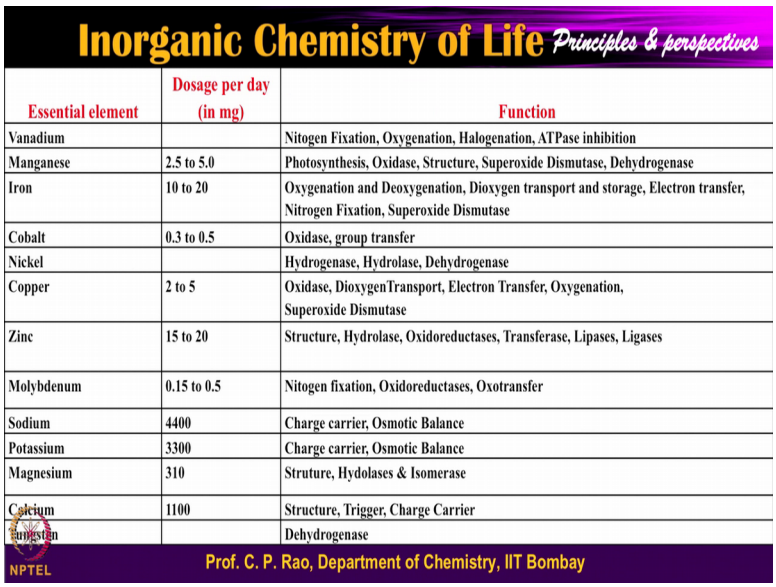

And, so whatever I have talked to you is about there are different essential enzymes you require specific dosage of this per day and they have certain functions. So, different

kinds of functions are there for each of this they manganese, vanadium, iron, cobalt etcetera in all these things they have different kinds of functions some other maybe showing only the carrier osmotic pressure, I will come to this a little bit more bit later stage on this.

So, to sum up let me tell the following, so we have seen that the metal ion is bonded to the side chains or the amino acid residues of the proteins and these amino acid residues in proteins bound a bind and make a complex.

So, therefore, it is like a metal iron complex is suspended in the protein, and the properties of such a complex is different from the properties of simple complexes that we see day to day or we see in the test tube, because the protein applies its on parameters of the confirmation and other hydrophobic or hydrophilic properties etcetera. As a result of that the metal iron centre properties are changed dramatically. Therefore, different enzymes function differently though the coordination's sphere may have very close by.

Thank you very much.