Inorganic Chemistry of Life Principles & Properties
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Lecture – 21
Role of vanadium in life - General perspectives

Welcome you all to the next lecture on Inorganic Chemistry of Life Principles and Perspectives. What have we done in the recent in the classes? In the recent classes we have looked at the aspects relevant to biology of those are the alkali and alkaline earth elements that is sodium, potassium, calcium and magnesium.

Now, we will transit into the transition metal biological chemistry.

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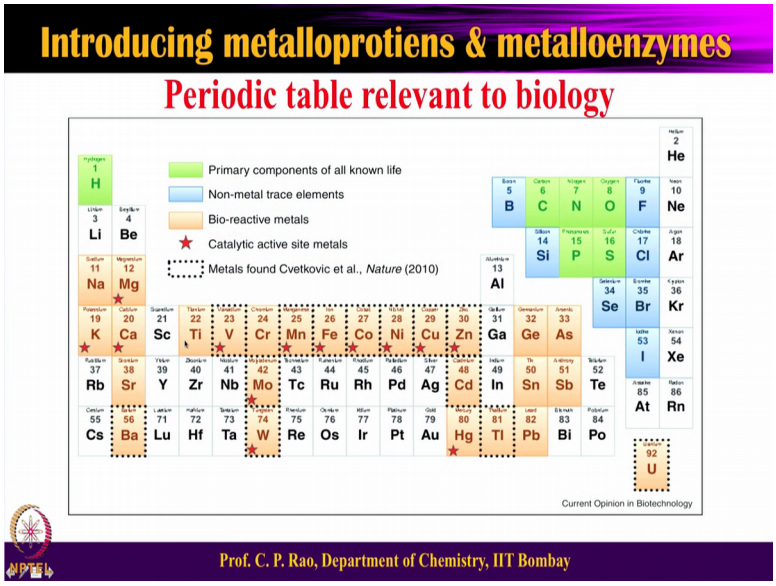

So, therefore, let us first look at the periodic table which is relevant to the biological systems and you know these are the words where you have a catalytic activities particularly we have looked at sodium, potassium, magnesium, calcium. The next comes is the transition metal series, the titanium till zinc. Though the titanium is sort of as a micro or nutrient element is understood, but there is no enzyme yet been identified therefore, we will not take up this case of the titanium, we will look at vanadium and chromium is also not (Refer Time: 01:30). So will be leaving out that manganese, iron, cobalt, nickel copper, zinc.

So, we will go in this particular order of the transition metal series, look at the enzymes. I would be spending a lot of time with iron enzymes because we have both the heap based and not heap based. Then we will spend a lot of time on copper and zinc as well, maybe some extent to molybdenum. In other cases will be spending only a limited number of a examples of each of these ok.

So, let us start with the Biological Inorganic Chemistry of Vanadium. Vanadium as you know as a deliberate as a chemical element, can show a variety of oxidation states. Anybody has a guess what kind of oxidation states; yeah take a moment it can show from plus 5 to minus 1.

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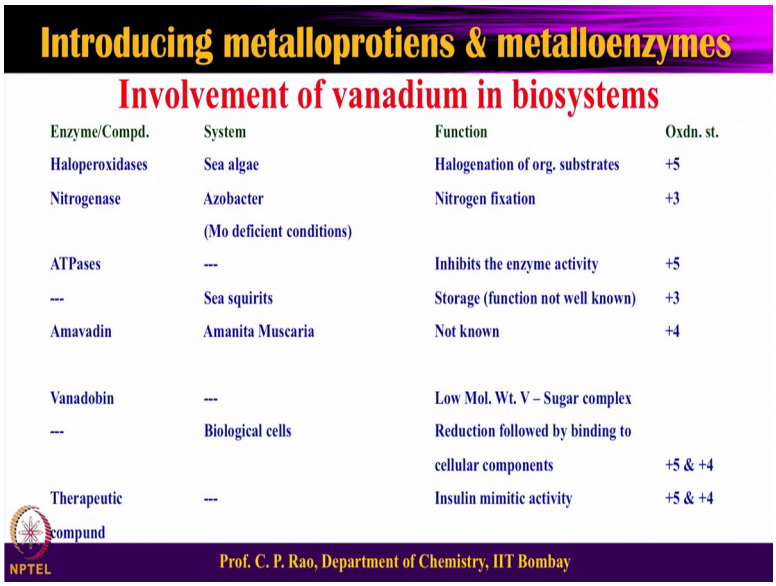

So, it can show a large number of a oxidation states, but all of these oxidation states are not well favored, some of them or more frequently found than the others. And in the biological system also we should always keep in mind the kind of a oxidation states that are favored or most common oxidation states. And if you look at the most common oxidation states in the in the vanadium or the plus 5 plus 4 and plus 3. We will see the reasons why plus 2 and all are not so, common just in a while ok.

So, before we go to that let us look at this particular slide may some enzymes are shown and the corresponding oxidation state. Haloperoxidase and these are some information which you can read any time like the source, system the function. The function is it halogenates the organic substrates, and the oxidation state this is the plus 5 ok. And the

next one you see that it is the nitrogenase in the nitrogenase you have nitrogen fixation and the main oxidation state in this is plus 3.

Then a ATPases etcetera it store and there is something called amavadin which is a storing kind of a protein, not so, much details are known is a plus 4 and there is vanadobin its biological cells it can be plus 5, plus 4 in a few cases even plus 3. A lot of therapeutic compounds are also plus 5 and plus 4 and some of their activities in the insulin based activity.

So, what do we understand out of this particular slide or table is that the vanadium is involved in the biological systems, it is of course, limited number of enzymes and the main oxidation states are plus 5, plus 4 into some extent plus 3 ok.

Now, it is good to do the nature of the vanadium species. The nature of the vanadium species or kind of oligoporus that is found are dependent on the concentration of the vanadium and as well as a p H. Most of the times these vanadium species or generally found in there plus oxygen 5 oxidation state as vanadates ok.

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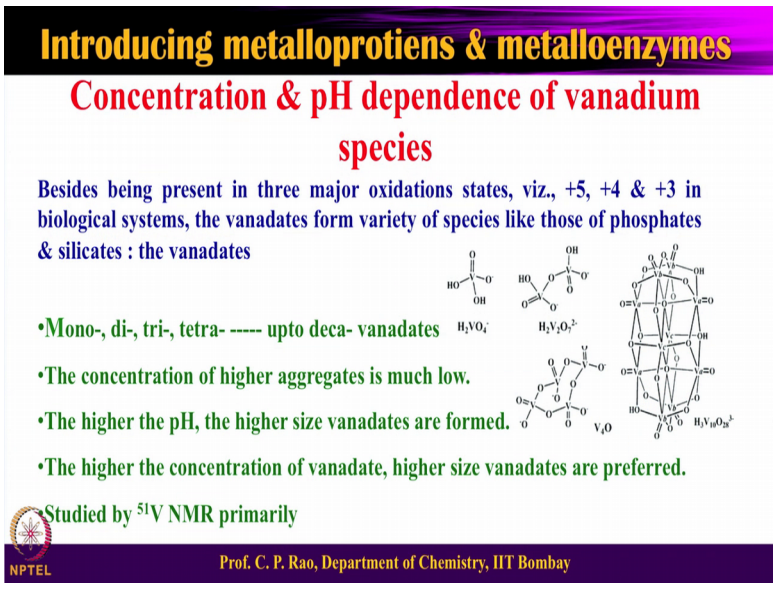

So, this vanadates like phosphates, like silicates, molymbdates, you have a vanadates also. So, the vanadates are Mono-, di-, tri-, tetra- up to about deca- kind of things are reasonably known the so concentration of the higher vanadates are generally low. So, if you go for the higher p H the higher size vanadates are generally little bit more favored.

So, the higher the concentration of the vanadate the higher the sizes of the vanadates are preferred how do we study these vanadates are all plus 5 based vanadates.

So, therefore, the study is suitable by 51 V NMR because plus 5 vanadium is what? What is the d configuration? D configuration is 0; d 0 there are no electrons in the d system. What is the d configuration of vanadium in plus 4 oxidation states? It is plus 1 because plus 5 oxidation state is 0 therefore, plus 4 oxidation state should be 1 this one electron in d therefore, it is a nice system for EPR studies and 0 electrons in d plus 5 is very good for NMR studies ok.

And what I mentioned to you about vanadates, how these formed? Oligo vanadates or polyoxovanadates I mentioned their aggregation or their vanadate formation, I would take back the word aggregation, but I would say their vanadate formations.

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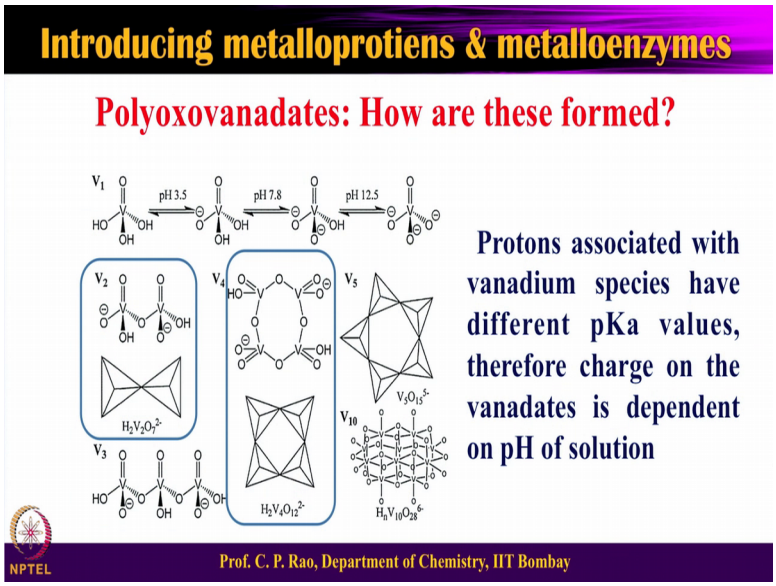

So, aggregated vanadate formations or joined of vanadate formations or dependent on not only of the vanadium concentration in the medium in its vanadium plus 5 oxidation state, but also on the p H.

Suppose you take a p H as acidic as 3.5 so the entire thing will we have protonated that is H 3 V O 4 just like H 3 PO 4 phosphoric acid. So, H 3 PO 4 and then you slowly increase the p H to somewhere neutral or a little bit more than neutral, and you start increasing the thing it will become mono negative then you make it beyond neutral; it

will become di negative you go to p H like 12 or above then it will become tri negative. Because there are only 3 OH s it can only lose 3 protons. So, therefore, at very highly acidic below 3.5 around 2 to 3, it will be all 3 protons are intact above 3.5 4 one of the proton is lost so mono anionic when it is beyond 7 to 8 then 2 protons are lost there is a di anionic. When it is beyond 12, 13 p H all the 3 protons are lost so it is V O 4 3 minus.

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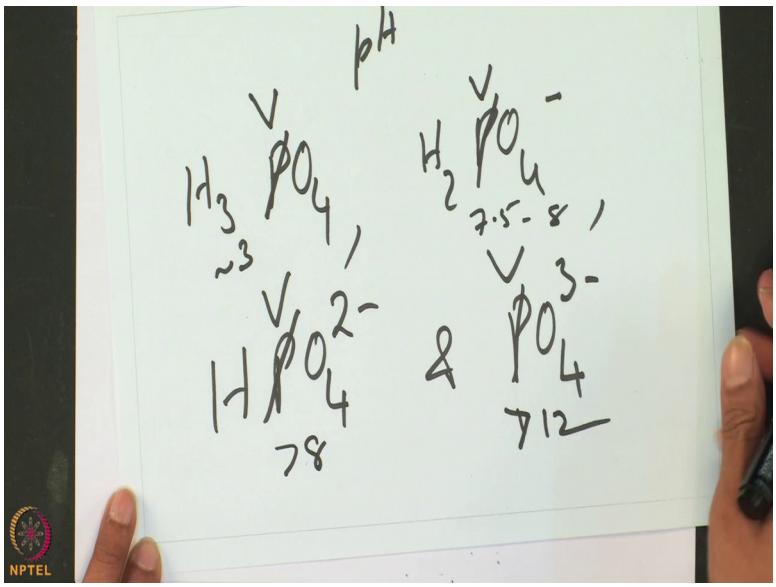

So, you have species of this type as a function of p H as a function of p H. So, you have H 3 PO 4, then H 2 PO 4 minus H PO 4 2 minus and PO 4 3 minus not P, in each of this you take it as V it is a vanadium.

So so it is a vanadium. So, therefore, H 3 V O 4, H 2 V O 4 minus H V O 4 2 minus V O 4 3 minus its very similar to the phosphate that is how I just got into the phosphate part of it so, but we are in the vanadate. As you go like 2 to 3 p H up to about up to around 3 p H around 7.5 to 8 p H and the p H beyond 8 greater than 8 and then greater than 12. So, you can see the slide that we have this.

Now at these concentrations, because you are forming the negatively charged species so therefore, they can combine they can combine by the elimination of the water. So, if the 2 such things are combined as you can see here. So, you can get the H 2 V 2 O 7. So, one oxygen is less; that means one water is gone and then you have further 1 2 3 4. So, 4 oxygens are less. So, like that 3 oxygens. So, you have H 2 V 2 O 7 and then you have V 3 combination, then V 4, then the V 4 it showed as 1 2 3 and 4 and this is for V 5 and for

V 10 and these are joined together the individual vanadate units are joined together through oxo bridge by the elimination of the water ok.

So, it is basically by 2 of the you know VOH groups coming closer it is like this.

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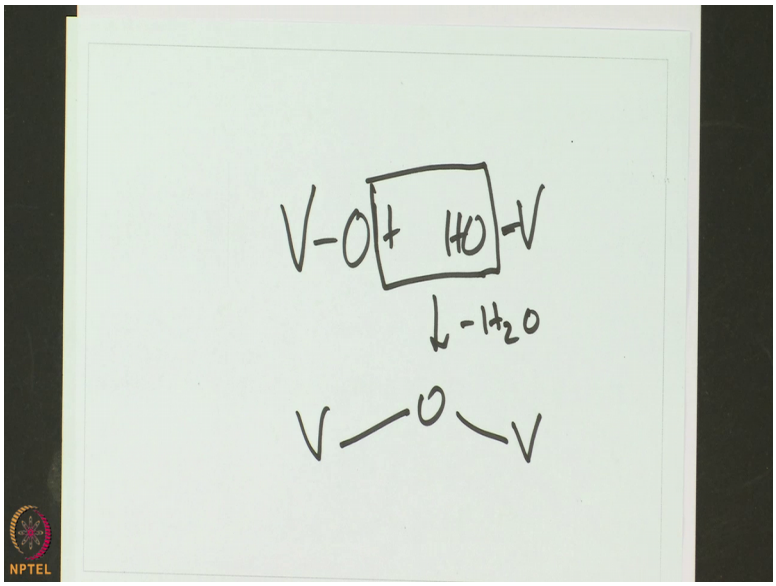

You have a with V 1 with OH, V with another species. So, of which you live minus H 2 O. So, you get V O V; that is how the links are formed therefore, the polyoxovanadates are found because of that. So, you can see that these are all depended on the concentration at the p H as you can see, then p different p K a values are there.

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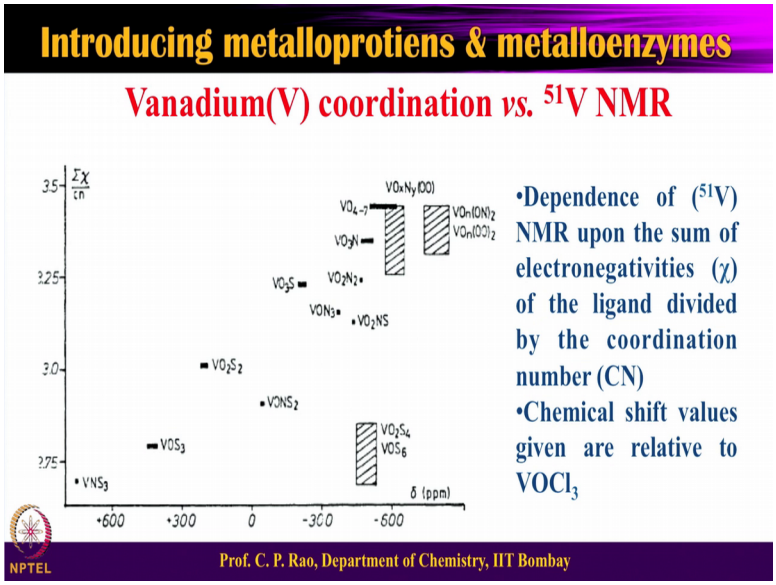

Now, I talked to you about in the vanadates mostly these are all vanadium 5, and the vanadium 5 is do system and vanadium 5 which is d 0 system can be studied by 51 V NMR.

Now, here is a very interesting curious plot here. So, have a look at this; this is a vanadium NMR plot what you have here is a vanadium surrounded by different kinds of ligands. So, if I take this case; that means, there are 2 oxo kind of ligands, 2 sulfur kind of ligands. This does not mean 2 OZ 2 S 2 sulfurs. It is 2 oxo ligands, 2 sulfur ligands take here there are 3 oxo ligands, 1 sulfur ligand. If you take this one 1 oxo ligand, 3 nitrogen kind of ligands; so this is what we have.

So, therefore, you have a vanadium which is surrounded by some all oxygen, some oxygen, some nitrogen, some oxygen, some sulfur, some nitrogen, some sulfur, some oxygen nitrogen sulfur. So that means, what you are changing the coordination sphere. You are changing the a ligand nature from oxygen to nitrogen to sulfur and we know why we are talking about? Because we already explained in this particular course, several lectures ago hard soft acid base concept I explain to you. So, therefore, oxygen, nitrogen, sulfur follows that kind of a thing.

Second thing is their electronegativities; in this case the what you have at the x axis is a is the chemical shift of not proton, it is vanadium 51 NMR. And on the y axis you have in this something called sigma n a chi. So, chi is electronegativity of the atom that is attached to the vanadium and sigma is summation, summation of all the atoms has so attached to vanadium say term, by the coordination number cn coordination number.

So, the coordination number here it is a 4, here it is 4, here it is 4 etcetera here it is 6 here it is 6 so, things so, that kind. So, you have different kinds of coordination number. So, this is normalized with respect to coordination number, taking the summation of the electronegativities of the surrounding ligating centers to the vanadium. It is very interesting as you can see, leaving this one aside you see that there is a fairly linear kind of a correlation we can draw to this. So, fairly linear correlation you can draw.

So, you see on this end you have more of a oxo base ligands, and if you come here more oxygen is less, nitrogen is more and oxygen is less, sulfur is more, and nitrogen and sulfur. So, it is absolutely going by the electronegativity kind of a principle. So, the greater the electronegativity of all the surrounding atoms, the more negative is a

vanadium chemical shift then lesser electronegativity around the vanadium the more positive is the chemical shift vanadium. And another thing that you need to notice is that, you have chemical shifts going from something like minus 7 800, to plus 7 800. So, the huge range of the chemical shifts.

So, this means, what are we conveying in terms of the biological vanadium chemistry. Biological vanadium chemistry if I have a vanadium 5 in some enzyme, in some protein, if I measure its vanadium 51 NMR and try to use this plot I can get roughly what is the surrounding atoms, what is the surrounding coordination sphere, whether there are all oxygens, oxygens of nitrogens, oxide nitrogens nitrogen sulfur that kind of a coordination primary coordination details can be obtained primary coordination details can be obtained that is why we are studying this plot. So, this plot has a relevance with a biological vanadium chemistry, if the vanadium is vanadium 5.

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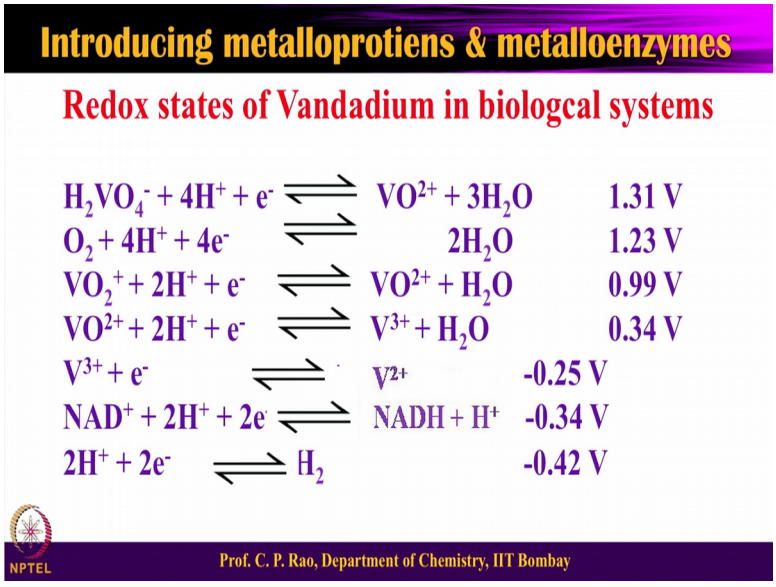

Now, having looked at that the vanadium plus 5 oxidation state is 0, plus 4 oxidation state is d 1, plus d oxidation state is d 2 etcetera. Let us look at their redox potentials so how easily one can reduce, how easily one can oxidize, how difficult one to reduce, how difficult one to oxidize. So, these are the things that we need to understand. So, if you take H 2 V O 4 minus, H 2 V O 4 minus which is vanadium is obviously, 5 just I am talked to you about this then you add 1 electron to this. When you add 1 electron to this what will happen? Vanadium 5 will become vanadium 4. So, this is vanadium 4 V O 2

plus this is also has a name called vanadyl. So, this is generally referred as the species of vanadyl in nature.

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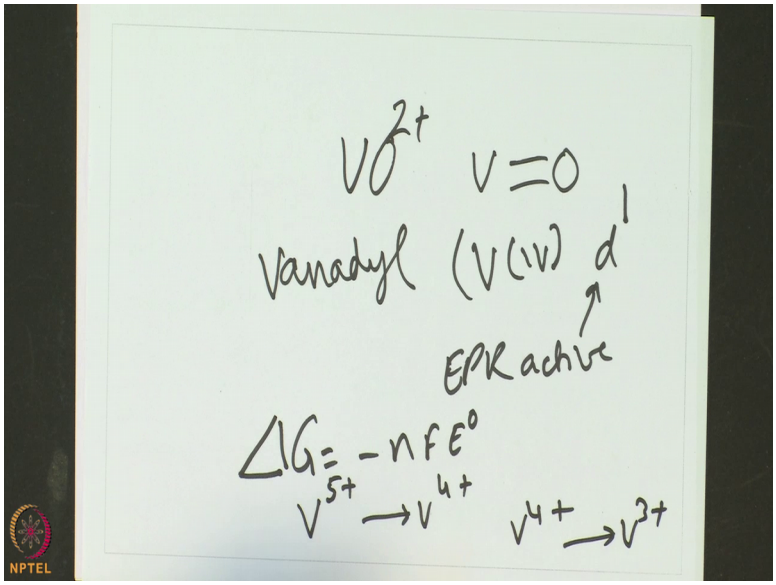

So, V O 2 plus is also shown as V O and this is called vanadyl. So, this is vanadium 4 and this is d 1 system. So, this is; obviously, EPR active. So, one can study the EPR spectroscopy etcetera.

Now, coming to this electrochemical potentials on these. So, vanadium 5 reduce to vanadium 4 and the rest of the oxygen is going into the water has a very high positive potential ok. There is 1.31 V O 2 plus this is again the vanadium 5. So, it is a vanadium species if your electron will get V O 2 plus, in this particular situation this is much somewhat little lower, but its good amount of positive about 1 volt and there is 1.3 volt, that difference is because you are doing from a vanadate, which is anionic species and here you are doing from V O 2 plus which is a cationic species that is ok.

Now, you take this one, and further add one electron ok. So, you are taking vanadium 4 and then take an electron, it will become vanadium 3 and this potential redox potential is only plus 0.3. And you take vanadium 3 plus plus electron is minus and so; that means, as you go from 5 to 4 is quite easy because more positive potential, if you put into the formula delta G is minus n F E naught and the positive value of E naught will become these minus. So, therefore, there is a great minus and which feasible, 5 to 4 is quite V 5

plus to V 4 plus is more favored and V 4 plus to V 3 plus is somewhat less favored because the potential is plus 0.3. So, this is plus 1 plus 0.3 etcetera.

So, therefore, vanadium 4 to vanadium 5 to 4 is very easy in the biological systems also and 4 to 3 is not impossible, but with some difficult you can make, but going to vanadium 2 from 3 is a negative potential and that means, it is strongly reducing it will get easily oxidized. That is probably the reason why biological species did not prefer to have vanadium 2 plus, because vanadium 2 plus is a strong reducing agent and its reactivity is also very high. Therefore, the vanadium biological system is very happy with for plus 5, plus 4 and plus 3.

Now, come to the other redox couples the oxygen, which I will go to explain when the oxygeneous properties etcetera, but still we can see right now the oxygen O 2, there are 2 bonds are there; that means, 4 electrons. So, you can add 4 electrons to this and therefore, reduce into the O 2 minus kind of thing that will be 2 protons. So, water 2 of such.

So, this is almost equal to reducing oxygen to water. So, the vanadium 5 to 4 and if you see the vanadium 3 to 2 is as good as the NAD plus reducing the NAD plus to NADH. So, NAD plus to NADH; so minus point is as much as that and or 2 H plus plus 2 electron hydrogen. So, therefore, the vanadium 3 plus 2 plus electron is as much as the as NAD plus reduction or proton reduction kind of a thing.

So, from this slide what are we our conclusions, our conclusions are that the it is rather easy to reduce the vanadium 5 plus to vanadium 3 4 plus and somewhat difficult, but not impossible from 4 plus to 3 plus. But 3 plus to 2 plus is going to be extremely difficult and this whatever the 2 plus species that is product is going to be highly reactive and strongly reducing agent probably, then the reason why it has not prefer the biological systems.

Now, let us look at the these species being present in the biological systems.

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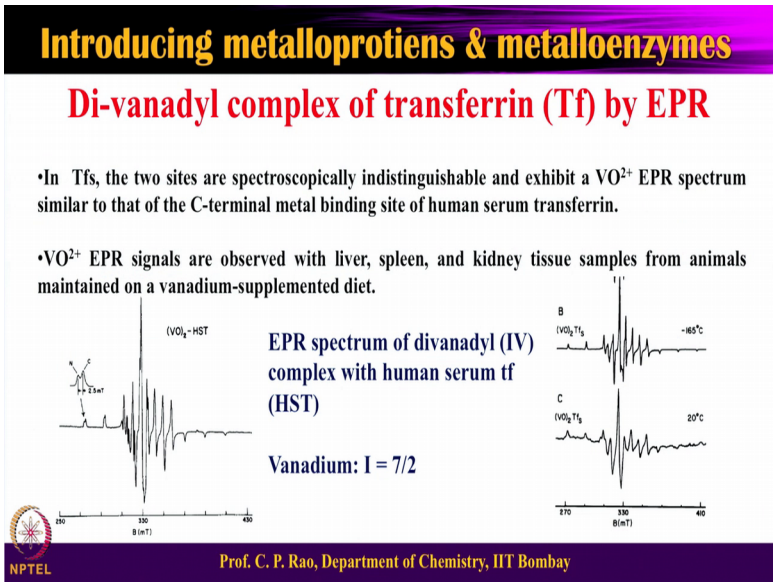

These species are being present as an example we see that the vanadyl species is being found, to bind to the transferrin human serum transferrin and vanadium vanadyl is vanadium 4 plus and I said vanadium 4 plus is d 1 and I said this is a EPR active therefore, one can study this by EPR. In fact, if you take a vanadate and incubate with the with the protein over a period of time, you would get the vana V O 2 plus which is bound to which is vanadyl species bound to the protein 2.

So, now here we have examples shown over there this is for the human serum transferrin. So, human serum transferrin later on I am going to explain when I come to the iron story, this is a the iron transferrin protein; it has 2 lobes one is called the n terminal lobe, one is called the c terminal lobe and in both the regions you have the iron clusters.

Now, this vanadyl will bind at both of these clusters, but both of these centers. So, the n terminal center and C terminal center and you know I explained to you earlier in the EPR.

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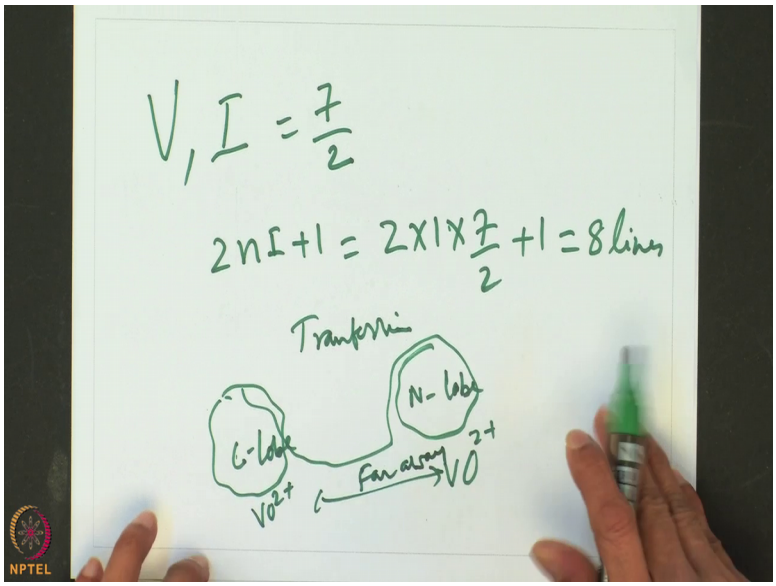

You will get the hype super hyperfine coupling based on the for vanadium the I is 7 over 2. So, how many vanadium are there in one vanadyl? Only one so 2 n I plus 1. So, 2 into 1 into 7 over 2 plus 1 that is 8 lines.

So, what you expect is there are 2 vanadyls, but both the vanadyls are not in the same place, they are in 2 different regions and because this protein transferrin has got. So, transferrin I will show I will be showing later on. So, I will say there is one this lobe and there is another lobe this is let us say c terminal lobe and this is stay n terminal lobe. So, it binds at both of these. So, 1 V O 2 plus is bound here, another V O 2 plus is bound here, but they are not communicate they are very far away so far away.

So, therefore, there is no interaction between them. So, individually you will find you can see all these things are one 1 2 3 4 5 6 7 8 9 lines, but this is coming from the different source. So, these are the actual lines coming from the hyperfine splitting lines for these. So, therefore, you can explain all of them very well ok.

So, the 9 lines coming these are perpendicular kind of a situation and each of this if you see we are closed by you have a splitting of each of this peak into 2, this one is coming from the C table another is coming from the n terminal kind of thing. So, that is that is why one can study these ones too. Here we have shown for a different case, because this kind of a vanadyl species is found in biological systems, even in samples of the man

animal samples or my samples the liver, spleen, kidney tissue etcetera kidney all these tissues and they can be studied.

So, if you study at the room temperature you find not so very nice spectrum, but if you go to the lower temperature you will find the spectrum to be very nice and very well very well resolved kind of thing so. So, therefore, one can study this presence of the vanadium 4 plus species in the biological systems, by using the EPR spectroscopy ok.

Let us look at some few other cases where the vanadium is being accumulated.

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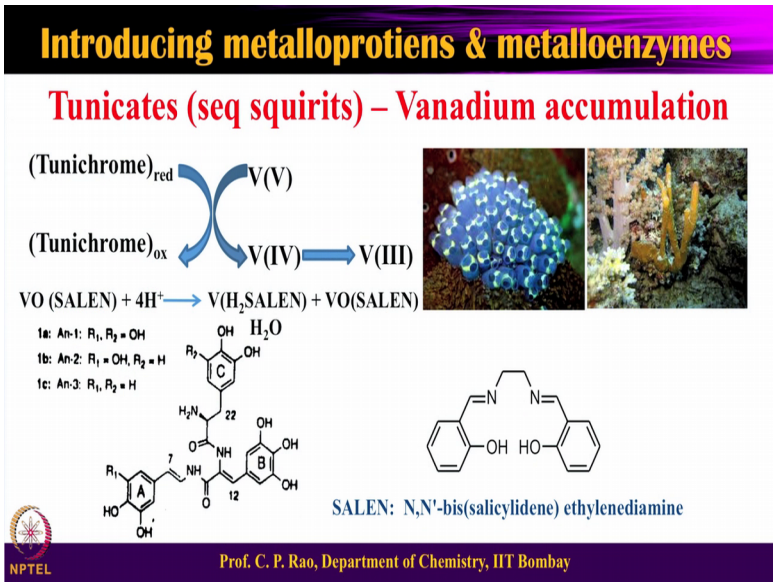

In fact there is some see small sized animal seq squirits, tunicates when where vanadium is accumulated and this vanadium accumulation is found in their body. So, seq squirits body is 80 percent of his body is by the vanadium o vanadium based compounds.

So, what happens in these things? So, what happens in these things is, these tunicates have got some chromophore called tunichrome and this tunichrome can undergo oxi redox process; as a result of that it can bring a redox in the vanadium 5. So, therefore, tunichrome reduce going to oxidized will convert the oxidized vanadium to reduce the vanadyl. So, oxidized vanadium is vanadium 5 reduced vanadium is vanadium 4 and further this is this forms a vanadium 3.

So, you can have a some part of a vanadium 5, some of the vanadium 4, some of the vanadium 3 all of these are found in this and in fact, for the evidence for a vanadium of

these species have been worked out by small molecular systems as well ok. So, this is for the vanadayl vanadyl vanadium 4 compound, this is for the vanadium 3 compound these are from synthetic analogs. So, salen is a salen is this kind of a molecule that synthetic analogs you can in fact, make 4 and 3 and show this.

So that means, in the biological system whatever the vanadiator is being taken up from the let us say seawater, because these are sea tunicates the vanadium 5 is not sitting in the 5 it will go into 4 and 3 and the vanadochrome is somewhat having a structure on this kind. So, what is this one? You have a catechol kind of a groups and you know that the catechol kind of a groups, we will undergo very nicely very easily redox.

So, reduced form is catechol or phenol or oh oxidized form is a quinone or semi quinone cat o quinone and these are the things. So, oxidized form and reduced forms can be formed. So, therefore, the vanadium present in these sea animals is in the form of a vanadium 4 and 3, though the entry is vanadium 5; they are not entered as vanadium 4 that should be noted. Kindly note that these are the entry point is vanadium 5 not the vanadium 4.

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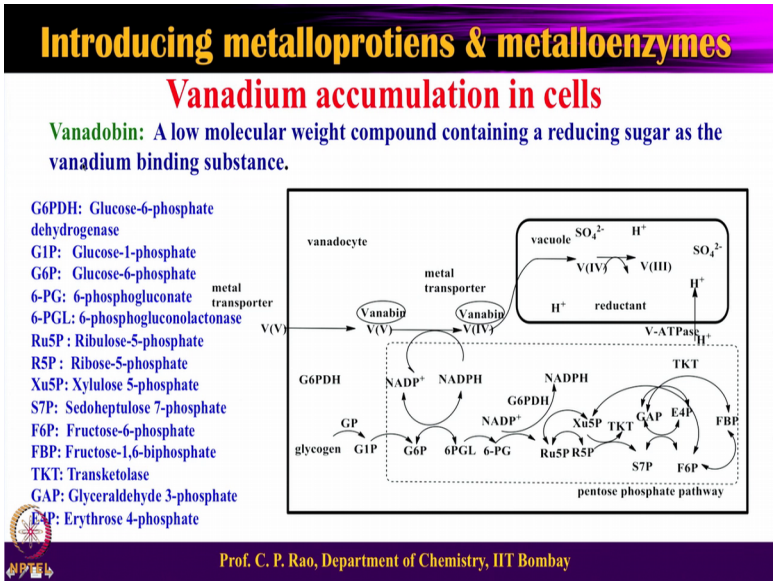

In some of the species there is a low molecular weight compound containing reducing sugar which is called vanadobin. In fact, the vanadobin also do very similar kind of thing. In this whole figure what I need is your attention is this is if you take a central line here, only the above portion you do not need to so much worry about the portion below.

So, vanadium 5 and is captured by the vanadobin and then it will convert vanadium 4 and then this can go into 3 and so vanadium 5, vanadium 4 to vanadium 3 and you have other anions to stabilize some of these.

So, therefore, in another system with the previous one was the sea squirit and this is in some of the cells. So, even in cells the vanadium 5 that is being taken in cannot be ideally sitting as vanadium 5, it will go in to vanadium 4 and vanadium 3 and this goes very well with what we studied the redox potential. 5 to 4 absolutely very easy, 4 to 3 is somewhat not as easy, but; however, with certain reducing agent this is possible and that is what we are basically finding ok.

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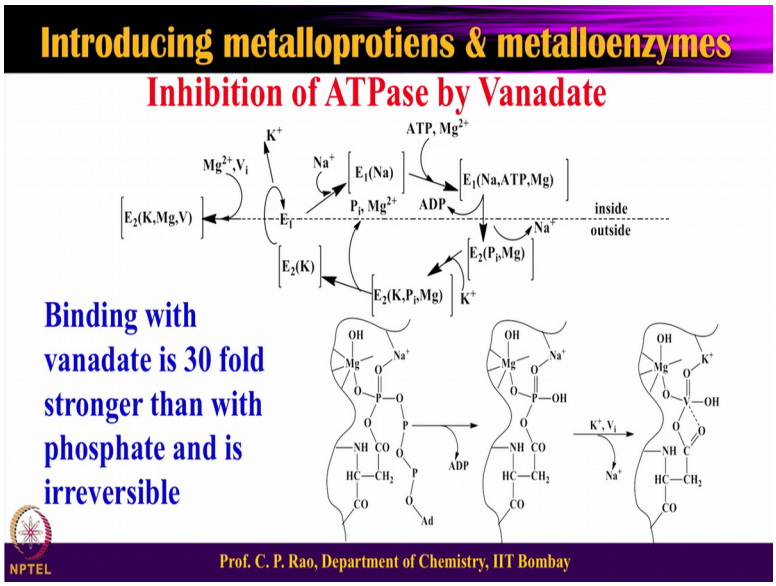

With the vanadate before we go into vanadium based enzyme, let us look at some effect of vanadate. At this stage I would like to recall your attention to the sodium potassium ATPase pump just in the previous class I have covered that you know what I mentioned there you have even confirmation of the protein ATPase, the sodium binds and then this triggers along with the magnesium 2 plus, the phosphorylation. So, the phosphorylation will be with the phosphate group and at that stage protein conformation changes sodium ions are gone and this whole thing happens in this particular half of the cycle.

And at that stage of the sodiums our lungs, the potassiums gain the affinity to bind to the science in the ATPase and at this the magnesium activates and then dephosphorylates. So, when it dephosphorylate at that moment if you have a vanadate in the presence, the

dephosphorylated protein is replaced by the vanade vanadate and the second part of the cycle is incomplete. So, thus presence of first vanadate will act as a inhibitor for the ATPase activity. So, ATPase is good, this is the half cycle goes very happily, the second half cycle, there is a phosphate dephosphorylation during the period vanadate is present, the vanadium will or vanadate will bind once the vanadate binds then it will not revert back to the normal state. Because the vanadate binds at least 30 fold stronger and also vanadate vanadate binds very much stronger to this particular system and it is irreversible. So, vanadate binding is absolutely irreversible.

So, therefore, this cannot be functioning. So, therefore, if in ATPase cycle, it is a you add some vanadate and vanadate with phosphate a very similar in terms of shape, charge, size etcetera were you close by and then vanadium vanadate can inhibit the enzyme. So, this is an inhibition of the enzyme, I am not talking about the enzyme activity ok.

So, the kinds of species that are present are shown over here the magnesium bound ATP and then vanadate bound. So, with the phosphate and the when the phosphate is gone vanadate is present you. So, the species looks very similar, but the vanadate species much more stronger by 30 fold and it is irreversible ok.

So, in this class what we have studied? We have studied the vanadium can exhibit plus 5 plus 4 and plus 3 in the biological systems, plus 5 to plus 4 is quite easy plus 4 to plus 3 is not impossible though not easy, but it is possible. So, therefore, in the biological systems the vanadium has been found in the form of plus 5 plus 4 and plus 3 and vanadate acts like a inhibitor to the ATPase cycle; in the second half that is the potassium part of the sub part of the cycle, that is in the this part of the half of the cycle. So, we will continue with the enzyme based on the vanadium, which is called vanadium haloperoxidase in the next class.

Thank you very much.