Bioinorganic Chemistry
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Lecture - 36
Vanadium Enzymes - IV

Welcome, we just finished today the part belonging to the enzymes, which can be motivated by the presence of the Vanadium.

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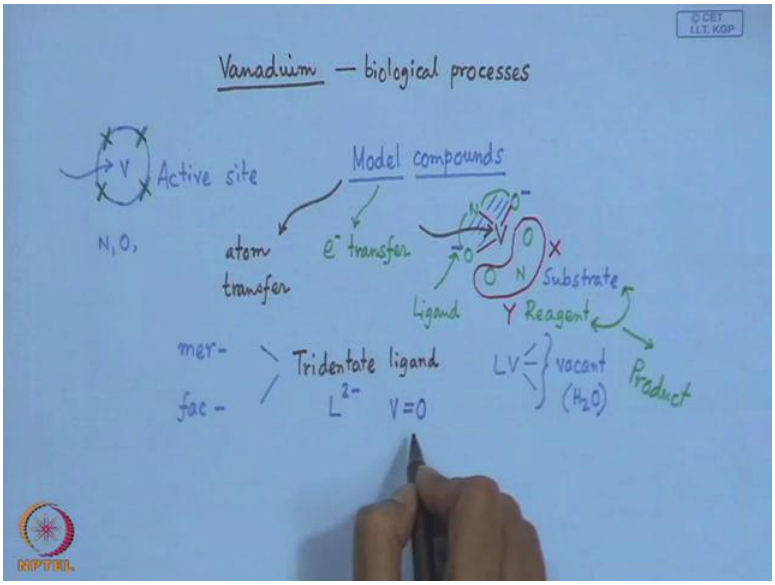

So, how vanadium can get inside the cell, how vanadium can show some interactions with different important biological processes. So, basically today will be talking about the interaction of all these groups related to the vanadium; so the part 4 of Vanadium Enzymes. And if we consider some of these as the model compounds, because the particular active site, what we can have in the biological system. So, if we have the active site in the biological system, and some of these positions having some useful donor atoms, like nitrogen, like oxygen or any other useful group, which can be identified by different techniques like, (( )) structure or other spectroscopic signatures.

So, how a particular active site can go for the vanadium interruptment and how the vanadium can go for several important reactions, which can also be mimicked in the laboratory by synthesizing some related model compounds. So, the synthesizes and characterization of these model compounds, play some important and interesting role in

understanding several important aspects related to vanadium chemistry. That, if we just simply consider whether this active site is participating or catalyzing some important reaction where electron transfer play some important and major role.

Then we should have a related model compound, where the environment the coordination environment compared to the active site environment, where definitely these groups are the immediate donor atoms, which are bond to the metal center, the metal ion center. But in case of model compound these are the useful donor atoms, can be nitrogen, can be oxygen and how this particular donor atoms can be a part of the ligand system; it can be a part of the ligand system.

And when the metal center is not present that means, several other oxygen, oxygen or nitrogen donor atoms may be available there, may not be originating from the same ligand system; that means, the same proteins backbone. But some other small groups can enter over there, where the same passage of the metal ion that means, the passage of metal ion as vanadium can also be studied very nicely. So, is model compound plays some vital and important role, in understanding the type of chemical reaction, which is being catalyzed by these vanadium centers, for electron transfer or some atom transfer reactions.

So, if it is an atom transfer, so we can also see the same atom transfer reaction with the help of these model compounds. So, one such example for that is that, when these model systems can have some water as the ligand. And if water is occupying a position which is correspondingly trans to the oxo group, which is important for the labialization from the strong trans influence. So, we have chosen one such system, which is reported in the literature also, that if we have these backbones, as a saleslady high backbone with bromine substitution to the para position of the phenol oxygen. And which is being condensed with one mole of glycine, so we get very simple O A, O N O tridentates ligand.

So, this is one part of the cavity, what we are just talking about that this particular part is available for coordination of the vanadium. So, if the system the cell can par meet, the entry of vanadium center to this particular part. So, vanadium can go and immediately form three bonds, one is this vanadium oxygen, second is this vanadium nitrogen, and

third is this vanadium oxygen bond. So, the same is also true, when vanadium is bond to this particular ligand system in a typical coordination compound.

So, what happens there that immediately depending upon the major of the vanadium salt, what we are using over there, immediately this vanadium is coordinated to this tridentate ligand. So, the binding of this tridentate ligand is very important, so model compounds we can have from the choice of this ligands, so first of these is a simple tridentate ligand. So, why we are taking this particular tridentate ligand is that, we have this oxygen nitrogen oxygen binding, and vanadium is forming three bonds to that. And we will we do not know what other positions would be, and what are these positions will come and bind to the vanadium center. So, this particular phase is it is tridentate to vanadium, and two more positions are occupied by two other groups which are unknown, which can be x or which can be y.

So, this particular species that means, x and y you already know all this thing that, x can be our very good substrate species, so when this ligand bond system that means, the vanadium is there, and ligand was already present there. So, depending upon that these V L species can have two to three positions vacant, it is not vacant in the true sense, it can be occupied by water molecules, which is present in the system. And which is already there when vanadium is bond to these water molecules to give us the corresponding ACO compound. So, these vacant sites can go for bending this x and some other reagent this y can be our reagent.

So, there are positions where the substrate can bind to directly to the vanadium center, the reagent can also bind to the vanadium center. And in the next step, these two that means, the reagent and substrate can react to give rise to our product. So, product is formed from there, so very important thing is that how this tridentate ligand is binding to the vanadium center.

So, we all know that depending upon the flexibility of the ligand backbone, we can have two different types of binding, one is meridional binding; that means, this three can bind to the vanadium and they are in the same plane. So, when they are not in the same plane, the same tridentate ligand occupy one particular phase, so if they occupy one particular phase, we call these as a corresponding facial binding. So, the choice of ligand is therefore, can dictate us whether we should take a corresponding tridentate ligand, which

can bind in meridional fashion. Or the same tridentate ligand, which can go and bind the metal center in the facial mode.

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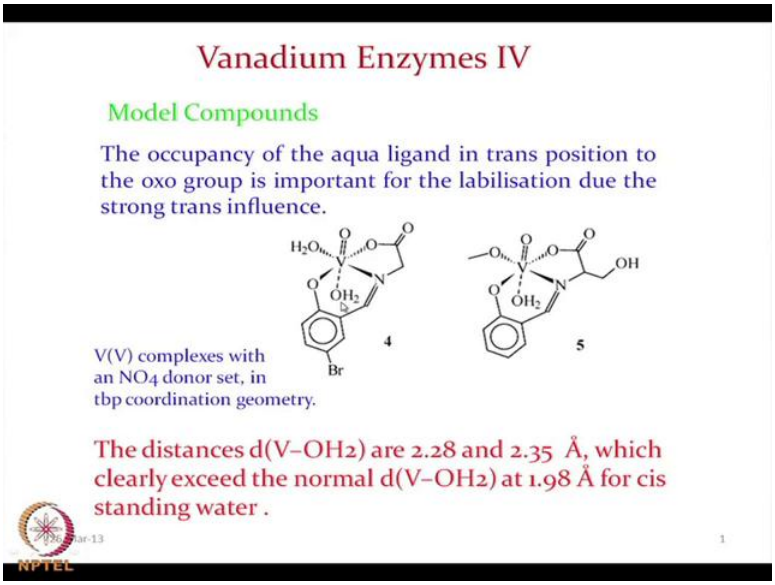

So, in this particular case, what we see that, this particular ligand as well as the other ligand, where we have some different part of the glycine derivative. We have some alcohol part also to check whether, this vanadium has higher affinity for this carboxylate oxygen; this is the carboxylate oxygen or it has some binding affinity to the alcohol oxygen. So, when you get the compound, when you synthesize the compound, and characterize the compound. We can identify that vanadium has more affinity for the carboxylate oxygen, rather than the alcohol oxygen.

Because, these to have different p k values, and the basicity of the remaining oxygen, what is getting from there as O minus has also different, so vanadium will have direct affinity for binding to the carboxylate oxygen. So, when these three positions are blocked in a meridional mode, we can have three other remaining positions. And these three remaining positions are interestingly shifted over there, that if we get the immediate vanadyl-oxygen. Because, vanadium compound very easily formed the corresponding vanadyl complex, it is directly coming from the oxygen of the water molecule also. So, initially if we have the vanadium water bond, then after deprotonation, it goes to vanadium hydroxide; and then finally, to vanadium oxo bond.

So, when oxo is there, and if we just see that three of these are coming from the ligand, fourth is also another aqua molecule. So, initially when this dotted water molecule is not present, we have a situation, where the geometry of the coordination environment can be considered as a square pyramidal one. So, if this particular vanadium oxygen bond is not so short, and if we cannot have a corresponding pyramidal distortion of the geometry.

This water molecule can come opposite to that of our vanadium center with respect to the oxo group, and quickly start interacting with the water molecule. Similar thing also happens this is compound number 5, where this vanadium instead of water coordination, it can bind to some alkoxide anion. So, this is an ionic coordination and also during hexa coordination, it has some weak coordination from the water molecule trans to that of our vanadium oxygen double bond.

So, this particular occupancy that means, why this water molecules should be there or not that is being dictated by the oxo group. So, this particular presence of this oxo group, if it is not transforming from oxo to hydroxide or hydroxide to aqua molecule. This oxo function can weaken the corresponding vanadium oxygen bond coming from the water molecule trans to this vanadium oxygen double bond.

So, what we get that we can make these compounds in the vanadium plus 5 oxidation state. So, initially what we get if we the your ligand is tridentate dinegative in this form, this ligand, this L if we can have charge on this oxygen, and charge on this oxygen, we can have a corresponding compound of the ligand, where L is giving rise to two negative charges. So, vanadium is there, so we can have 2 negative charges from the ligand, and also since it is coordinating with the oxo, so vanadium oxo can also 2 negative charges.

So, immediate neutralization of 4 negative charges by vanadium 4 plus. And if it goes for one more step towards oxidation, it can go to vanadium in 5 plus oxidation state, so modeling of this particular oxidation state is very easy. And we can have the corresponding vanadium pentavalent compound that means, vanadium in plus 5 oxidation state. If we can have NO 4 donor set, in roughly trigonal bipyramidal coordination geometry, so what should be the most preferred coordination geometry.

So, instead of this particular square pyramidal or octahedral geometry, the info O donor set, here also we can have 3 oxygen, and to 5 oxygen anion. So, this is an NO 5 donor set, this is also NO 5 donor set for an octahedral geometry around this vanadium as well

as on this vanadium. But if we can have a NO 4 donor set around the same vanadium center, it can distort itself to a corresponding trigonal bipyramidal geometry, which is a preferred geometry, for this particular vanadium center.

And we also see we can compare this vanadate groups or vanadate anions to that of our phosphate. And the phosphate anions will see in case of phosphate is hydrolyte reactions that this vanadium center will have some preference for trigonal bipyramidal geometry, compared to square pyramidal geometries. So, here the this particular labialization that means, the presence of vanadium oxygen bond, how they are weakening the corresponding vanadium water group can be seen.

If we determine the corresponding single crystal x-ray, structure of this synthesize compound in a good crystalline form. And determination of these vanadium oxygen bond this particular bond, this dotted bond we find that the corresponding bond distance for this vanadium oxygen bond, lies in the range of 2.28 to 2.35 Armstrong, which is clearly a bigger value a longer value. Where we see that the normal distance falls in the range of 1.98.

Because, within the same system we can have another bond which is this particular vanadium oxygen bond, which is cis to this vanadium oxygen double bond, but this bond is pretty shorter in the range of 1.98 Armstrong, compared to these bond, which is in the range of 2.35 or 2.28. So, this particular bond is pretty weak, and when substrate comes and bind this particular centre it immediately can displace; these two positions that means, either these two water molecules can be replaced.

One can be considered as the binding of x the substrate and another can be bond as the corresponding reagent, for the usable transformation centre at the vanadium site.

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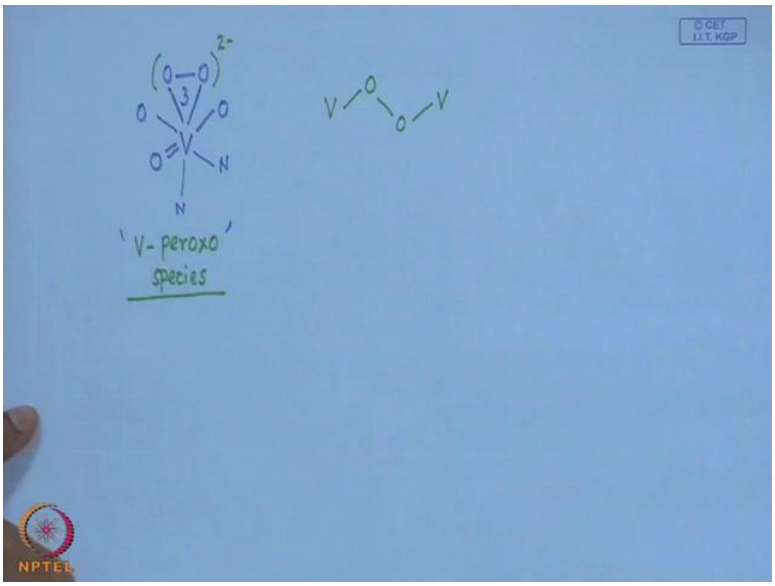

So, interestingly also that this particular vanadium complexes, if they go for some amount of interaction, what we see that already we have this vanadium oxygen double bond, and we can have other groups. So, if the plane, the square plane is formed from three other donor atoms, one is nitrogen and two oxygen, and this other oxygen. So, if five positions are occupied, and if one of these positions can be taken up by the corresponding substrate molecule.

And we see that this particular centre having some vacant site that means, this particular area or this particular space is very important such that, we can consider a corresponding binding of peroxide anion. So, we have seen large number of vanadium compound, whether it is in the living organism or in some model compound that vanadium is forming a corresponding peroxide bond. In this particular fashion that means, in cis mode and it is forming a very tight bonding pattern for a three membered ring.

Because, this is a corresponding three membered ring for the corresponding coordination of both the oxygen atom, instead of any such bridging type of coordination involving two vanadium centers. So, we can have these and this particular group, basically this peroxide compound which has a corresponding charge of 2 minus. So, the vanadium peroxo compound is very important.

This case, and we should have sufficient vacant space such that, the peroxide anion can go and bind to vanadium in this form. So, once it is bond we have this oxygen and this

oxygen, so we need further stabilization. So, if possible that means, this particular linkage is not very much stable, compare to our oxo binding, oxygen binding or nitrogen binding. So, to stabilize this particular peroxo group to the vanadium site, we need some other type of interactions which can stabilize the enter vanadium peroxo fragment.

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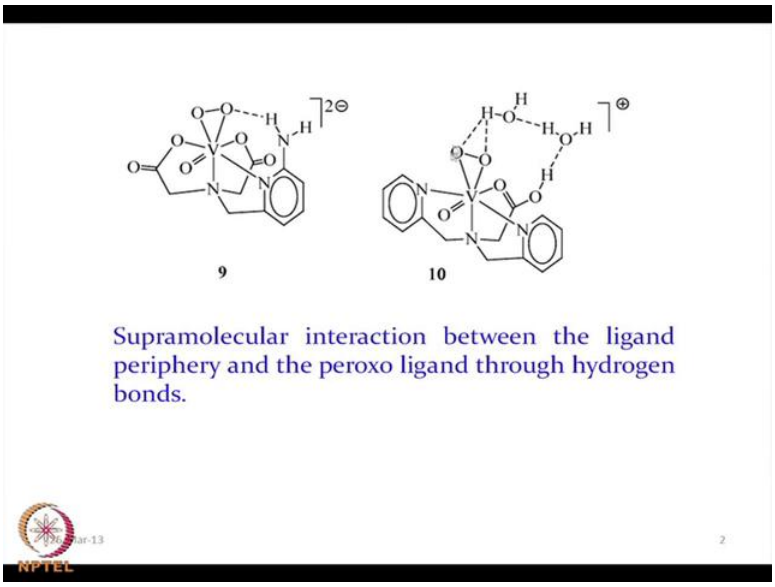

So, what is that, we see that in this particular case, this vanadium peroxo group, and we already know that it has two negative charges, so some residual delta negative charges are there, which is present on these oxygen atoms. And if we have some group attached to this (( )) ring of the ligand system that means, if we have some ortho NH 2 function, so this NH 2 groups if they are available. So, when it forms corresponding complex, this NH group is in close vicinity to this particular, and it can form some hydrogen bonding interaction. So, through such hydrogen bonding interaction, this particular vanadium peroxo species can be stabilized.

And that also give us some important information, that if this particular group is your reagent, and if this particular vanadium peroxo reagent can show some hydrogen bonding interaction on the substrate molecule. Then this particular substrate can be reacted towards this activated peroxo anion, which is bond to the vanadium group. Similarly, not only the NH 2 function of the ligand system, but simple water molecules. So, if we have water molecules as well as protons present in the systems, like that of our pyramidal structure of the ice molecule.

So, one water molecule over here, which is already hydrogen bonded to another molecule of water. And we can have the corresponding proton either this is bond to this carboxyl function, so if the carboxyl function which is already bond to the vanadium centre, have instead of O minus group it can have the OH function. And this OH function can be stabilized by this fast water group of these water dimmers. So, this is the water dimmer which is getting stabilized through hydrogen bonding through internal hydrogen bonding between two water molecules.

And this oxygen further shows hydrogen bonding interaction with the OH group of the (( )), and the peroxide linkage showing some other type of hydrogen bonding interaction which is different from compound 9. That means, this hydrogen is forming interaction with both the two oxygen atoms of the peroxide groups, so it is a different type of stabilization of the vanadium peroxo unit. So, not only this stabilization helps this particular entity, but it also helps the presence of the OH function or the carboxyl end of the ligand.

Because, in the long polypeptide chain on the protein chain, we can have several of such OH groups attached to the polypeptide backbone, it can be originating from the amide backbone or it can be originating from the corresponding carboxyl backbone. So, these backbone hydrogen atom available on oxygen or nitrogen, if it is amide can further be stabilized in the presence of water molecules. And these water molecules can further interact with the peroxide (( )) to stabilize this vanadium with respect to that of our peroxide link.

So, we call these interactions, these hydrogen bonding interactions we all know that these interactions we call as non covalent interactions. So, non covalent interactions are beyond the molecular interaction, so we call them as the corresponding supramolecular interaction. So, we have the vanadium compound is one molecule, and then we can have some other part of the species like this NH 2 or the water molecules, coming from the separate water molecules it can be present in the system as the lattice water molecule.

Or some other water molecules which is trapped within the crystal lattice for that, so this interaction with the ligand periphery that means, the peroxide functions are present at the ligand periphery. Because this particular part is blocked only the part which is available

for this hydrogen bonding interactions is that site where the peroxide linkage is coordinating to vanadium.

As already I mentioned that, if we can have some vacant space or vacant area in this particular area, then only the peroxide can show this sort of coordination to the vanadium centre, and which further shows hydrogen bonding interactions with the water molecules. So, hydrogen bonds in all these complexes plays some important role is stabilizing the entity, where we can have the direct coordinate bond between vanadium and the peroxide anion. So, these peroxide groups we can have, so in this particular entity where we can have the corresponding vanadium, as the corresponding vanadium oxo function, and the peroxo function, so we can consider this as vanadium oxo peroxo species.

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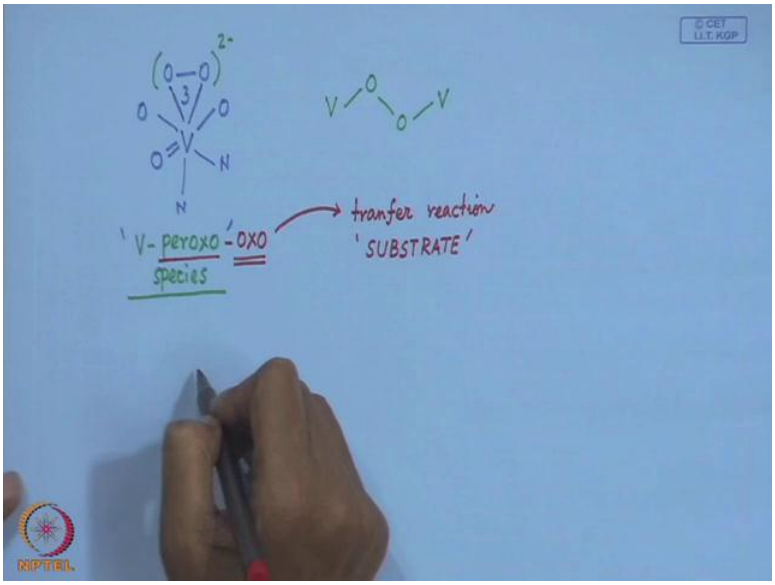

So, if we can go for some reaction, where we want to study the corresponding oxo transfer reaction, we can see that this particular oxo group can be transferred to some other substrate. So, substrates should be there, and we can transfer the oxo group to the substrate, in some cases if we have the species which is a composite of both the oxo group, as well as the peroxo group. We can see that whether this particular oxygen atom is being transferred from vanadium centre, from this oxo end or from the peroxo end.

So, several of these reactions, these peroxidase activity we have seen, which has been obtained, in case of vanadium chloro peroxidase, vanadium bromoperoxidase species

where the vanadium peroxo group is interacting with the corresponding Cl minus and Br minus, which is found from the marine origin.

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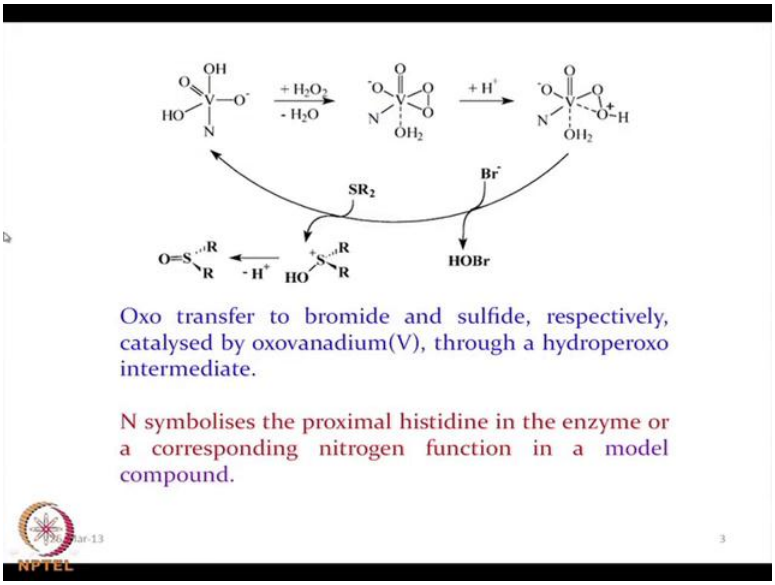

So, if we consider the same oxo transfer reaction to bromide that means the bromoperoxidase activity. Or if we just consider the corresponding oxo transfer reaction on the sulfide group, we can see that they are all catalyzed by the oxo vanadium species through some hydroperoxo intermediate. That means, initially if we can have a non oxo vanadium compound, that non oxo vanadium compound can be transformed to some oxo vanadium compound.

And that oxo vanadium compound can interact with hydroperoxides, forming the corresponding stabilization of the peroxide unit. Either the neat peroxide anion or the protonation of one end giving the hydro peroxide unit, which is originally started giving us through the hydrogen bonding interaction of the peroxide anion to some hydrogen bond donor. So, what we see that this these particular corresponding transaction state, where now the vanadium is present in a trigonal bipyramidal geometry, not in some square pyramidal geometry or octahedral geometry; but it is present in a typical trigonal bipyramidal geometry.

So, all these species are very important that means, if we can have this nitrogen, we can have these as one donor atom, and another is to this site, but also if we have the simple nitrogen atom from the protein chain. And this particular position can be occupied by

simple hydroxide group, this is oxo group, this is a second hydroxide group, and this is O, this is the third hydroxide function, and it can go for deprotonation giving O minus.

So, if they react with hydrogen peroxide, what happens that when hydrogen peroxide is bond to the vanadium centre, this position of this nitrogen getting changed, it is coming from this particular position is occupying, this particular OH group. And nitrogen is over here this oxygen O minus is moving over here, and one new water molecule is coming over there, and this has been converted to a corresponding vanadium oxo function. And which is trans to this particular water molecule that we have seen just now.

That the labialization of this water molecule in a typical octahedral environment is due to the presence of this vanadium oxygen double bond or the vanadium oxo form. So, from a trigonal bipyramidal geometry, we move to a (( )) octahedral geometry, because this particular bond is little bit squeezed one, and this we can also consider as a one bond. So, if we consider this as one bond, so which is the trigonal plane and these are the two sites for the trigonal bipyramidal geometry.

Otherwise, we can consider if these two are considered as two bonds, this can be considered as a typical example of octahedral geometry. So, when we put some proton that means, this particular peroxide anion is getting protonated, and the centre what is generated over there is our vanadium oxo plus hydroperoxide anion. So, this not the simple peroxide anion, this is now the hydroperoxide anion, so this hydroperoxide anion is useful to react, so this is the most reactive species.

And this reactive species is basically responsible for interacting with the substrate group, if the substrate is the bromide anion which can supply this particular HO group, this is the giving you HO Br species. So, OH group is coming from here, and this peroxide group due to this particular reaction is going back to this oxo hydroxide species. So, peroxide species is therefore, no longer will be present over there, so this peroxide group is getting consumed over there.

And we have the corresponding transformation of Br minus to HO Br. Similarly, this oxo can transfer to the sulfide group R 2 S, so sulfide group is also taking this HO plus species. That means, this particular part of the peroxide, hydroperoxide unit giving rise to this immediate attack on the sulfur. And finally, to the sulfoxide formation, so that we

know that how we can transfer this oxygen atom to simple dimethyl sulfide group, to form the corresponding dimethyl sulfoxide.

So, dime reducates reactions we already know that dime, so reducates type of reaction where the sulfides are getting transformed to sulfoxides, can also be seen through this sort of reaction where vanadium is interacting through a vanadium oxo peroxide unit. Therefore, the presence of all these three groups that means, the presence of this nitrogen, presence of this oxo group, and the presence of these peroxide linkages are important for the reaction, where we transfer this HO plus unit to Br minus or S R 2 unit.

So, if we just consider what is this nitrogen, if this nitrogen we can consider that the corresponding immune nitrogen of the ligand system in the model compound, or this nitrogen can be considered as a corresponding enzyme nitrogen of the histidine, and the nitrogen function of the model compound. So, the presence of this nitrogen is crucial, and which is important. Because in all these cases, whatever species we are getting in the form of the oxo hydroxo species, which is reacting with the substrate molecule is all these cases not only the vanadium oxo peroxo unit is present, which is all the time bond to the nitrogen.

And this nitrogen is coming from the enzyme histidine or it is coming from the immune group of the nitrogen ligand. So, all these vanadium oxo peroxo species, we have some unique nitrogen donor atom, so this is therefore, crucial for all these compounds, we can have the specific nitrogen donor, which can control the reactivity, And these nitrogen can come from the enzyme also, and this can also come from the model compound.

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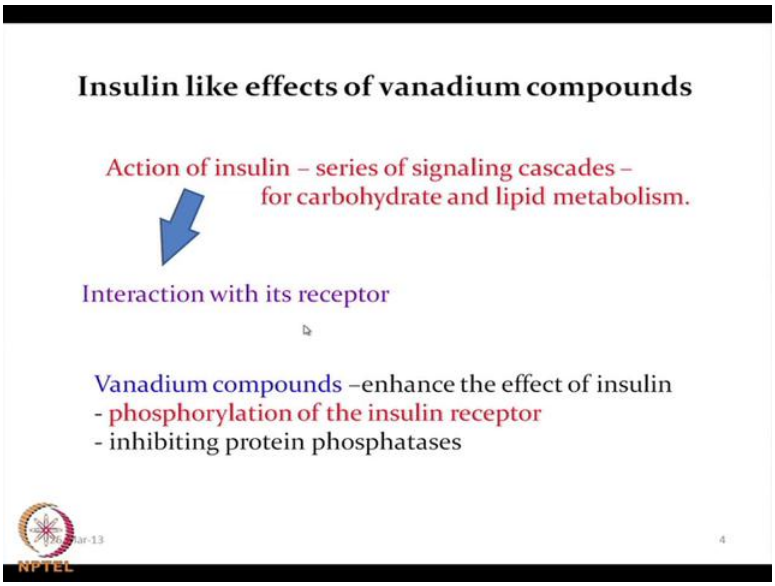

So, what we see next that, some of these vanadium compounds can show some insulin like effect, so the concern condition where insulin is responsible for glucose metabolism is very important. And this particular biomolecule can handle can tackle the corresponding degradation of glucose molecule, in the case of glucose metabolism reaction. So, the effect of this insulin can be mimicked, if we consider some vanadium compound, some important vanadium compound can be a good substitute of this particular insulin compounds by showing some insulin type of effects.

So, what we know that in this particular case, the action of insulin which is responsible for our carbohydrate, and lipid metabolism in our body, when insulin is enactive in our body is not interacting. We can have some diabetic condition that means the insufficient carbohydrate metabolism and lipid metabolism, so action of this insulin molecule is important. And how it is acting on this carbohydrate or lipid molecule is that, during this interaction a syringe of signaling processes are taking place.

That means, when insulin is entering into the system, it can give rise to some signaling process; and that signaling process is responsible for the assimilation of the glucose or the carbohydrate molecule to the system. So, basically this particular insulin is interacting with the insulin receptor system, so there are some receptor sites and those receptor sites are useful to bind this insulin molecule, and this insulin goes and interact with these insulin receptor site.

So, if we can have some equivalent vanadium compound of that nature which can function as insulin, so, these vanadium compounds can have some property of interacting to these receptor sites. So, that we see that, some of the vanadium compounds which are of very special type, and we can choose these vanadium compound from a large number of such vanadium compounds, varying from one particular ligand system to the other.

In this case, these vanadium compounds show some insulin like effect and therefore, can show some enhancement of the effect of insulin by two step things, one is the phosphor relation of the insulin receptor. Because how this particular molecule that means, the vanadium compound which is a synthetic compound, coordination compound of vanadium can go and interact with the insulin receptor through the corresponding phosphor relation state.

And in some case it can inhabit the protein phosphatases that means, the proteins phosphatases are responsible for phosphate hydrolysis reaction. And if we are able to inhabit or stop the corresponding hydrolytic reaction of these phosphatases, we can consider that these vanadium compounds are useful in inhabiting the phosphatases activities on the phosphate extract groups. So, therefore, this action of insulin is directly related to the corresponding interaction with the insulin receptor, and vanadium molecules with some interacting sites which we have seen. In that, it can interact with some site, where it can show some hydrogen bonding interaction, in a similar fashion this synthetic compound can show some interaction with that of our receptor site.

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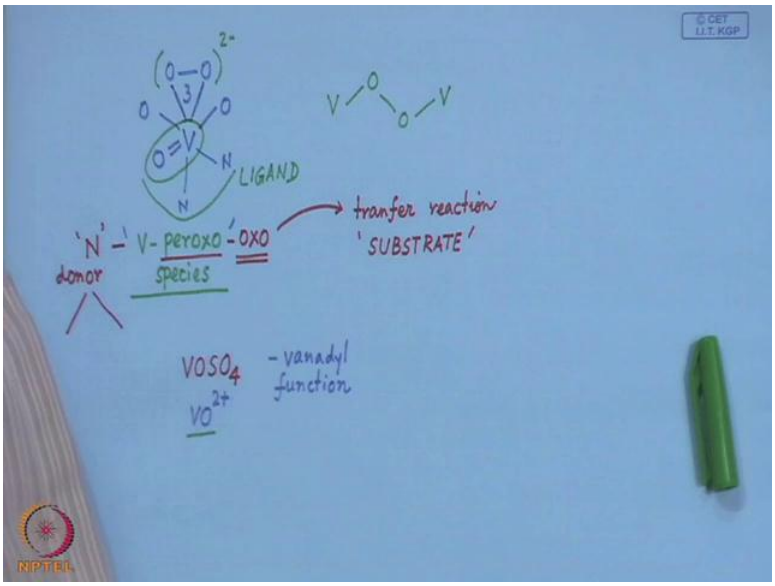

So, we can see that very simple compound that means, the vanadium sulfide not a complex, metal complex, so vanadyl sulfide is the corresponding typical inorganic compound where we have the vanadium oxygen group. So, we have the vanadyl function, so vanadyl function is present and therefore, in this particular case this V O is present as 2 plus. And in this particular case also what we have seen in the compound, where we have the corresponding ligand environment this was our ligand.

So, you have the ligand environment, and in this ligand environment we have the same vanadyl unit is present. So, this is a bigger molecule or rather complex molecule, and if we consider that this should go and pass the cell membrane to entire into the cell to show some interaction, which is similar to that of our insulin molecule. Before that if we just consider that the simple vanadyl compound where the vanadyl sulfate. So, we can check whether the vanadyl sulfate with V O 2 plus unit, can interact to the corresponding receptor site for the insulin molecule.

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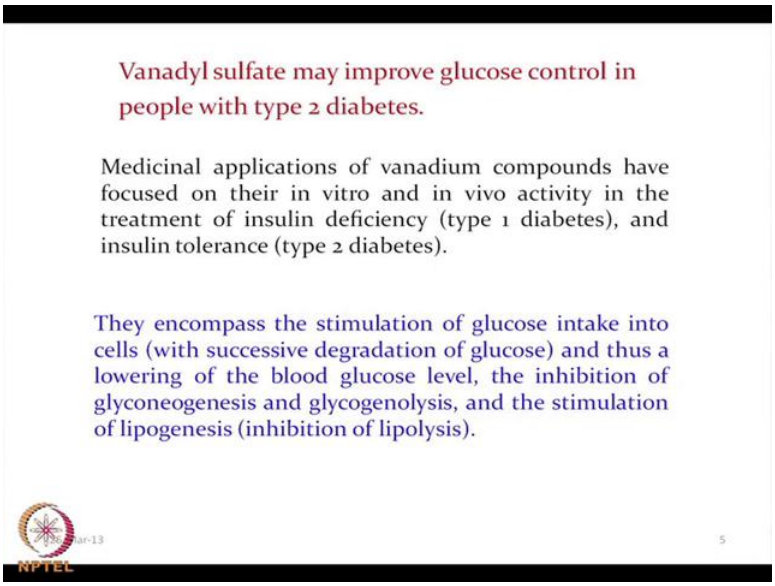

So, when we use vanadyl sulfate, we see that the simple vanadyl sulfate can show some glucose control activity with some people or it is on the experimental animals, like rat it can experimented on some rat to see that the type two diabetes can be controlled by the simple interaction with the vanadyl sulfide molecules. So, that gives rise to the typical medicinal applications of these vanadium compounds, so in vitro and in vivo studies both inside the cell, and outside the cell.

We can study the corresponding activity for glucose control of these vanadium compounds of two different types of patients; one is type one diabetic patients, and another is type two diabetic patients. In the formal case they have the corresponding insulin deficiency that means, their pancreas cannot produce sufficient amount of insulin to control, the glucose metabolism, and in the second case it has some insulin tolerance.

So, both this two types can be seen whether they can show some affect, if we use vanadyl sulfate as a medium for controlling the glucose. So, they can stimulate the glucose intake into the cell, so how we can go and we can put the glucose inside the cell, so glucose should enter into the cell; and then we can go for the degradation of the glucose, and thus it can lower the corresponding blood glucose level of the diabetic patients.

So, these diabetic patients have high blood glucose level, and this high blood glucose level can be counter acted, if we can take the glucose inside the cell, and we can go for

the metabolism. And in this process it can thus interact with the glycol genesis, and glycogenolysis, so in this two cases which is also related to lipogenesis where the lipolysis are hydrolyzed. So, all these hydrolysis reaction that means, the glucose hydrolysis reaction, and the lipid hydrolysis reaction can be controlled by the simple administration of vanadyl sulfate. So, some of these sites can be activated, and through that activation we can see that, it can show some corresponding mimetic reactions.

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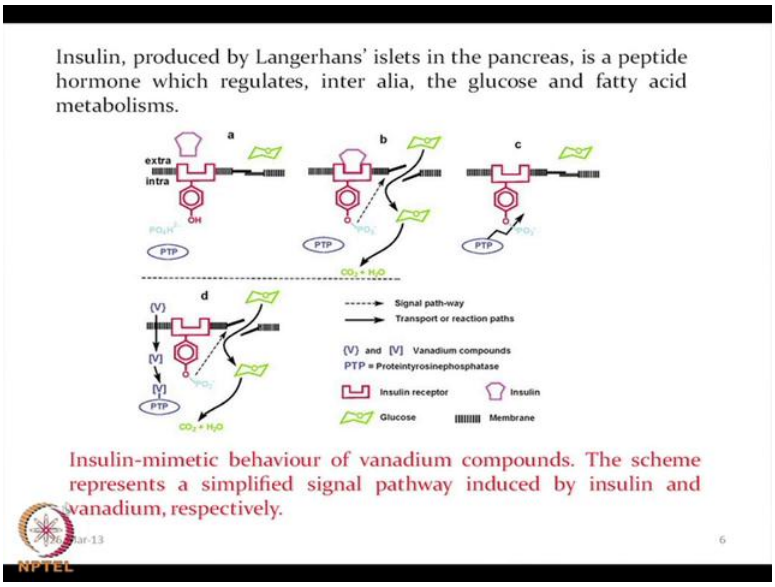

So, insulin the molecule which can produce in Langerhans' islets or pancreas, so there are some site where pancreas is responsible for the production of insulin, and basically this is a peptide hormone. And it has a typical organic molecule only having a peptide backbone only, and which regulates the glucose and fatty acid or the lipid metabolism. So, insulin is responsible for both the glucose and fatty acid metabolism, and if we can have shortage of insulin we cannot see the corresponding control of this glucose metabolism.

So, this is a typical flowchart for several of this complex reactions, and where we see that the signaling cascades we have considered that during this particular interaction, it shows some signaling pathway. So, signaling cascades are important, and where we have the phosphatester bond which is responsible for showing that signaling process. So, in the first step in figure a that means, this part of figure which shows that, this is our

insulin molecule, so this hormone is coming and within the cell membrane it is coming and this is our receptor site.

So, this particular part is the extra cellular part and this is the intra cellular part. And this particular part is responsible to put this particular glucose molecule inside the cell, so when this insulin coming and sitting comfortably on the receptor site, and receptor site has some tyrosine part which is very important. And this tyrosine part which is basically responsible for showing this particular receptor site, whether this phenol group this is the OH function. Whether this OH function is phosphorelated or not that basically gives us some information, whether this insulin can come over here.

And whether this particular gate, this is a gate for the entry of the glucose molecule from the extracellular site to the intracellular site, so in this particular case this PTP is nothing but protein tyrosine phosphatases. So, PTP that is Protein Tyrosine Phosphatases is the corresponding enzyme, showing the corresponding phosphatase activity. That means, if we have the oxygen phosphorous bond of the phosphate ester, the PTP can interact with these and can break this oxygen phosphorous bond showing the phosphor hydrolysis reaction.

So, this phospho ester reactivity can be seen, if we can break this particular oxygen phosphorous bond, so during that process when we have this oxygen phosphorous bond, it shows the corresponding signal pathway. And this signaling pathway can open up this particular gate and this through this particular path we basically this arrow shows which is nothing but the transport reaction path. So, basically this path when the gate is open insulin is sitting over here, so when the gate is open the glucose molecule can come and enter through this gate.

So, here was the glucose, here in the figure a, so in figure b we have the glucose molecule which is entered in the extra intra cellular a region, and this particular one molecule when it is entered within the cell system can go for the corresponding burning process that means, the glucose is metabolized. So, glucose metabolism can only take place, where we can have this particular glucose molecule inside this particular cell. So, this PTP basically, this PTP then if it can walk on this oxygen phosphorous bond can responsible for this corresponding metabolism.

So, insulin basically giving us some information that when insulin seats over there, the gate opens up and glucose can enter inside the cell. So, in the figure c, where we see that the insulin is not there the gate is closed, and the PTP, if the PTP is available the PTP can work on this and which can click the corresponding ester bond, so the PTP is active. And the activity of the PTP is responsible for the breaking of this oxygen phosphorous bond, giving rise to the corresponding tyrosine unit, tyrosine that means, the bearing the phenol group, and the phosphate anion.

So, this situation we do not like, so if this situation is there we require the insulin to come over here to open up the gate, so if PTP is active it should break the corresponding bond, and if this bond is no longer there the signaling cascade is stopped. So, what happens that if we have some vanadium compound, see the vanadium compound is there and which can pass through the membrane. And this vanadium can go inside with some modification which is curly bracketed vanadium, and which is square bracketed vanadium.

So, some modification on the vanadium compound can take place through it is passage through the cell membrane, and this vanadium can interact with the PTP. So, the enzyme PTP is now interactive with the vanadium, and this vanadium compound can be considered as the corresponding phosphatase inhibiter. So, this phosphatase inhibiter that means, this PTP molecules will no longer be utilized for breaking this OP bond of the phosphor ester.

So, OP bond is will remain intact, and it shows the corresponding signaling process that means, it can produce the giving the signal to open up the corresponding gate. So, in absence of insulin only the presence of this vanadium, which inhabits the corresponding activity of the PTP. So, the gate is opened up and the glucose molecule can enter inside the cell, and can go for the corresponding metabolic pathway that means, the glucose molecule can be metabolized producing carbon dioxide and water molecule.

So, this vanadium compounds therefore, showing the same effect what we have seen, in case of the presence of the insulin molecule, only thing that it basically inhibiting the corresponding action of this PTP molecule. So, this PTP if we can go for the corresponding inhibited design for that, so we engage this PTP with this vanadium, so it is no longer available for the hydrolysis reaction.

So, insulin mimetic behavior, we can see from this vanadium compounds and the entire scheme basically what we have discussed just now, can represent simplified is very simple form of signal pathway, which is induced either by the insulin or by the vanadium. So, this path, this dotted line this dotted line the signal pathways can be seen only, when we have insulin in our system or we can have the corresponding vanadium compound within the system.

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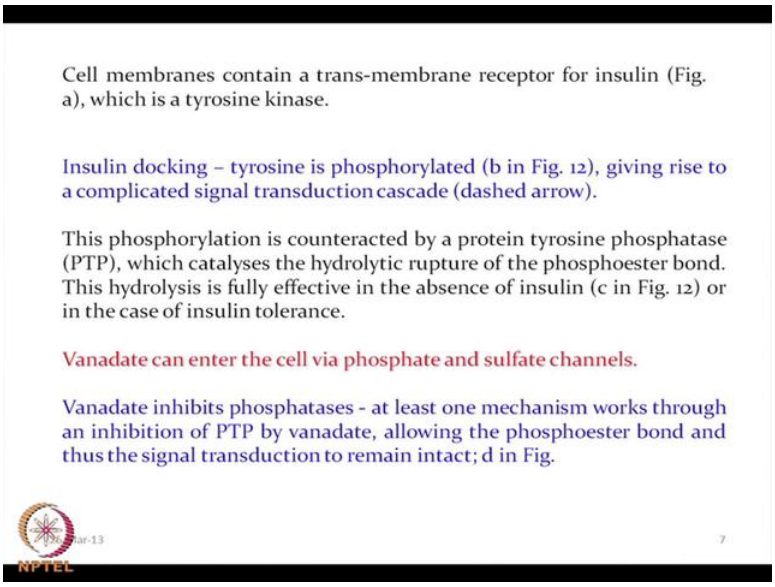

So, if we have the cell membrane, it contains the trans membrane receptor for insulin, and which is basically the corresponding tyrosine kinase. So, this tyrosine kinase is responsible for insulin docking, an insulin is docking is nothing but insulin is coming and sitting at the receptor site of the insulin, and tyrosine is getting basically phosphorelated and in during this phosphorylation it gives rise to a complicated signal transduction cascade.

So, the dotted line what we are showing in the previous scheme is that, it is basically a corresponding signal transduction cascade pathway. And this phosphorylation can be counteracted, if the PTP which is responsible for the hydrolytic rupture of the phosphoester bond that means, the phosphatester hydrolysis reaction, and during this phosphatester hydrolysis reaction, the signal process is taking place.

So, this particular hydrolysis reaction is fully effective in absence of insulin or in case of insulin tolerance, so how we can control this hydrolytic reaction, so we bring the

vanadate; so the vanadate can come and enter the cell via some phosphate and sulfate channels. So, these are not some receptors sites, unlike the insulin molecule, insulin need some receptor site through that receptor site insulin can enter the cell, but in case of vanadium these are the phosphate and sulfate channels, which are very important channel sites.

And through those phosphate and sulfate channels, vanadate can enter into the system, and through that entrance the vanadate inhibits the phosphatases, and one such mechanism is that inhibition of PTP by vanadate only. And which allows the phosphoester bond, and thus the signal transduction to remain intact, the signal transduction should remain operative which allows the gate to open, and which can bring the corresponding glucose molecule within the cell for glucose metabolism. So, that is the basic function for all these vanadium compound for glucose control, and which is showing some corresponding insulin mimetic activity.

Thank you very much.