Biological Inorganic Chemistry
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Lecture No. 07
Occurrence and availability

Hello everybody so welcome to this class where we will be talking about the example of ligands and we all know what a ligands. How they are controlling the coordination to your metal ions centers, then they are biological origin. So, once they are available from the biological world we can consider them as the biological ligand. So, definitely they are occurrence and availability we can discuss.

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So, what are the things we will be discussing in this particular class in terms of their concept that how they are occurring. Whether a simple amino acid can be available and whether that amino acid can function as a ligand for any particular type of metal ion and what sort of amino acid is it that means the donor groups available in it. Then the corresponding elemental composition that means in terms of your oxygen, carbon, hydrogen, and nitrogen for a basic amino acid say like glycine.

Then metallacycle ring formation when the metal ion is binding to that particular side how the ligand part is can give you the corresponding cycle formation including that metal ion. And the thermodynamic and kinetic aspects of the stabilization of the metal ion complexes.

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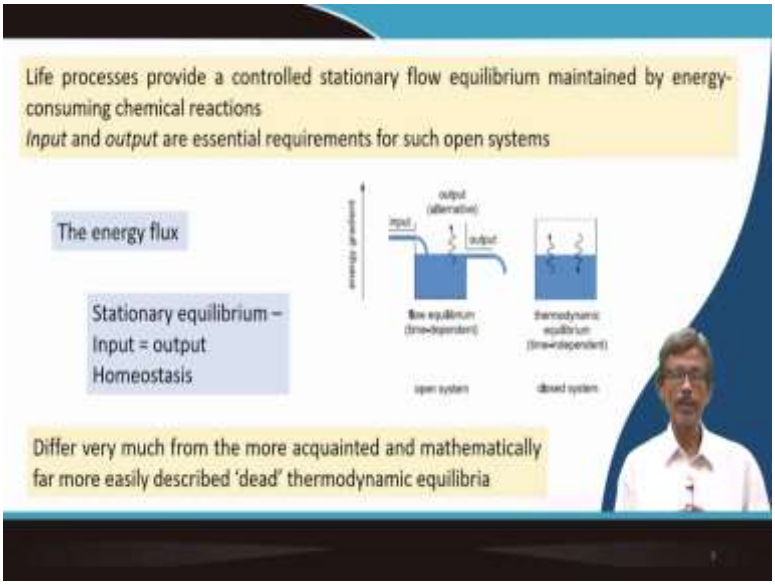

So, all these different life processes what we will be talking and what we are discussing they are dependent on something which can be discussed and which can be considered in terms of a particular thermodynamic quantity or the equilibrium process or equilibrium thermodynamic quantity is basically maintained by energy consuming chemical reactions. So, if you find some simple reaction from left to right A plus B is reacting giving you C plus D but that should be energy driven.

Otherwise, it will not go from left to right they are very highly reactive A is the acting with B producing C and D, but you must have something the affinity for that particular reaction such that you can move from left side to the right side. For the energetic point of view and the rate point of view also the input and output which are essential for thermodynamic quantities for a particular open system when we talk in terms of energy flux.

If we think that this particular energy flux is required for your typical supply of energy in terms of your number of ATP molecules also we can find in that way. So, if we have a particular stationary equilibrium we can have the input and output and is in equilibrium. So, the amount of input that means amount of a thing going from by reacting A plus B to giving you a C plus D similarly, after some time when some amount of C plus D has been accumulated in the medium in the cell environment or within the cell can start reacting.

The C plus D can also react together giving back your A plus B then whole thing will be in the equilibrium. And that is why we maintained the corresponding metal ion concentrations also not only any other important biological molecules like your glucose, like your amino

acids, like your peptides and other things is the homeostasis of the metal ions and we will be focusing in all these classes on the homeostasis of the metal ions.

So, if we have a particular thing that mean the energy gradient if we have from the lower to the higher one. And if we consider to flow equilibrium but in a closed system which is a thermodynamic equilibrium we know everything we study in our regular thermodynamic classes or the physical chemistry classes that they are time independent processes.

But if you have a open system we have the output which is alternative one also the input and output thing how they are correlated for that open system is also a time dependent process is not independent. So, this particular thermodynamics consideration is very much different but mathematically we can access in terms of its corresponding thermodynamic equilibria that adopts equilibria and all this.

So, and the proton transport it will be also the pH of that particular medium also can be correlated little bit with the thermodynamic equilibria. What we study for the laboratory consideration so the cellular considerations will be completely different.

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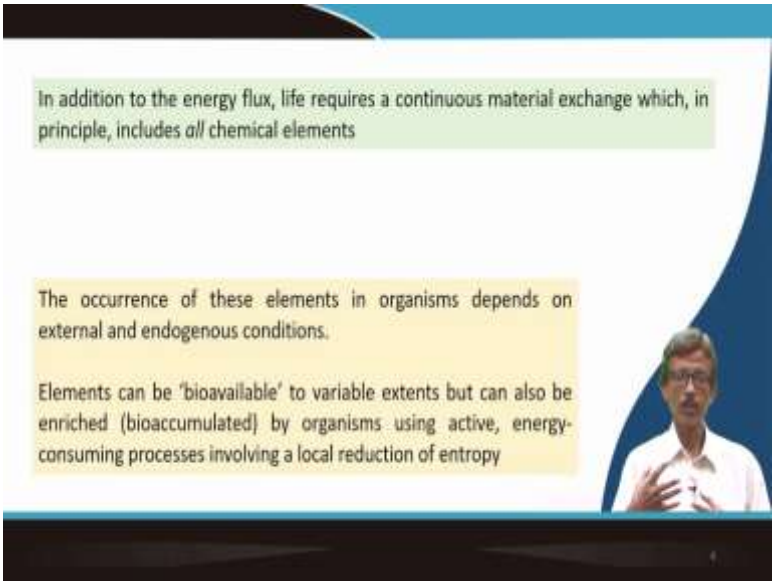

So, when you find that this particular energy flux we get, then the life basically requiring a continuous material exchange. That is why you can have from one particular part to the other which is in principle includes all chemical elements. So, if we consider if we just focus our attention what I told you for your first slide or second slide that you have oxygen, you have carbon, you have nitrogen, and you have hydrogen.

So, the elemental composition wise way we write that some CX HY OZ like these the formula offers the molecular formula or the chemical formula of a particular compound, then when they are going for a different environment such that it can react with something. So, how they are occurring all these elements elemental compositions basically the occurrence of these elements in organisms like in our body how we are made up of different proteins, polypeptides, metal ions, amino acids and all these.

So, they are basically dependent on the external and the endogenous conditions. That means not the internal or other conditions is the external as well as the endogenous conditions which is within. So, these elements starting from your metal ions can be available in the biological world. So, thereby availability of different extent is not that when you take food and our intestine is absorbing all this food material is that, that you can absorb one particular metal ion to a particular extent but not that the other. But it should be in this there.

So, first thing is that how much it is available what sort of food you are consuming. And they that particular consumption basically tells us that okay I have taken this much amount of that particular food which is rich in protein, which is rich in carbohydrate, or which is rich in fat. But the typical absorption process, the typical assimilation process can go for some amount of these materials. We can store iron ion, we can store sodium ion at some point if possible.

So, if they are stored and if they are accumulated from the food material we can consider them they are as bio accumulated. So, organisms any animals, any mammal, or any human being therefore can use some active mechanism which is energy consuming processes involving a low reduction of entropy. So, entropy is not rising entropy is basically reducing in this particular process.

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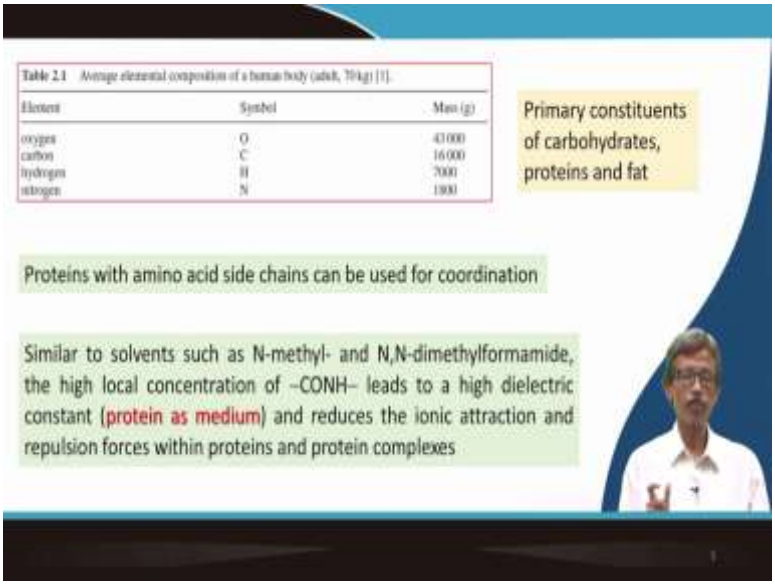

So, the energy what is being supplied for a typical adult that these 4 elements O, C, H, N. So, the typical amount basically because we should have the higher amount of oxygen in terms of your water molecule, in terms of your oxygen in the carboxy and of the amino acid, in terms of your CONH O function of the polypeptide chain as well as in the protein chain. So, the amount of in total the amount of oxygen should be very high.

So, this particular one in terms of a human body having 70 kilogram of weight, then next comes the carbon. So, how you get these carbons so if your food material can supply carbohydrate we all know the carbohydrate is made up of carbon, hydrogen, and oxygen. So, from there you can take up sub carbon. So, the biosynthetic route in our body also if the amino acids are not available from the external sources.

You have to synthesize all these amino acids in our body and carbon oxygen, nitrogen, and hydrogen are the most fundamental quantities in all these amino acids to proteins. So, then you have the hydrogen lesser amount and finally the nitrogen which is the least amount. So, these 4 are the basically constituents for all these sources what I just telling you that is the for the source for your carbohydrate is source for your protein and is also the source for your fat molecules.

Then, once you have these nitrogen bearing molecules you have the corresponding acids thing is not the acetic acid but these amino acids. So, you have to bring the NH2 function to it. Then you have the amino acid. So, amino acids giving you the peptides then polypeptides and then finally proteins in one particular structure. So, the whole protein molecule if you have a big protein molecule not that all these donor groups which are available.

Not only the CONH backbone but also the pendant or the dangling groups or the dangling functions which are available can be useful for the coordination to the metal ions. But sometimes we see that this protein can function as a test tube or a round bottom flask. What do you use for your laboratory reactions. So, this gives you an environment.

So, it is similar to a particular environment when you dissolve some metal ion complex or metal ion salt in some solvent like DMF. Which is nothing but your NN dimethyl formamide so is amid is there. So, remember it nicely how we can correlate it. So, definitely it will have a basic CONH function but that can function as a solvent. So, whether your polypeptide environment or the protein environment can function little bit about that sort of solvent environment.

Then not only dimethyl the monomethyl also N methyl formamide also can function with this particular way. And the whey protein gives us this medium the environment the biological environment these solvent medium can also give that sort of environment. So, if you consider something that he can have a biomimetic solvent environment. So, you can think of having these dimethyl or mono methyl formamide to be taken as your corresponding substitute for the protein environments.

Such that you can monitor the ion ion interactions as well as the protein protein interactions in these particular complex environments.

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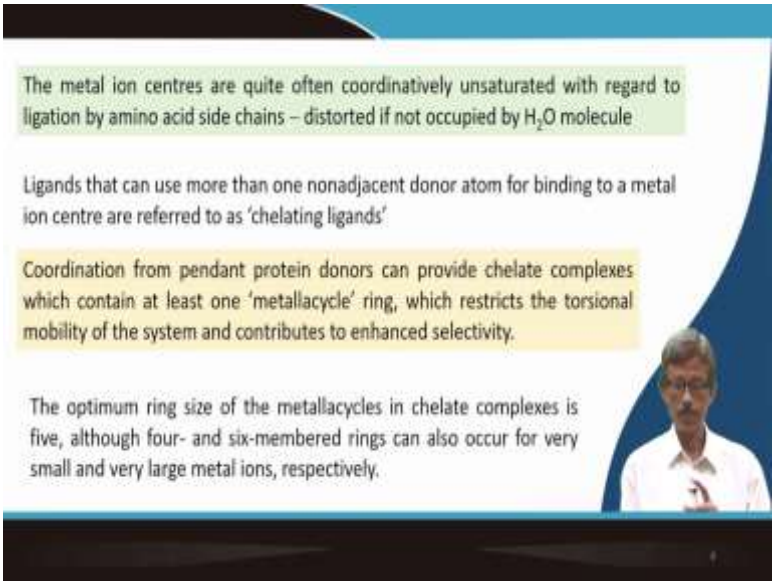

So, you bring now the metal ions and the metal ions centers are quite often coordinatively unsaturated. That if you bring some iron iron into our system is not that when it is not

available for coordinating to your protein part or globing chain it is fully coordinated by 6 water molecules giving you a octahedral environment around say ferric Ion F3 plus. Sometimes it is not there it is not getting water molecules.

But it is so post to some particular wall or somewhere that you do not get that particular space for water coordination. So, with respect to the ligation the amino acid side chains. So, they are unsaturated with regard to the ligation so amino acid ligations are not taking place. And if they are not occupied by all other water molecules. So, these ligands then can use one non adjacent donor atom for binding to a metal ion center as referred to as a chelating ligand.

So, if you take a simple glycine molecule, glycine molecule is NH2 CH2 COH. So, what are its donor groups? So, his donor groups are nothing but you have the oxygen and you have the nitrogen. So, that basically gives us some very good idea that if we have one donor groups like your ammonia which is NH2 function of glycine. And another is your oxygen like water as a carboxy end.

So, if we are able to bring both of them together around the same metal ion center is a very important thing so that it can have the bite. So, the ligand can bite the metal ion and the metal ion is here. So, that biting mechanism can give you a corresponding ligands simple glycine you write the glycine know the formula write it down that is why we are not writing over here.

You exercise yourself from your mind you know the glycine I am telling you the formula. Then put it is that one nitrogen and one oxygen so it will be bi dented NO donal ligand. Your metal ion is there and it is forming two bonds the metal ion oxygen bond and the metal ion nitrogen bond. And you get a whole metal a cycle. So, you have a chelating ligand so that chelating ligand is nothing but your glycine or the glycinate anion.

And afterwards when you have more complicated amino acid residues not the simple glycine you can have the histidine also. The imidazole residue is pendant or the hanging from the chain that also can come and bind giving a metallacycle ring. And some time it restricts the torsional mobility of the system and contributes to the enhanced selectivity. So, this particular thing due to the coordination you are fixing something you are stabilizing something.

So, the torsion of the backbone, the backbone CH2 sometime if we have the CH2 for the ethylene diamine say. So, how the torsion can take place. So, the torsional angle also will tell you how the backbone of the ethylene backbone of ethylene diamine or the bigger molecule

like EDTA, EDTA 4 minus how the torsional thing can give rise to some torsional mobility of the system and contributes to the enhanced selectivity such that in one conformation it will only bind one particular metal ion in a particular coordinate geometry.

Then the ring size of the chelating ligand if you are ethylene diamine NH2 CH2 CH2 NH2 with the metal ion forming a 5 member ring. But if you have a propane diamine you have a backbone of 3 carbon 2 nitrogen. So, 3 plus 2 5 plus 1 metal ion is a 6 membered ring. So, these are the most stable thing the 5 members as well as the 6 member one.

Sometimes you find that you can have the 4 membered ring with the bigger donor groups like it ethyl ejanthey you have bigger sulphur your sulphur. And then is the RO R is a methyl function or the ethyl function RO SS and binding the metal ion. So, it is forming a 4 member ring. So, C CS and another S and the metal ion.

So, these 4 and 5 members so all 3 together the 4 5 and 6 membered rings are there some are small the bite angle can be small you need a bigger metal ion and sometimes the bite angle is bigger you need a smaller metal line for the coordination.

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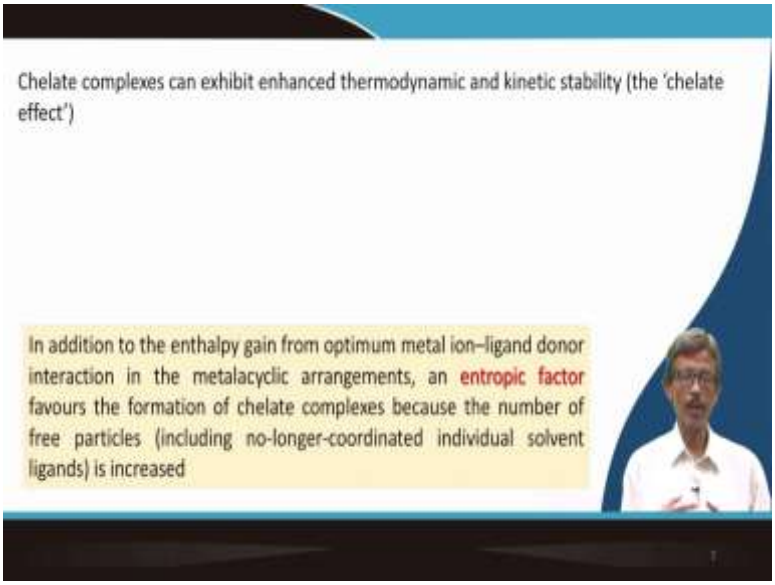

So, that chelating complexes then can exhibit enhanced thermodynamic as well as kinetic stability and that chelate effect. So, once you have the chelate which is binding the metal ion and the driving force for that particular case that how quickly we are getting that means the corresponding equilibrium constant for your formation of the metal ion complex is important. Then one other factor that how quickly they are forming the stability factor in terms of its kinetics the rate of the reaction.

So, finally, the delta H naught or delta H0 is the enthalpy gain. What do we get out of these so you have the free energy change the delta G0 and for the optimum metal ion ligand donor interaction that means the coordination for the metalacyclic arrangement or the metal cycle formation can be controlled also by the entropic factor. Because if you have the corresponding aqua complex of Fe 3 plus and you allow it to react with bi dented ligand.

So, when it is forming a triskillet that means three bidentate an ionic ligands or neutral ligands or a mono anionic ligand binding to your metal ion center forming a whole entity. Where you have 1 metal ion center and 3 ligands. So, is a species of 4 components; 3 individual ligands and the metal ion by doing so you are removing 6 water molecules from the surroundings of the iron center.

Fe 3 plus already bound to 6 water molecules. So, those 6 water molecules will be removed in the medium that means large number of particles are removed in the medium. So, you will have the entropy gain. So, the entropy gain out of that basically favouring that particular complexation reaction. So, this particular also favoured the chelate formation.

And because of the removal of the water molecules or any other small donor groups like ammonia or any other species like chloride sometimes or fluoride sometimes and iodide also. So, that basically enhancing your corresponding complex formation.

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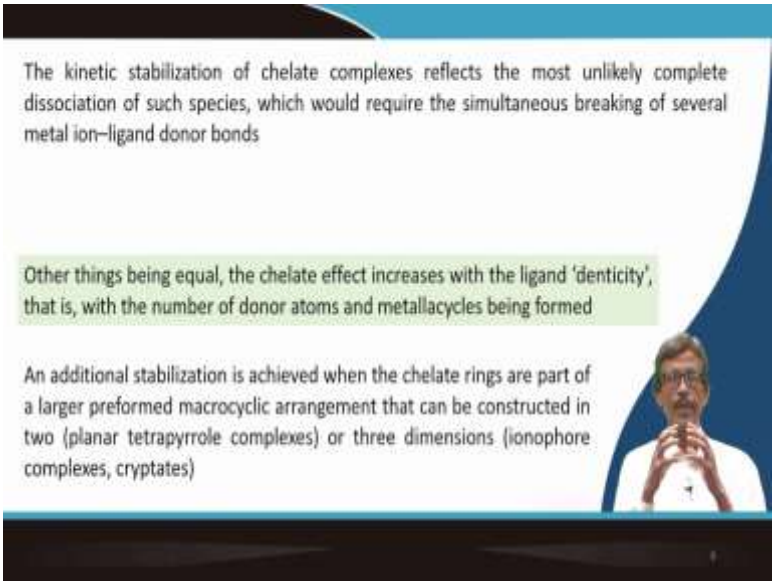

So, the stimulation with respect to the kinetic form of the chelate complex is basically reflects that most unlikely complete dissociation of such species which would require the simultaneous breaking of several metal ion ligand donor bonds. So, why this you can have

the stability. So, if you have 6 ammonia molecules or 6 water molecules surrounding the ferric ion center, then you bring 6 nitrogen in terms of 3 ethylene diamine groups or you bring 3 nitrogen as well as 3 oxygen in terms of your binding of glycinate anion to the same iron center or any other metal ion center.

And finally, you bring the EDTA the bigger exadented ligand having 2 nitrogen donor and 4 oxygen donor. So, all we are thinking or talking in terms of nitrogen in isolation like ammonia or oxygen in isolation like water molecule or the bidentate ethylene diamine or the combination of nitrogen and oxygen giving you a glycinate anion.

Or another bigger combination where you can have the 6 donor ions available from 1 single molecule that is your EDTA 4 minus. So, that is why the kinetic stabilization if we are able to monitor everywhere able to measure will have some effect when the bigger protein chain will come and trap the metal ion. So, if the other things are same of same type then the chelate effect increases the ligand density.

Whether you have a bidentate or a tridented or exadented ligand. So, the number of donor atoms available for coordinating the metal ion is changing. When it is EDTA the 6 numbers 2 nitrogen and 4 oxygen will come and bind to the metal ion center. And at the same time you try to see and try to find out how many metallacyclic rings are forming when EDTA 4 minus that is binding to your metal ion center.

This can you can consider as your assignment you work it out you know it from your school days you are studying. But now you should remember it because this particular information and knowledge is are always important that what is the number of metallacyclic rings are forming out of that particular coordination. So, this additional stabilisation when a chelate ring is forming is also can be given to us if we have certain things that okay I have not the bidentate I have not the tridented but I have a tetradentate ligand.

So, the tetradentate amine based ligand what you can consider and what you can think of is your N 4 ligand N 4 ligand N 4 tetradentate linear MN. So diamine is your ethylene diamine triamine is your diethylene triamine. Then the tetra amine mean will be you will have the 3 ethylene backbone. NH2 CH2 CH2 NH CH2 CH2 NH and then CH2 CH2 NH2. So, these are basically at 2 ends you have the NH2 function and 2 NH functions is a secondary amine and the end amine is a primary amine.

So, name of this molecule would be triethylene tetramine. So, that can also bind to your metal ion and that can also give you many such mental cycling information as well as the stability and the corresponding stabilization we can compare. But if we are able to connect if we are able to connect these two end NH2 functions the primary NH2 functions you will be getting a macro cyclically ring.

So, is basically a garland what we are putting on the metal ion. So, that particular things we can consider as the macro cyclically ring or the macro cyclic arrangement such as we all know for our hemoglobin and myoglobin it is that tetrapyrrole unit the porphyl entering the porphyl end is nothing but your macro cyclically ring. And if we can have a 3 dimensional arrangement that means your crown ethers ionophore are there which can bind nicely your sodium ion as well as the potassium ion.

And sometimes if you have the one cyclic thing and then another ring in from the 1 nitrogen end or one other end through the other end you get a cryptid. Because you have the basic idea of, what is the basic idea, basic idea is that you have to provide 3 plus 3 6 donor groups. So, 3 plus 3 but your macrocycles the N4 macrocyclic like your tetrapyrrole giving my fingertips basically 1 2 3 4. So, these are your 4 nitrogen which is a tetradentate macrocyclic ligand.

But if you bring like this arrangement so this is connected and this is also connected. So, you will get a cryptid. So, this basically the cryptid the cryptid a type of ligand basically can enclose the metal ion within this particular pocket is a very useful very good dumbbell say pocket. And basically the this basically enclosed and the stability will be much higher even if you consider only the binding of sodium ion as well as the potassium ion.

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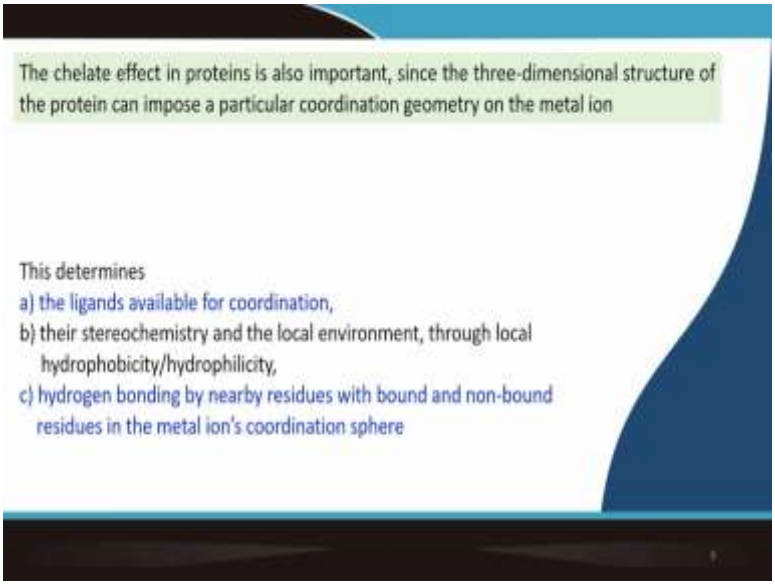

So, those elements are basically very important and you should know about all these ligands you go back your study table and open up the books. What do you have studied so far all the different sorts of ligands. Otherwise, you will not enjoy these classes in terms of your metal ion and the ligand coordinations. Because the many biological and the complicated things will come but before that the very basic ligand part we should have some very good idea on that particular point.

So, since the chelate is forming definitely will have the chelate effect which have higher stability and the energy gain also in terms of that particular coordination. And you have the 3 dimensional structure and if your protein is coming and the protein can give you that supply all these 3 plus 3 coordination inside like your cryptid. So, you have this so you have the planar ring. And then the planar ring is basically the if you have a ring and then you have the corresponding connectivity like a handle another basket handle.

So, these basically able to determine something that what are the ligands which are available for the coordination to your metal ion whether you have only oxygen centric donor atoms available for your typical ionophores which are required for coordination of your sodium and potassium ion or the typical nitrogen for binding your iron in your haemoglobin and myoglobin molecule in your blood.

They are stereochemistry that means the corresponding geometry the corresponding geometrical isomers. What are forming whether you are getting sis isomer or trans isomer facial isomer or a mini donor isomer sometimes the optical activity also. And the local hydrophobicity and the hydrophilicity. What is that?

That means how much your corresponding benzene rings or the hydrophobic organic part is there or the hydrophilic and anionic donor groups like the carboxyl attend or some other eminent which is forming a ammonium ion or any (())(25:25) ionic form. So, that can balance also because everywhere the environment is your aqueous environment.

Then finally, the secondary sphere of attractions which in terms of your hydrogen bonding. So, that hydrogen bonding by nearby residues can also tell us that whether you can have some non-binding residues and the metal ion can give you or fulfill or stabilize that particular metal and coordination.

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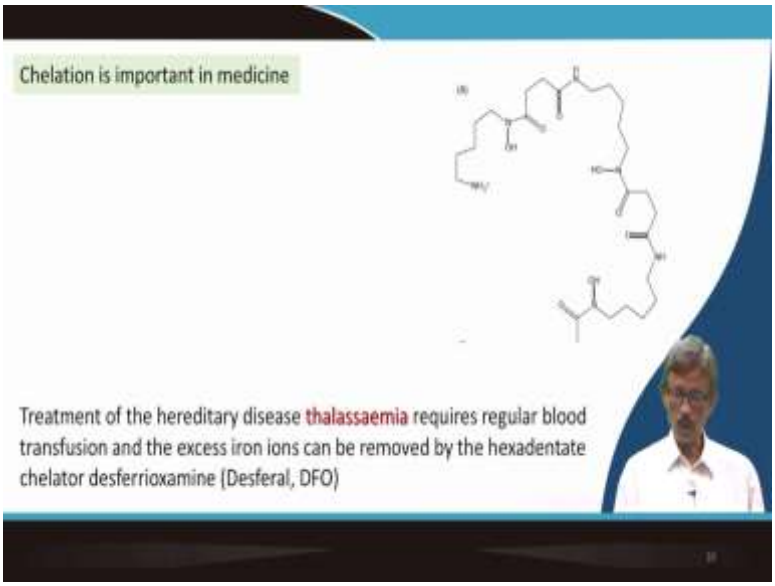

So, now that particular chelation how we can apply to not only your biological inorganic chemistry, the biological inorganic chemistry with special emphasis to metal ions. What the biological world or what the biological information can give us in terms of your corresponding coordination chemistry it can also be applied to your medicinal chemistry. So, it can be considered as a medicinal metal ion chemistry or medicinal inorganic chemistry also.

So, this chelation is very much important we have the corresponding metal ion in our body if we want to supply the typical metal ion. But that will not be very much are very nicely assimilated in our body like your Platinum we know that the Platinum you can supply as a anti-cancer drug in the form of your cisplatin. But we are not injecting the percent with that of yours Platinum salt the Platinum chloride or your tetrachloropalatinate or your H2 PTCL6 some any many number of these Platinum salts that are available.

But a particular type of coordination complex which is your cisplatin is given for your corresponding treatment. So, one such example now I take here is your that particular thing which is a very huge and a long molecule. But is not of your type what we are discussing we will be discussing about your polypeptide chain. But is a very long molecule and what we can synthesize in our laboratory also.

And what we will be looking for when you get a long chain like your triethylene tetramine. It has many other things many other applications starting from your organic chemistry to the polymer chemistry. Those titanium tetramine molecules are very useful for all these purposes. Similarly one such long chain organic molecule is available to us. And if we look at the adjacent bidentate part the NOH CO is NOH CO part so this particular NOH CO.

Then another NOH CO part and then lie at the end basically CH3 CO NOH part. So, is basically the hydroxamate function what we are looking for. And that Hydroxamate function is very much useful if you are facing the toxic effect of your iron centers. That means you have many number of iron by doing some medical treatment on all these things you have accumulated huge amount of iron and that is getting stored in your liver.

So, at what time what will happen the storing of these iron there like your iron nail or iron rod or iron knife or anything getting rusted. So, immediate accumulation of these iron over your liver is basically or your pancreas or any other vital organ if it is deposited over there. You will all be rusted your liver will be rusted then. So, a particular type of disease a hereditary disease you cannot avoid is a genetically transmitted disease is your thalassemia.

And in particular thalassemia occasionally we required the new blood supply the blood transfusion. So, more and more blood is given to your system but your system is not accustomed to remove the other metal ions. We excrete some amount some amount of metal ions we definitely we removed from our body. But when you are consuming some extra amount of iron in terms of your blood and the blood after some time is getting degraded.

It has some lifetime around 120 days. So, 120 days after 120 days this blood will not be useful you have to synthesize your known a new blood. So, to remove that particular one this particular chelator which is desferrioxamine which is known as desferrioxamine desferriol is DFO is a commercial trade name having these things. So, these the very useful chelate which can bind that particular free iron ion. And can remove all these iron or iron overload or the toxic effect of iron from your body.

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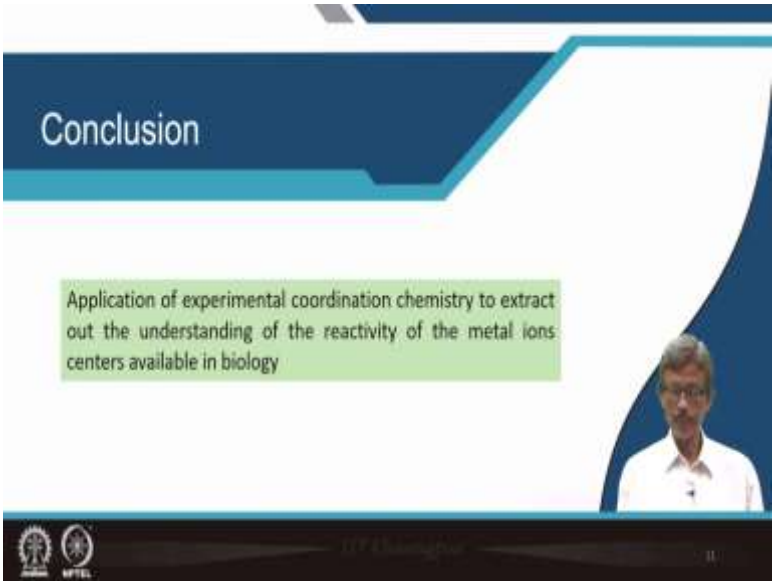

So, what we have seen in this particular class and what we have tried to understand in this particular class by showing these examples of this starting from your ligand your metal ion. And how it is binding and finally the corresponding application one such application all you should know about the application of this particular drug molecule is a typical drug molecule to remove your iron from your body when you are undergoing some treatment.

So, the application of these experimental coordination and chemistry what we are doing in your laboratory is not that theoretically we are talking about the ligand and the metal ion and okay it can bind or it may not bind but the experimental thing is always important which can support the clinical understanding the doctors are doing the pathologists are doing or they are serving all these purposes.

Because we the chemists also read teach and learn the biochemistry. Similarly, the doctors the practicing doctors also they also study the biochemistry. But they are understanding is towards the clinical chemistry. So, this particular part that is the coordinates in chemistry what we can understand from these in terms of the metal ions. And the metal ions which are available in the biological world like the availability of the iron from our food material for the synthesis of new haemoglobin and myoglobin molecules.

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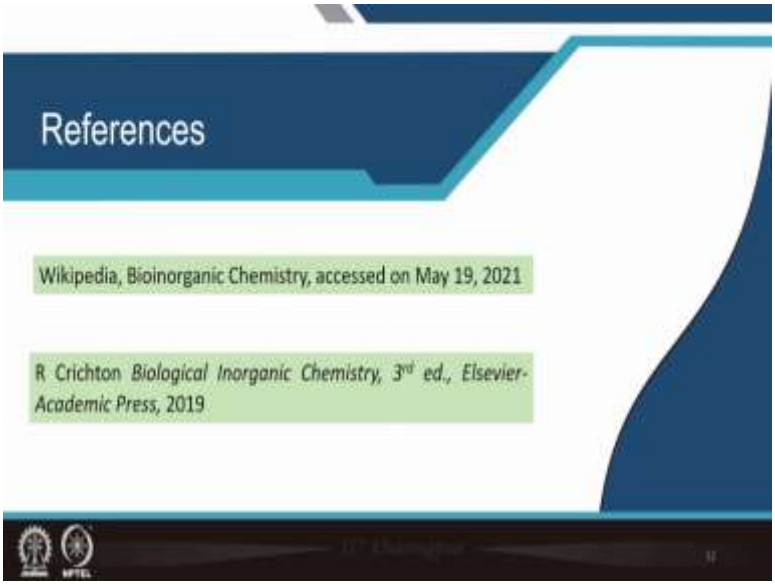

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