**Basics in Inorganic Chemistry**
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**Lecture - 17**
**Introduction to Bio-Inorganic Chemistry**

So today's class is on Inorganic Chemistry in Biology ok.

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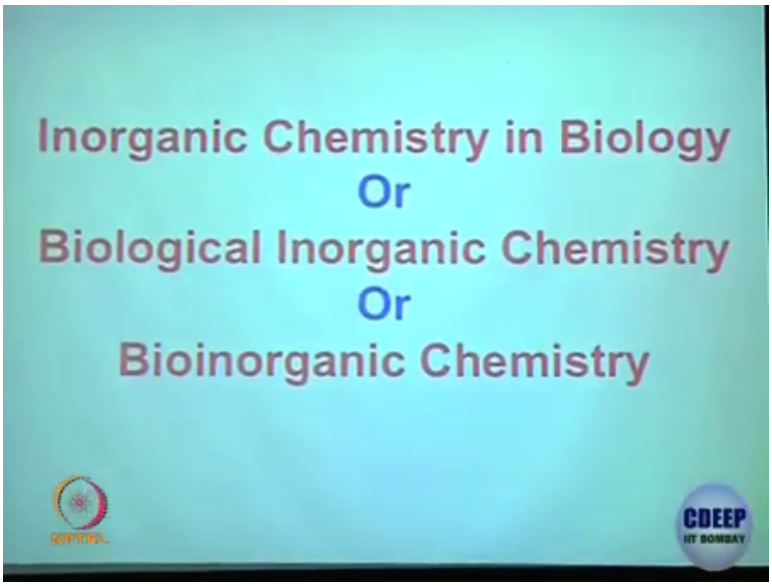


What is inorganic chemistry we have seen so, far is the role of metal in different field. Let us say, we have seen role of metal in periodic table of course, they are full of them and then we have seen extraction techniques, they are again we have metal subsequently we have seen, crystal field theory or the coordination chemistry chapter of course, metal was there.

In the last class we were discussing magneto chemistry, or you know that is the chapter right, or whatever the name of the chapter was it is essentially magnetic chemistry or in a magnetism we are trying to discussed. And, now, today we will try to see if there is any role of metal in biological system or in us ok. It is a vast topic, it is literally impossible to do justice in one class.

So, we will try to bring few topics trying to keep it as brief as possible and try to convince you, that there is an essential role of metal in our body, or biological system, or in nature in general ok, that is the roughly going to be the topic so, role of metal ions in biology ok.

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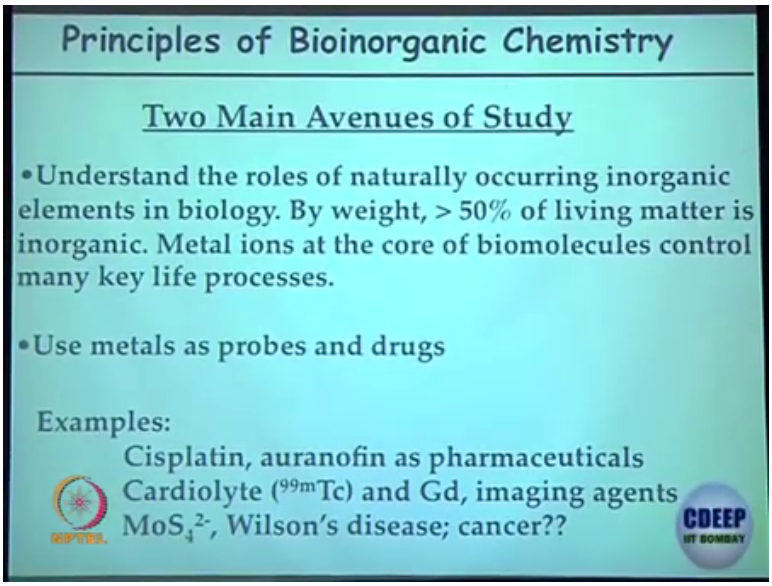


Now, I was I think discussing little bit that, nearly 50 percent, actually greater than 50 percent body weight is having metal it is due to the metal. Of course, there must be some role; see in

nature the most important thing to understand is nothing is done in nature without a cause, we may not understand right.

Now, or we may not discuss in the class or maybe it is not understood by scientist yet, but nothing absolutely nothing in our body is without a reason, that is I think definitely a big take home message ok.

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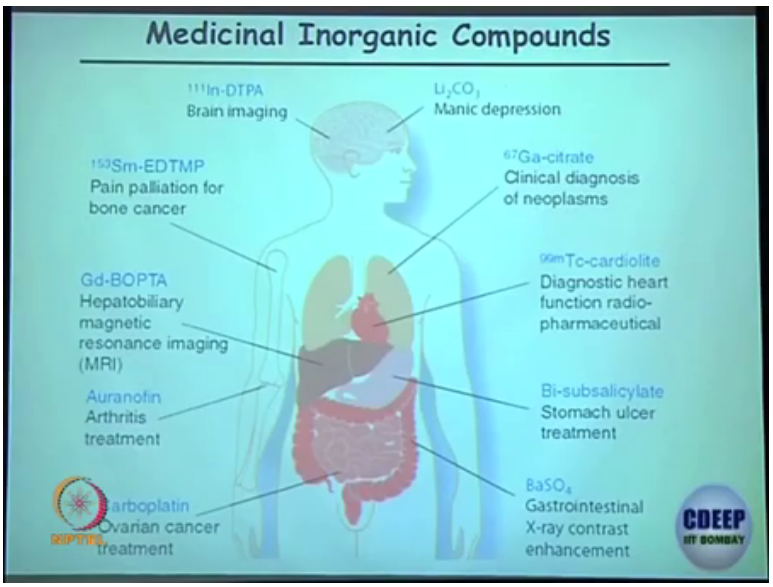


Now, of course, metal complexes can act as drugs. The drugs we take the drugs the doctors prescribe a lot of them are having metal. Some of them may not be lifesaving some of them it could be for flu, for fever, for you know indigestion this that some of them could be lifesaving such as cancer, like advanced stage of cancer. They are is a metal.

Metal actually is saving human being from getting demolished or from getting you know, they are being killed in lot of cases there are some examples say, I am not expecting again this chapter, I am not expecting each and every details of things you have to remember I do not think say. So, I am saying that it is important to understand what is there in terms of medicine in terms of biology.

So, there are for example, there are some drugs it is shown in here, which is operating on our different parts of body. For example, you know any anything you can pick up, I think we will go for one of those that says platin, cisplatin you have heard of it is a platinum containing drug, carboplatin. These are specific drugs for some specific type of cancer.

Of course, as you know cancer truly has no you know 100 percent cure medicine so, far different medicines are effective for cancer, for different type of cancer ok. So, cisplatin carboplatin happened to be two specific platinum containing drug, which are effective for a particular type of cancer and, it saves a lot of people. Of course, it has side effect lot of side effect, but nothing is more precious than life.

So, you know when there is no alternative. I think it is still better not every medicine has side effect; I think I mean not every medicine has huge side effect. Almost every medicine has some side effect for sure, but some of them has more some of them have less, but essentially at the end we end up having the best possible one at this given time ok.

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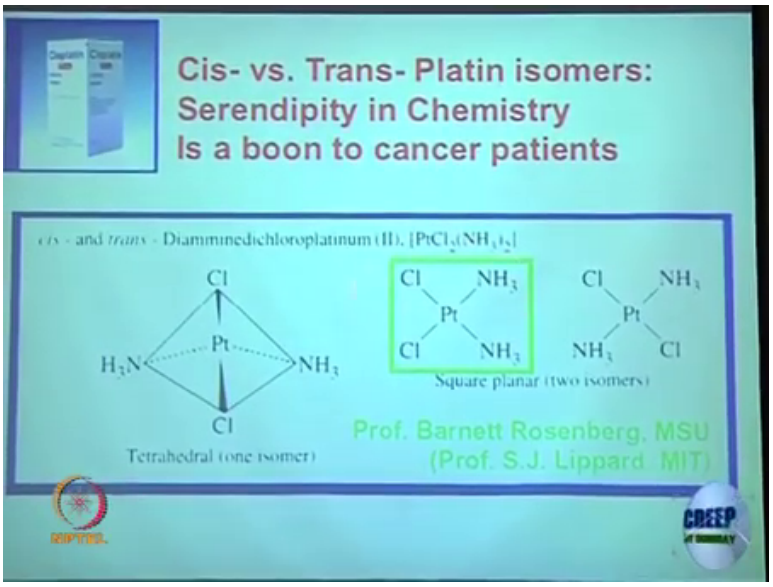


This is what is Cisplaten all about, cisplatin is a simple platinum containing molecule? So, once again we are trying to keep this class as simple as possible. So, that we can correlate, but there are more complex thing, which definitely you can understand just we do not have time to discuss that much it is a one class will try to give you an overview.

So, this is a cisplatin this is the transplatin, why it is cis? You can see that two chloro are cis 2 amino groups are or an ammonia are cis. So, this is cisplatin Trans means, they are Trans to each other.

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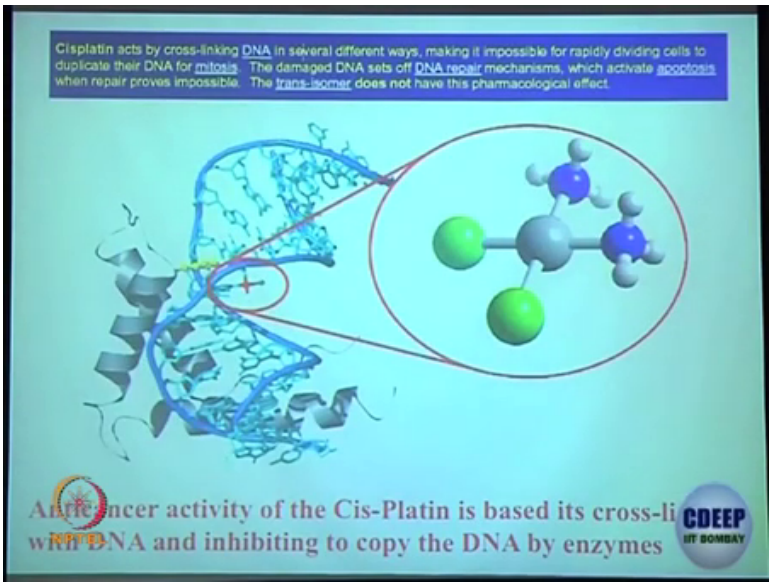


Now, Trans platin is not effective as drug. Only cisplatin is, that is mainly, because the cisplatin this amino group let us say which is labile ok. I think let us say this is the amino group or whatever, there are these amino groups which are labile; labile means they can fall off ok.

They can fall off under a given condition let us say if you give a better ligand, metal is nothing, but hold with the ligand. If, you provide a better ligand, that better ligand can displace the existing ligand it is like exchange right. So, what happens this cisplatin can exchange let us say two of it is ligand as is drawn in here let us say, two of these ligands and it can coordinate the better picture is not there, it is this question is also there in that tutorial part, will come and show you a little better picture.

How it coordinates with that DNA?. So, the major problem of the cancer patients is you know you cannot prevent the growth of the cancerous cell. Cancer is nothing, but uncontrolled growth of your d diseasegious cell or diseased cell right that is why we see that swelling right tumor you see it is growing there is no control ok.

If something like let us say you know any part is having cancer, if it grows of course, almost everything will get affected inside our body right. So, since the growth cannot be controlled people are trying different way to stop the growth of the cancerous cell. One of the way to stop you know to stop the growth is to just cleave the DNA, you have DNA all of you have studied even if you do not at this point may not understand 100 percent that is ok.

So, their DNA is a base pair right it is a helical system. So, this drug particularly can go and intercalate or two of it is ligand can be displaced by let us say to guanine, you know guanine is there, adenine is there. So, 2 base pair can displace let us say this ammonia definitely 2, 2 of this ammonia can be displaced by those of the; those of the base pair of the DNA.

Therefore, what happens is? Once you have such displacement, you will not be of course; there are more involved strategy how it exactly prevents? The moment such EG complex forms over there in DNA, you will not be able to carry out the cell growth. It gives a message thereby you know your cell growth process; you have heard of mitosis definitely, that overall process stops. There by you are able to prevent the cell growth indirectly you are killing the cancer or you know cancerous cell.

If you do not allow cancerous cell to grow it is that is it perhaps that is that you know one of the cure of the cancer right. And, then of course, you can do other treatment thereby of by once it binds actually then there is a mechanism called apoptosis by which it can kill the cell, even those cancerous cell.

So, what we have learned so, far a simple compound such as cisplatin, which is a platinum complex, you can write down the crystal field splitting and everything ok. It is a 4 ligand over there on platinum, 2 of the ligand can be displaced by the DNA base pair you have heard of

adenine, guanine, guanine thymine cytosine uracil and so on. Let us say guanine go up the guanine in from the nearby residue, let us say it is a big thing right.

DNA means, it is a big thing it is a long polymer type of thing it is a peptide right from peptide backbone, from that protein backbone. You are taking two selective chord selective ligand those are ligand again right; if you look at guanine this is nothing, but a ligand for metal. They can also undergo hydrogen bonding that is how they are giving the helical structure and so on ok.

But, once again they can be ligand; ligands are nothing, but having a hetero atom. What is hetero atom nitrogen, oxygen, sulfur? It has lone pair usually or a negative charge and those negative charge is going to bind with the positively charged metal ion. Thereby, if you give an opportunity for all those ligand present in our body, some of them not definitely all of them, some of them will bind with the metal and form metal complex ok.

So, that is what is happening in cisplatin as I say the base pair or this backbone, protein backbone can bind with the platinum center displacing two of the ammonia let us say. And, then we get a complex which will not allow the cancerous cell to grow, if you let us say break the DNA base pair. So, that the region where the plat cisplatin binds from their own these DNA duplex will not exist, DNA structure will not exist. So, the moment that collapses lot of things changes it triggers lot of things.

So, your mitosis or the cell division will not be progressing further, this is a simple way to explain of course, it is little more complex, but essentially that is how we see that it can be prevented ok. So, I think you got an idea how simple complex can be effective as drug. As deadly as cancer, which are even you know a very late stage of cancer can be cured by this drug. Of course, this drug has a lot of side effect, but still I think when this the cisplatin was not there nearly 90 or 85 percent patient was dying ok.

For, now after cisplatin so, these are cisplatin and carboplatin carboplatin is specifically for prostate cancer ok. These disease, now can be cured up to 95 percent, which is a lot 90 85 to 90 percent people who are dying before this medicine.

Now, the people having this specific type of cancer, where cisplatin is effective nearly 90 to 95 percent people are surviving. Of course, you know it comes with a side effect, but still people are using it and it is not that costly, another thing is cost how costly it is right anyway let us move on. But, then essentially what this example shows you, that you have control on things cisplatin works transplanting does not work ok.

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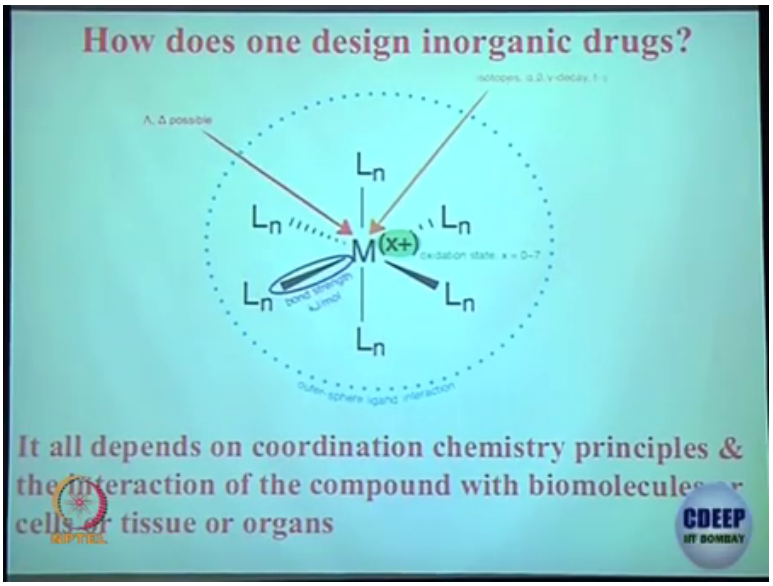


Therefore, you would be able to understand where to design your drug or how to design your drug, one component in which metal to choose?. For example, let us say you take a drug with iron or copper, iron center can get oxidized, iron 2 plus, 2 iron 3 plus and that is how we see

the rust formation right? Copper, copper you know copper 1 plus, copper 2 plus the oxidation state occurs very quickly, because that potential is achievable right.

Therefore, these are called redox active metal center, because you can switch between your you know switch between the oxidized state reduced form and the oxidized form. Reduced form is for what iron 2 plus is reduced form, oxidized form is iron 3 plus copper 1 is reduced form copper 1 plus copper 2 plus is oxidized form.

Now, these are the proteins you may not be able to use as drug, because let us say you use iron 2 plus. Iron 2 plus in air is also not stable, you put it in body it may not be iron 2 plus if got oxidized to iron 3 plus let us say iron 3 plus is not drug anymore right. So, you have problem. So, you usually do not use some metal center, which are having easily oxidizable or reducible center ok.

Now, these centers such as iron copper they can be electron carrier, because they can travel between the 2 oxidation state very easily lot of reactions are happening in our body where we need electron. You have done the balancing of electron some equation a plus b, goes to c plus b. You see that some electron is required somewhere oxygen plus for proton plus you know for electron going to water. That electron, where those electrons are coming from?.

Those are coming from some of these redox active site these are nothing, but enzyme what is enzyme I mean it is let us loosely define enzyme. Enzyme some center or someplace in our body where a particular thing is going on.

Let us say, we are inhaling oxygen, we will discuss today oxygen is going to bind with something, that is the power firing center hemoglobin you have heard of right that one will be calling metallo enzyme, because it has metal in it. It is not necessary that every enzyme has to have metal in it, but those enzyme which are having metal we will be calling it metallo enzyme. Enzyme are nothing, but made of the peptides lot of those amino acid ok.

So, we have heard of amino acid one amino acid can be put together with another amino acid though are called amide bonding right. So, small amino acid put together I have slide I will

discuss briefly put together will be a peptide backbone. Let us say we have how many 23 amino acid naturally occurring, essential amino acids. Different sequence of these you can put let us say you know different different type all these in different sequence, let us say amino acid 1, amino acid 2, amino acid 3, then again 1, 2 and 3, this show a different sequence, you can give amino acid will form peptide backbone.

Those peptide backbone, are the one can organize in different fashion alphas it because it ok. All those you may have heard of if not do not worry, then there by will give you a big enzyme structure. So, essentially if you look at the enzyme and cut it down into pieces what you get is amino acid. Different orientation of amino acid there could be hydrogen bonding among them there could be covalent bonding they can you know form the amide bond, but enzyme is nothing, but collection of amino acid in different sequence I will be coming ok.

Student: (Refer Time: 17:27).

All right. So, over here you have different way to control or design a drug, you can control the metal center, you can control the different ligand. What type of ligand you want, whether you want a high spin complex, whether you want a low spin complex. How the properties can differ? Even from high spin to low spin, this conversion is crucial for our existence will discuss the oxygen binding with the porphyrin iron center hemoglobin ok.

We will show how these high spin low spin change is essential for our surviving without that oxygen not even bind will not even bind ok. So, it all depends on coordination chemistry principles and the interaction of the compound with biomolecules or cells or tissue or organs ok.

Sometime you know amino acids are there and in between some metals are there. The role of metal could be different ok. Sometime, what metal does is very simply metal can hold different protein backbone together how, because metal can have ligand the way metal stays in our bodies either if nothing is there water is there as a ligand. If water can be displaced

with those amino acid backbones, amino acid has some ligand let us say histidine, which is like a 5 membered ring with a nitrogenated.

So, everywhere you will see if whatever is binding with the metal it has a hetero atom, nitrogen, oxygen, sulfur this sort of thing are there, either those lone pair or the negative charge is binding with the metal. So, as I said amino acid has these units, where it can act as a ligand these are monodentate ligand, it is not bidented ligand.

We have discussed bidented ligand right, where you bind like is you know bind very tightly, but the monodentate ligand may not bind tight, but if they are in the right place, where the metal is there, metal binding site is there. If there is a space for metal to sit down metal sits down, there those amino acid backbone can hold metal tightly enough to do lot of chemistry ok, it can act as drug, it can destroy a drug, you can it can create a lot of things.

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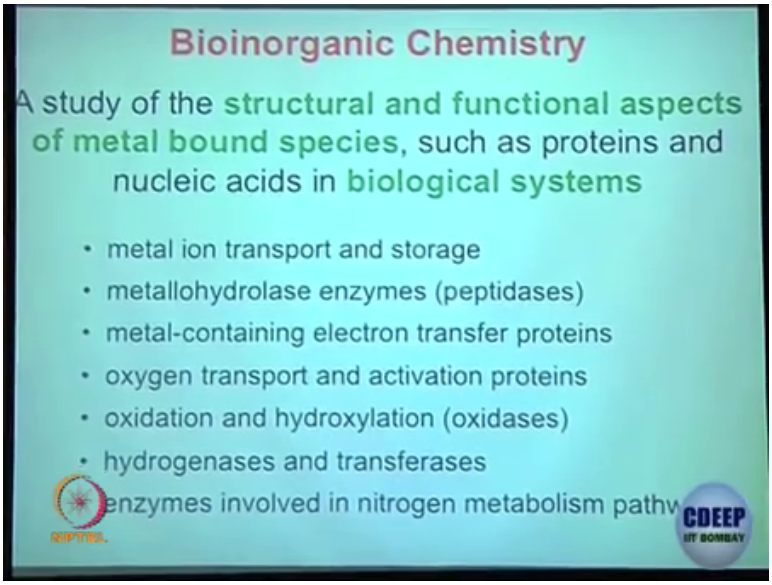

So, that is this is what essential so, bio inorganic chemistry is nothing, but structural and functional activities of the different metal ions, that is what we will try to discuss you just read I will essentially discuss these in the class ok.

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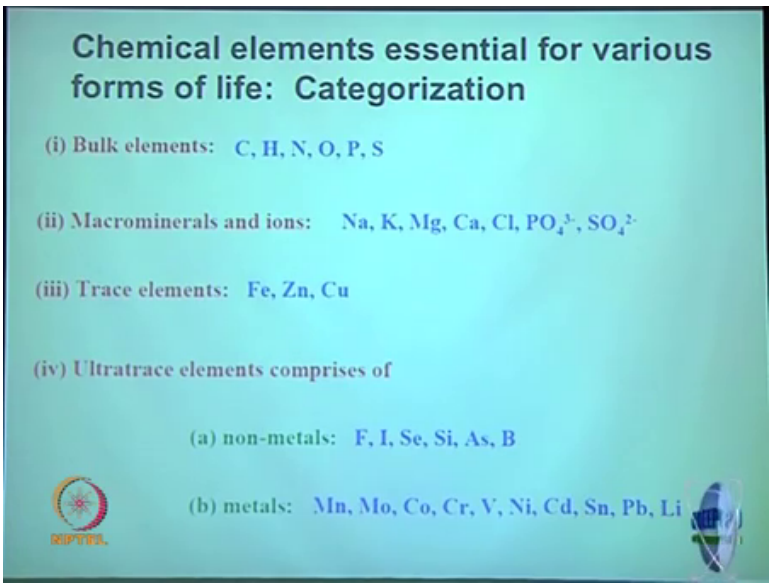


Now, of course, every element in the periodic table is not readily available you have learned. So, therefore, what we see in our body is usually the one which is available in large quantity iron for example, it is available in decent quantity. Bulk element like carbon hydrogen, nitrogen, oxygen, phosphorus, sulfur these are present in our body in large amount in any biological system like, organic molecules are made of these carbon, hydrogen mostly and then nitrogen oxygen sulfur.

So, those are bulk, but then there are trace elements although very little present, but still they are there in our body iron zinc copper and so on. Other different you know percentage of

metal makes it makes the makes really our body. Overall I think every time I see that there is a question let us say give an example of trace element, this is one trace element, which is essential for essential for biological activity let us say over here.

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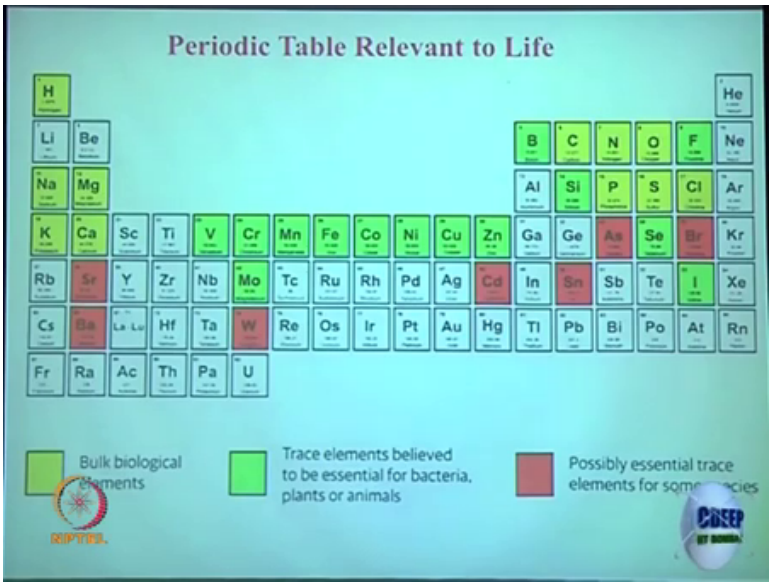


These are the one in the blue which are trace elements, but it is essential for biological activity, this is kind of periodic table with the biological perspective. You do not have to remember all these one or two example, if you remember I think that is good enough trace element means small amount present, but those are going to be very important for us anyway these are possibly essential ok. Forget it let us move on.

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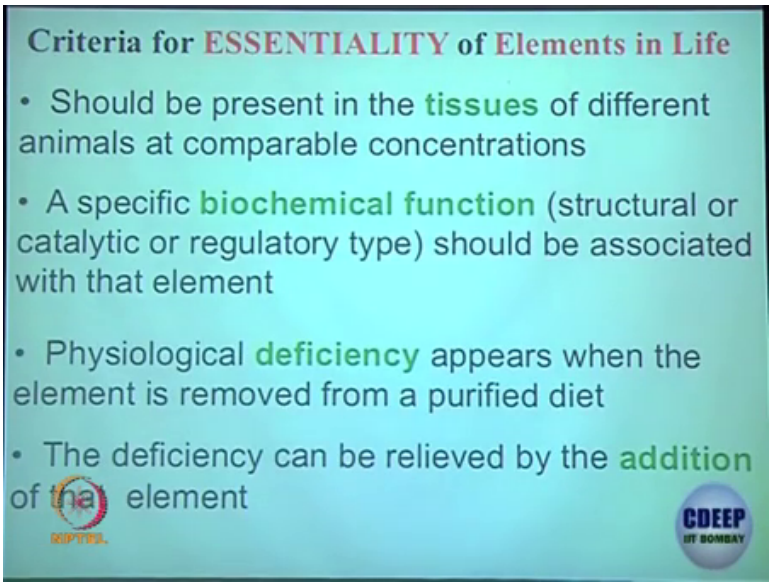


Now, what is the essential element? I will not go through all these writing that is for you can read.

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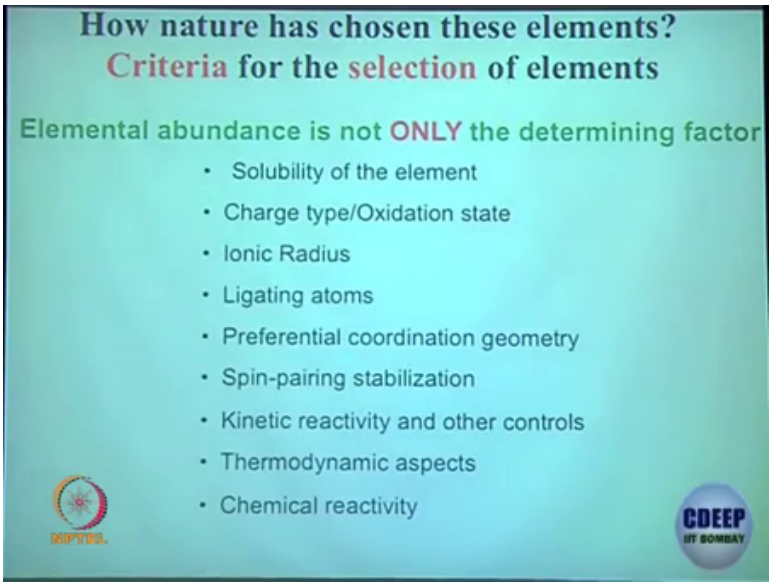


I will explain this.

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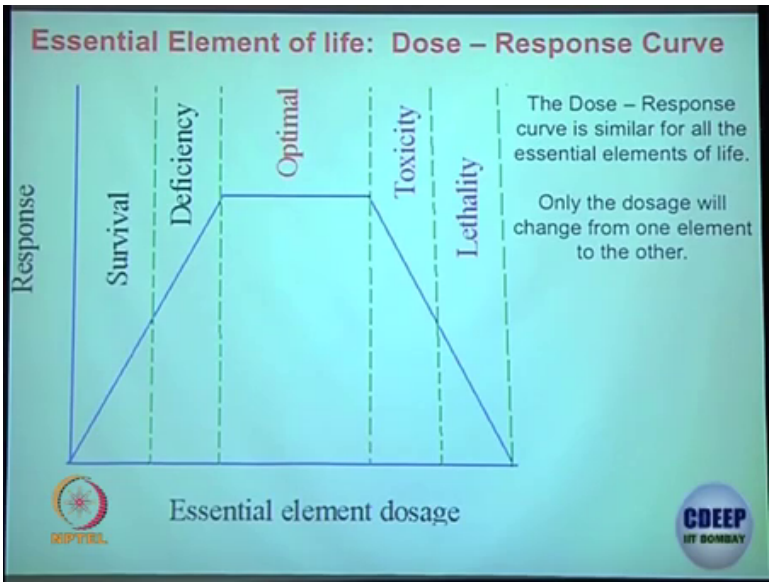


This chart; this chart is very simple. See every metal is good may not be for our body for other purpose, but those metal which are good for our body is not good, if you give a lot to our body. Let us say iron if you keep on taking the iron tablet or calcium tablet like supplements, you take even over the counter, you can get without prescription do you think it is going to be good for your body no.

So, there is always this curve, if you have a very less amount of some metal then your survival is questioned you may not survive ok. If of course, you may be dead, if you do not have a certain percentage of metal ok, if you do not have enough then it is going to be deficient you do not want to be deficient, you do not have want to be super deficient, then you will die, you want to stay in this region where it is optimal pretty understandable right.

If let us say 5 milligram is optimal for your body you should have around 4 to 6 milligram, if you go 1 milligram range you may be not surviving, but if 5 milligram is good, if you have 5 gram of it you may be again.

Student: (Refer Time: 23:40).

Going to here ok. So, that is all this graph is going to tell you. It is going to be toxic up to certain level after that ok; we will see you in the afterlife ok. Now, what determines, which metal is going to be in our body or in biological system ok? What actually determines, what controls the selectivity? Let us say in porphyrin that hemoglobin there is iron right. What controls these things?.

First criteria is definitely the metal has to be abundant somewhat abundant on the earth crust. We should have some enough amount in nature, for those metal to be here. Of course, every metal or every element that present on the earth may not be relevant in biological system, but whatever is in our biological system in any biological system those should be somewhat abundant, that is the natural abundance has to be somewhat there it may not be the maximum some what it is there.

In the addition, it should be soluble you know if something is not soluble, how can you really have in our bodies during you know our growth we are eating food. So, from food we get let us say, iron we copper lot of other metal it should be soluble. So, that body can intake it body can you know digest it and it can be delivered ok.

So, essentially what happens is let us say we are eating food; food had some minerals food have this metal center different things. And, then from our intestine let us say, it is a series of events. One it is almost like a pizza delivery, pizza is made somewhere you place an order ok. The delivery guy with a bike nowadays will come.

Now, it will deliver to a desired or to a ordered order place, wherever the order has come from. So, that is how it happens? So, your food gets in from there on whatever an essential a

lot of things are going on and then there are different enzyme and of course, they are specific, they are very very selective as well. Let us say iron is there some guys there I have to deliver iron.

He picks up iron goes and then dump it somewhere right, they dump it somewhere, then it could be further transported to some other place or it could be stored. It is not necessarily everything we are eating, it is going to be digested or you know it is useful right away, it can be stored at a certain point right, it can be stored or it can be delivered at a desired point ok, anyway.

So, solubility is essential oxidation state is essential you know oxidation state determines size ok. So, let us say that delivery guy, if you give a huge pizza, it is not going to fit in his bucket right, he is not going to deliver. So, size is going to matter ionic radius ligating atoms see always no metal ions is free. Metal ions comes with a luggage of ligand. Now, the delivery guy, if you do not give him enough money he is not going to deliver right, you have to pay him salary.

Similarly, the metal ions if they do not find that right ligand, they will not be ready to go, there they will not be transported, they will not be storing right. So, all those things are essential to form or to do anything with the metal ion how they are delivered, how they are there in the very first place, how they came it depends on a lot of factor? It is not just, it has to be abundant, it has to be abundant we have to have it on the earth crust in addition to that, what is the other there you know, what is their characteristics, what they are made of that determines?.

Let us some zinc 2 plus you know zinc 2 plus is not redox active right. So, if you have some active site; active site means, where the chemistry is happening, where you are doing some organic reaction that is the active site. In our body lots of active site is there ok, where a particular reaction is going on, which is essential for our survival right. Now, if you put something like zinc 2 plus in such site, where a redox activity is required, it is not going to do it right zinc 2 plus.

Let us say usually can do a structural job means, it does not change the oxidation state, it stays there and thereby if different protein backbone has to be hold together zinc 2 plus it is best. But, then if you in that site, instead of zinc 2 plus, if you end up putting copper 2 copper 1 plus or 2 plus or iron 2 plus. They can undergo oxidation reaction, they can undergo redox reaction.

Therefore, though your structural job what you want may not be done by them, you want somebody spectator some dumb guy to be there like zinc 2 plus, which is feeling like a dumb, because they can do any chemistry, they cannot do any redox chemistry. You want somebody to hold the structure of the protein backbone; you want somebody to be just there.

So, you have the hard of this Alzheimer disease lot of movies been made ok. Parkinson disease right these are again very deadly diseases, usually not many medicines are there, you know it is painful diseases. Usually what happened let us say for Alzheimer diseases. If somehow you know your body starts accumulating some metal center. In an appropriate manner, in an inappropriate manner means where it should not be there it started concentrating, it could be at brain it could be at lungs usually Alzheimer disease which could be at brain let us say.

So, what happens this let us say you are storing copper 1 plus ok? Then those protein backbone start connecting with those copper, copper 1 plus let us say and then it can agglomerate, it can precipitate out. You do not want that sort of things to happen, but you know it is happening, that is basically let us say Alzheimer disease, you know the in presence of a metal center, your protein backbone or proteins are getting kind of precipitated.

If it is precipitating some in some important place such as brain, your brain definitely getting affected and lot of side effect, lot of things happens over the time right. So, that is how important the metal centers are they are good kilter or when they are the metal center, they can do interact with lot of things. And, thereby can change the biological activity ok. Let us move on.

Student: What is spin pairing stabilization?

Sorry.

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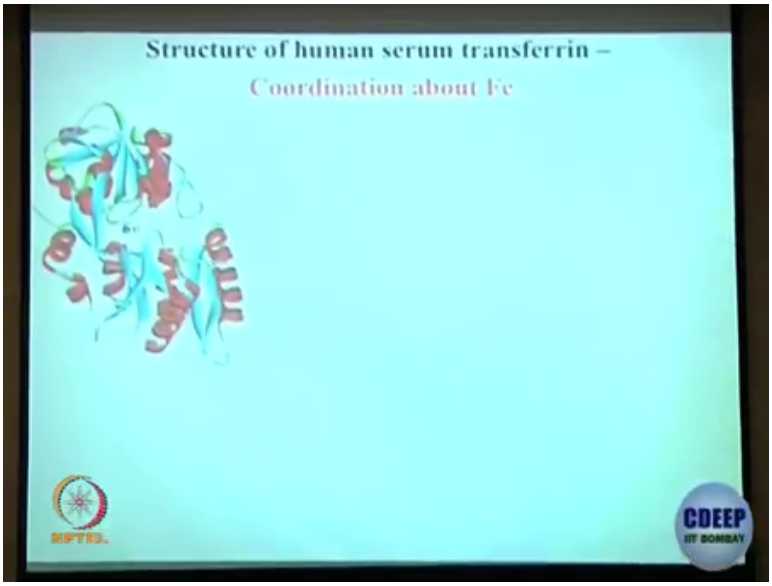


Student: Spin pairing stabilization.

Spin pairing stabilization. So, of course, high spin and low spin let us say ok. So, sometimes what happens let us say if you have unpaired electrons. Those unpaired electron means you are going to have a paramagnetic complex right. Compare to that if you have a pair not in every situation, sometime it can be paired, if it is high spin to low spin it can be paired, they are by those reactivity of those unpaired electrons can be somewhat minimized right.

Student: (Refer Time: 32:20) exchange the ligand which is doing this.

You can exchange the ligand right, I am coming to that, how can you exchange the ligand? One let us say water is there you replace that with another nitrogen ligand pyridine. Let us say you put pyridine instead of water what happens? If it is if it can change the spin state, then that chemistry will be completely different right ok. So, these are you know all these points you may not have to memorize, but I think it is essential that at least few points you understand what exactly brings out.