

Inorganic Chemistry of Life Principles & Properties
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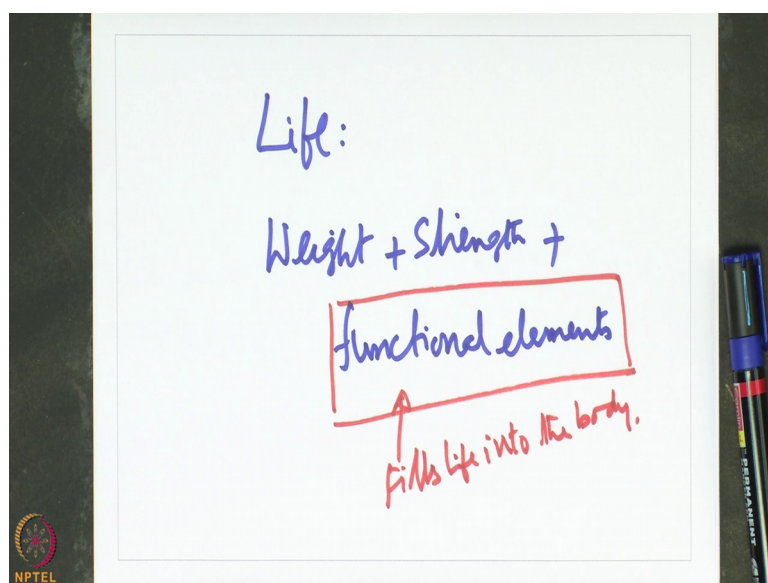
Lecture - 03
Selection and criteria for elements

Hello, welcome you back for the next part of the lecture on this topic and obviously, the Inorganic Chemistry of Life Principles and Perspectives. In the past two lectures we have looked at a few very basic components, that is required for this particular course: one of it is that there should be anion or inorganic species present in the biological system. I showed examples corresponding to that using so many different enzymes at least half a dozen different enzymes, whether they could be working in the human, they are in the plants then in the other kinds of organisms. So, therefore, that is concept or aspect number 1.

So, aspect number 1 is presence of the ion or species in the biological system ok. Aspect number 2 that we have try to look at is, what is the you know life made up of. So, for that we have understood that there are bulk elements like carbon, nitrogen, oxygen, sulfur etcetera. And these together will form almost 96 percent of the total body weight. Then you have some macro minerals like sodium potassium calcium magnesium phosphate chloride etcetera and this will add a few more percentage. And total will be come to about 99 to 99.9 percent of the total body weight, and then it is a 0.1 percentage the body weight that comes from the essential elements or essential trace elements or essential ultra trace elements.

Therefore, the life is a existent not just by the weight, not just by the bones, but it is by adding the elements, which basically you know give the functionality. So, as per that what we studied.

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So, life requires the weight and strength and functional elements ok. So, it is these functional elements, which basically tells you about the filling the life into the body. So, this fills life into the body ok. So, if you understand this yes definitely we can go to the next part of it and let us look at the same. Here as you can see from this slide.

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Inorganic Chemistry of Life *Principles & perspectives*

Categorization of elements essential for life

(i) Bulk Elements: C, H, N, O, P, S (involved in making proteins and nucleic acids, etc.)

(ii) Macrominerals & ions: Na, K, Mg, Ca, Cl⁻, PO₄²⁻, SO₄²⁻

(i) & (ii) together constitute >99% of human body weight

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So, I that we have bulk elements carbon, hydrogen, nitrogen, oxygen, phosphorous and sulphur and we have macrominerals, sodium, potassium, magnesium, calcium, chloride, phosphate, sulphate etcetera.

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Categorization of elements essential for life


Critical elements of metalloenzymes (Essential):

(iv) Trace Elements: Fe, Zn, Cu (present in few grams in human body)

(v) Ultra-Trace Elements: (each of these present to only few to several milligrams in human body)

(a) Metals: Mn, Mo, Co, Cr, V, Ni, Cd, Pb, Li

(b) Non-metals: F, I, Se, Si, As, B



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And we have several trace and ultra trace elements iron, zinc, copper, trace because they are present in terms of few grams to a body weight of 70 kilo grams, and whereas ultra trace elements are those where you have only a few milligrams for the total body weight of 70 kilograms and ultra trace elements can be further divided into metallic and non metallic.

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Criteria for ESSENTIALITY of Elements in biology

- Should be present in the tissues of different animals at comparable concentrations
- A specific biochemical function (structural or catalytic or regulatory type) should be associated with that particular element
- Physiological deficiency appears when the element is removed from a purified diet
- The deficiency can be relieved by the addition of that specific element



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So, this is the compositional aspects. So therefore, having understood that the elements should be present, the composition aspects, so probably we are at a stage where we can

start studying what is your known criteria for these kind of elements to be essential. So, what is the criteria for essentiality as the elements? As you can see first of all number 1, whatever the element we talk about that should be present in the tissue of the animal or any species or for a human in their tissue at a comparable or reasonable or recognizable concentrations ok.

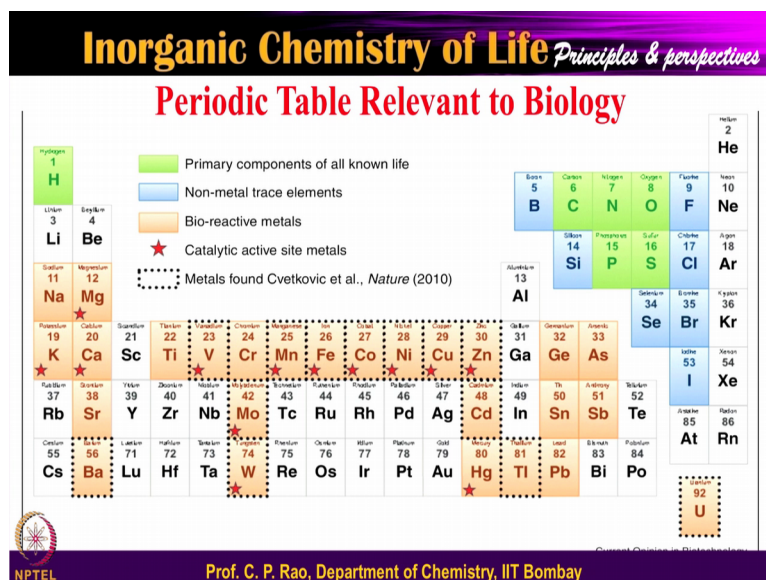
So, that is number 1. Number 2 just because it is present in the body, it does not mean that it is sufficient enough. It should have some kind of a function, it should have some kind of a role. The function is referred as a biochemical function some of them maybe a structural function, some of them maybe catalytic in function, some of them maybe regulatory. Now all of these three terms I will make it clear not now after a few more hours, when I come to the general aspects of the part 2, which refers to the general aspects of the metalloproteins and metalloenzymes. Till then just take it as a structural catalytic and regulatory. And so, to you are talking about the bio function, biochemical function. Then how do we know this particular function, what we claimed in point number 2 is really from that.

So, therefore, if that element is removed from the diet, is that element is made sure not available for the system, then that system must show some kind of a deficiency ok. So, this is nothing, but a physiological deficiency; what does it mean? It means that there is some kind of a physiological defect or in other words a proper reaction or proper function is not exhibited by an organism and that is what it basically means. Then how do we know it is happening because of this? Because we have so many different elements is it happening because of that x or something some other y or z? So, in order to identify this particular difference, you again put back that element x to the organism. When you put back this element x to the organism obviously the organism should rewind back to the normal or leave back to the normal must show the great function. So, therefore, then we can say that particular element x is essential for biological function, is essential for life ok.

So, now, let us look at once again back number 1 the element x should be present in the tissue of the animals in a particular concentration, number 2 it should carry a function, number 3 if you remove such an element availability to the system, then what you find is a kind of deficiency a deficient syndrome. So, and then the fourth is put back that element make that element available to it, then in that situation the species should get

back to the normalcy and normal function. So, if it get back gets back to the normal function; that means, the element x is an essential element.

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So, this is how the essentiality of the element being identified whether it is necessary or not. And let me remind you that the essentiality of the element is the one which among the elements which are present in the trace and the ultra trace not the other ones. Here we are referring mainly to the trace and ultra trace elements, and few of the macro mineral for example, sodium, potassium, calcium and magnesium these are the kinds of things ok. Having seen that; which are the bulk elements, which are the trace elements, which are the ultra trace elements I think now as a chemist what we need to see.

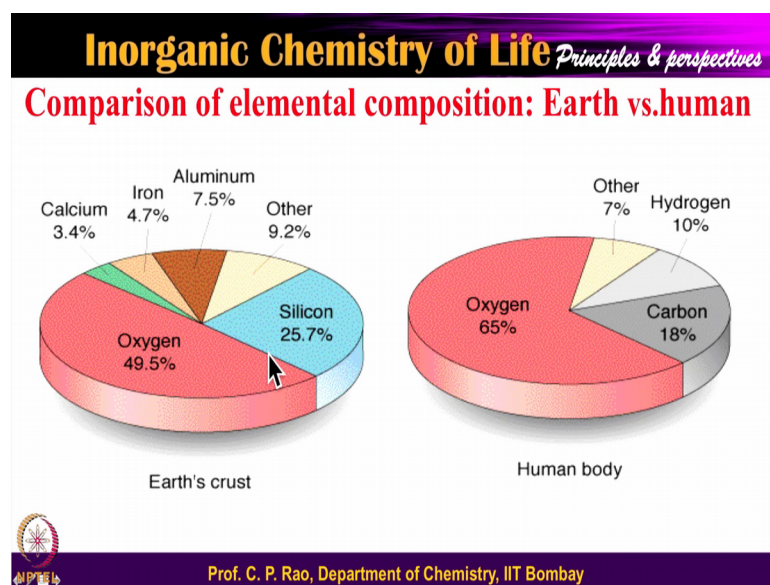
We put them in the regular position, what is the regular position? They have a position in the periodic table and that is what you can see here and you can find all of them. Now once which are colored with a green, the green color are the ones which are basically present as a bulk elements; there is a hydrogen, carbon, nitrogen, oxygen, phosphorous and sulphur these are known they are at the catalytic active sides. So, this is for example, titanium no enzyme is yet known, for example, chromium no enzyme is yet known, but a little presence of these elements are still present in the tissue of the animals of that.

Now, coming to the molybdenum and tungsten of course, there are enzymes are there, and there are for cadmium there are no enzyme known, but certain level of cadmium is always found in the tissue and mercury yes, there are mercury thio based enzymes are

there we will see towards the end of it what the thing and other elements are found in smaller concentrations like germanium, arsenic, tin, antimony, thallium lead and some of these act like a micronutrient which means that there are no enzymes are available for these; however, there is no enzymes, but still there is small concentrations are absolutely essential for running life ok. So, that has been understood very well.

So, they are present in ultra trace kind of things. So, there are other elements, which are given blue in color like fluorine, chlorine, bromine, iodine kind of thing selenium etcetera these are also found in the tissue and they are nonmetallic trace elements or nonmetallic ultra trace elements. So therefore, having seen the information of the previous slides, now I have tried to compile all these elements into this box; the box namely the periodic table. Now this will give a kind of a feel as how we should discuss the weight about these ones as we go along.

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So, I will get back to this later on how can we. So, how do we understand these are the elements only the ones, which are chosen by the life, why life has chosen these elements not other, for this for a moment let us have a look at the following. Let us say we have a human body, having oxygen, carbon, hydrogen, and other and having earth crust. So, if you see the some parts of that let us look at this comparison of these elemental composition between the earth and human body, the human body or the oxygen, carbon,

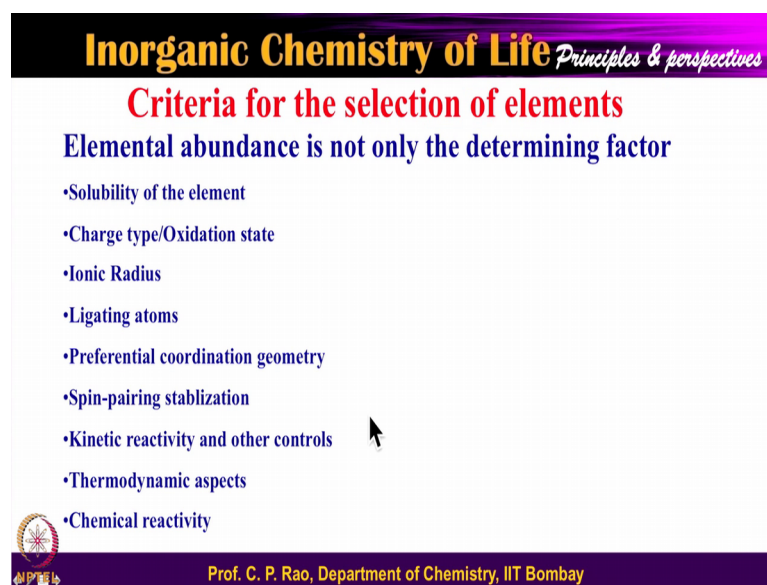
hydrogen and other elements and if you look at the earth crust you have the oxygen very similar almost 50 percent.

Silicon which is 25 percent there is hardly anything at all and of course, there is calcium, calcium is also present, here iron, iron is also present, aluminum 7.5 percent, which is very high in the earth crust we have no aluminum containing enzyme we have no silicon containing enzyme in a body. So, therefore, it is not easy to bring a direct correlation between the composition of the elements or the earth with that of the composition of the elements of the human body not directly, some are matched iron yes iron is very much existent in the body and the enzymes are very well known for this thing.

Calcium is very much existent and there is lot of enzymes are known, no enzyme of silicon no enzyme of aluminum is known. So, therefore, it is not easy to directly correlate and or conclude that the element which are present in the earth crust are the responsible ones for the human assimilation, because human the life starts at the interface of the earth crust and the sea water. So, these are called sea sedimental; areas the sea sedimental area the composition will be again different. So, sea sedimental area is a one which is in contact directly with sea water. So, therefore, sea water is available for the life to generate. So, the for that is where we have.

So, in any case also it is very not so, easy to compare between the either the earth crust composition or the sea water composition. Because in the sea water you have ppm, ppb level of many metal and other elements anions are also present and they are all available for life as well so. So, in absence of any kind of such a comparison between the concentration of the elements in the earth versus the concentration or importance in the human life we need to look for some important criteria that would have been necessary for the nature to choose these.

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Inorganic Chemistry of Life *Principles & perspectives*

Criteria for the selection of elements

Elemental abundance is not only the determining factor

- Solubility of the element
- Charge type/Oxidation state
- Ionic Radius
- Ligating atoms
- Preferential coordination geometry
- Spin-pairing stabilization
- Kinetic reactivity and other controls
- Thermodynamic aspects
- Chemical reactivity

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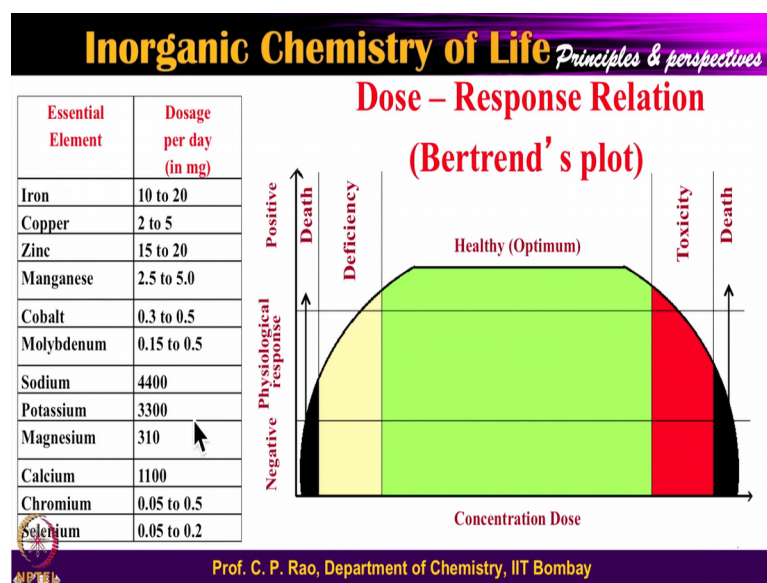
So, nature must have kept its mind in understanding all these.

So, it is not just the abundance other factors like solubility of the element, it could be charged, it could be oxidation state, it could be a size or radius ratio radius or legating centers in the proteins or what kind of geometry we have, what kind of a stabilization energy which is thermodynamic, thermodynamic aspects then even the kinetic aspects are also important and other controls and reactivity.

So, in effect what I would like to say is that the, nature has chosen those elements those elements which are shown over there these elements because of their coordination properties, because of their thermodynamic properties and because of their chemical properties. So, these are seem to be the responsible rather than just their concentration or abundance in these. I am sure you must have noticed the coordination chemistry aspects, these are all talking about coordination aspects and these are talking about the thermodynamic aspects and then kinetic aspects. So, the coordination, stability and liability these are important.

So, we will study these after a while its little more details, to make sure everyone understands these parameters in the long run.

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Now, let us say. So, we talked about certain elements and which elements etcetera. So, is there any kind of a limit to these concentration yes, in the body as you can see the iron, copper, zinc, these are all required in a higher level, this is a dosage per day in terms of milligrams. They are require 10 to 20 milligrams upto about 5, 10, 15 to 20 then you go to the manganese and cobalt they are required little bit less and you go further it is much less ok. So, therefore, we have the concentrations of these elements are to different extents why? Why the concentrations, why do you think this concentration of all the elements are not same or they should be different?

That is because the extent to which the enzymes on iron, the extent to which the enzymes on copper, the extent to which enzymes of zinc or manganese or their role in biological tissue biological aspects is different. So, iron has a greater role by copper then followed by zinc, then manganese in very few cases and molybdenum also in few cases etcetera. Therefore, the concentration that the body needs to maintain is seem to be a proportional to the extent to which utilizes the corresponding enzymes. So, you can always have look at all these aspects of not only the iron, copper, zinc, manganese, zinc, cobalt, molybdenum you also have other sodium potassium magnesium calcium things and you require other ion much smaller in concentration.

So, now you see that the different elements they their dosage per day is different because their involvement in enzymes is different in this ok; so having understood this. So, why

do not we look at the relation between the dose and how well the responses is? So, dose response relation is given over here, this dose response relation can be seen from this bertrend plot ok. So, what this plot has going to what? The x axis; x axis is the dose of the element or the concentration of the element required per day and what is the y axis?

Y axis is how well what is the functionality, how good is the function is a function is very good, is the function is not so good. So, not good could be deficiency. So, the extreme of the deficiency is death or too high toxicity, extreme of a toxicity is again death now. So, let us let me take you through this plot start from here as you keep going, you can start see seeing this it just slowly increases.

So, what is happening? On the x axis you are increasing the concentration, on the y axis the response is increasing. So, as you go from very low concentration towards the higher the concentration as the concentration increases the response increase, at some region this one even if the concentration is increasing the response is not so. Such a kind of region is called the optimum region, optimum concentration or healthy concentration for real health to be maintained.

Now, go beyond that the activity is falling down; activity is falling down. So, increase in concentration is a toxicity further increase in the concentration there is a death ok. So, what did I say now? I said the concentration versus this response has an increased direction, a decrease direction and plateau region. The plateau region is a healthy region that much concentration need to be maintained although and anything lower is called deficient very low can lead to death.

Higher can be toxic, very high can be death. So, so; that means, body happily functions within this green range and with some kind of a coupling, it can function deficiency, it can sustain some extent of toxicity, when the toxicity goes too high it dies and deficiency also goes too low then it becomes death. So, this is meant only for the trace and ultra trace elements not for the bulk elements not for the bulk elements at all.

So, I hope now you understand the concentration the concentration should be maintained by the body; that means, concentration should be supplemented to the body so, that is why we have to eat every day. So, you have to maintains balance the elements the iron t he copper, the zinc, manganese, the cobalt, etcetera all of these have to be maintained in

the body. So, because they are circulated in the throughout the body, they get into the enzyme they go out, they get into the enzymes and they go out as well.

So, otherwise we could have been just eating once in my in our life time and never need to take anything more. So, which is; obviously, not true; that means, there is a dynamic equilibrium working in this.

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Inorganic Chemistry of Life <i>Principles & perspectives</i> Dosage, Syndromes of deficiency & excess			
Essential Element	Dosage per day (in mg)	Disease arising from deficiency	Disease associated with an excess of the element
Iron	10 to 20	Anaemias	Haemochromatosis siderosis
Copper	2 to 5	Anaemia, kinky hair	S.A.K. Wilson's disease
Zinc	15 to 20	Dwarfism hypogonadism	Merkel's disease
Manganese	2.5 to 5.0	Skeletal deformities gonadal dysfunctions	Ataxia
Cobalt	0.3 to 0.5	Anaemia	Coronary failure poly cythaemia
Molybdenum	0.15 to 0.5	Cerebral atrophy	Carcinogenic
Sodium	4400	Addison's disease stoker's cramps	

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So, let us look at these things when you have a less of that element its deficiency, the more of that element we have a excess syndrome. So, one can look at these kind of a syndromes of example iron we know very well, everyone knows that when iron deficiency is there we call it is anaemia and when you have a excess of iron, we call it is a siderosis.

So, excess of iron is a problem in the body, less of an iron is also a problem to the body. Similarly zinc the deficiency is a dwarfism and excess is also a problem. So, there are many of these almost all of these irons as certain characteristics of a deficiency and excess copper has certain characteristics of a deficiency and excess zinc has got deficiency in excess, manganese has got deficiency in excess cobalt. So, the each one has one different deficient more than one deficient syndrome more than one excess based syndromes too.

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Inorganic Chemistry of Life <i>Principles & perspectives</i>			
Dosage, Syndromes of deficiency & excess			
Essential Element	Dosage per day (in mg)	Disease arising from deficiency	Disease associated within excess of the element
Potassium	3300		Addison's disease
Magnesium	310	Convulsions	Anaesthesia
Calcium	1100	Bone deformities, tetany	Cataracts, gall stones, atherosclerosis
Lithium		Manic depression	
Chromium	0.05 to 0.5	Incorrect glucose metabolism	Carcinogenic
Selenium	0.05 to 0.2	Necrosis of liver, white muscle disease	Blind staggers in cattle
Toxic Elements			
Cadmium			Nephritis
Lead & Mercury			Anaemia, Encephalitis, neuritis

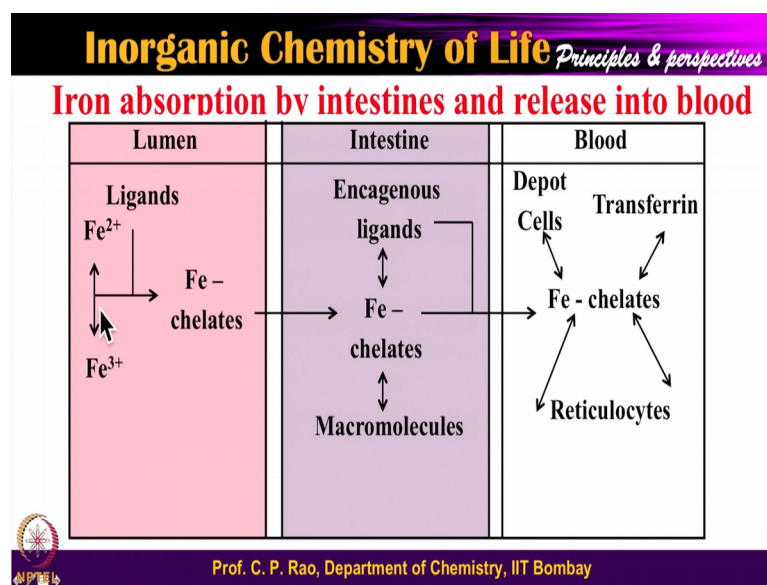
And it is not only for those elements even for the potassium, for the magnesium, for the calcium, for the chromium, for the selenium and cadmium lead and mercury all of these.

See these are toxic elements the cadmium and mercury. So, we talk about mainly high levels of doses of these the high levels of doses of these cadmium nephritis; that means, it is a disease that is associated with the with the kidneys ok; so all of these kinds of things. So, there are different kinds of the syndromes of the disease associated with the deficiency, there are some kind of things which are associated with the excess too defiant is a danger can lead to death, too excess is a danger can lead to the death as well.

So, I hope you have been able to understand this. So, I think I leave you for 30 seconds to understand what all I said ok. Hope you got a feel that what I was saying; what I was saying is these essential trace and ultra trace elements, we cannot have whatever the levels we want it should not be too low it should not be too high as well and that is where I have explained to you while ago that the dose response relationship.

So, this region is a happy region, beyond this is a danger below this is also a danger region ok. So, now, let us move to another aspect ok. So, this aspects is concerned with how such an elements you already see in that there is an different elements associated with the with the with the human life. So, many elements are there, but we will try to look at one of the element which is iron; so, the iron element how it is being absorbed.

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So, we cannot look at each one of these. So, iron absorption let us see this finally, it requires to be given in to the plant. At the lumen there are see you take some iron containing food. So, the iron ions are there, these iron should be taken up. So, these are taken up at a lumen, how who will take it they are all ligands. These ligands can capture iron 2, iron 3 it to form iron chelates. So, at the lumens surface you are forming iron chelates and these iron chelates are then passed. So, now, the iron is covered by the biological molecules, which is present at the lumen.

And this chelates is now taken inside is called intestine intestines; so again intestine. So, it will exchange these chelates to endogenous legends of macromolecules. So, from macromolecule then endogenous ligands and from the intestine this will get into these chelates are transported into the blood, and in the blood you know that you have a protein which is called transferrin this reticulocyte you have depot cells so many different kinds of things are there. So, therefore, iron is. So, it is not that whatever you take straight away into your body, whatever you eat as going is just straight away without any gate.

So, there is a first security check, then there is a second security check and there is finally, transferred to that. So, these are three different gated levels through which the iron is absorbed. Similarly zinc, similarly copper nickel any of the iron that you talk about the absorption by the intestine and releasing into the blood is a very common

phenomena, but the ligands involved are different in each case and the transporting proteins are also different in each case ok.

So, in this aspect what I would like to tell you is, that so far we have covered the following aspects; one is the biological entities contain inorganic elements, ions, species. For example, a lot of enzymes have got the inorganic elements present in the form of ions and they are very active they are very vital they in fact, play very crucial roles which I am going to explain in this course as we wait for some more time that is that is aspect number 1 and details will come later.

And aspect number 2 is these elements in the entire elements present in the periodic table and 118 elements which are known today, not all forms any kind of a role with the biological systems, about 30 different elements are known to find their role in the biological systems of which few are called bulk elements like carbon, hydrogen, nitrogen, phosphorus you know these sulphur all these kinds of things is a bulk element then you have a macro minerals, sodium, potassium, calcium, magnesium etcetera chloride sulphate and other things and that is the point number 2 that we have a many elements, which are present in this; so carbon the element which are nothing, but the bulk in nature.

These will constitute about 95 to 96 percent of this and if you add the bulk minerals also 99.9 percent of the body weight is filled by this. But it is those 0.1 percent of the element which are called the trace ultra trace element, which basically gives the life to the body and this is the second aspect. The third aspect we when land was. So, these elements when you place into the biological table biological periodic table, then you see that there are only certain elements which are the important essential not all of them.

So, how is this being decided? This being decided because of their coordination properties, this is decided because of the thermodynamic stability aspect, is at being decided because of their kinetic reactivity. So, all these things together will decide. The fourth factor is that the concentration levels, the essential ultra trace elements essential concentration should be maintained in the body. And if they are too little too low in concentration they give deficiency syndromes, if they are too high in concentration they give a they give toxicity both deficiency and toxicity are dangerous things. Then the fifth

point is how are these taken in? They are taken by the absorption from the lumen to the intestine to the blood.

So, I think if these factors you keep in mind, the next lecture I will concentrate and what binds to this how they are attached to the biological systems etcetera.

Thank you.