Inorganic Chemistry of Life Principles & Properties
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Lecture - 19
Role of Alkali, Alkaline earth elements in life - continuation Ion transport & ionophores

Welcome you all for the next lecture on the Inorganic Chemistry of Life Principles and Perspectives. In the previous class we have been looking at ion binding properties particularly, towards the end we have been looking at the ion binding properties with the synthetic analogue molecule such as crown ethers and kryptons and trying to understand the kind of parameters that influence the ion association or ion binding aspects; such as the cavity size or core size as well as the number of ligating centers that we have, and the lipophilicity or hydrophilicity present on the peripheral aspects of these particular molecules, all these affect the log K s values of the ions bound.

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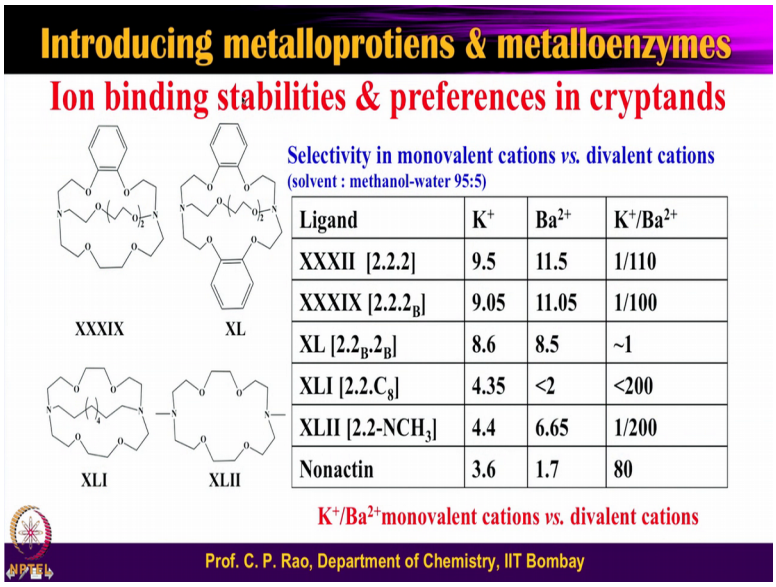

And particularly towards the end we were trying to look at some example, where we can and try to understand the monovalent versus the divalent ion transport. So, in this table I have some examples I explained to you earlier, in that when you have a 2 2 2 or 2 2 2 B there is 1 benzene ring still the selectivity is more towards the divalent cation. The

moment you make one more benzene ring on top of this, that is 2 2 B 2 B, then there is no specific preference either for the monovalent divalent.

So, but that does not mean that the both have been affected, what is more affected was the divalent. So, divalent gets more affected when you have more hydrophobic kind of a groups you know protruding outside like ferrall group in this particular case, and see the next example 2 2 2 C 8 2 2 C 8 case you have a much greater you know selectivity for binding towards the monovalent cation as compared to the divalent cation. As because the divalent preference is gone extremely down from 11, 8.5 to 2 whereas, the other one has gone down like monovalent is gone down to a smaller extent; so overall the preferences for the monovalent in this.

Now if you make in stuff that 2 2 C A way 2 2 NCH 3 as like the one which is should over there again it reverses state becomes a divalent cation. If you look at the natural antibiotic molecule one of the things as nonactin, you would see there is a preference for monovalent cation by about 84 differences.

So, all these clearly demonstrate that as you keep playing with the ion of pore molecule, in terms of the pore size in terms of the atoms that are being bound, in terms of the lipophilicity, hydrophilicity all of these aspects will change the monovalent versus the divalent transport; a divalent association constraints of these.

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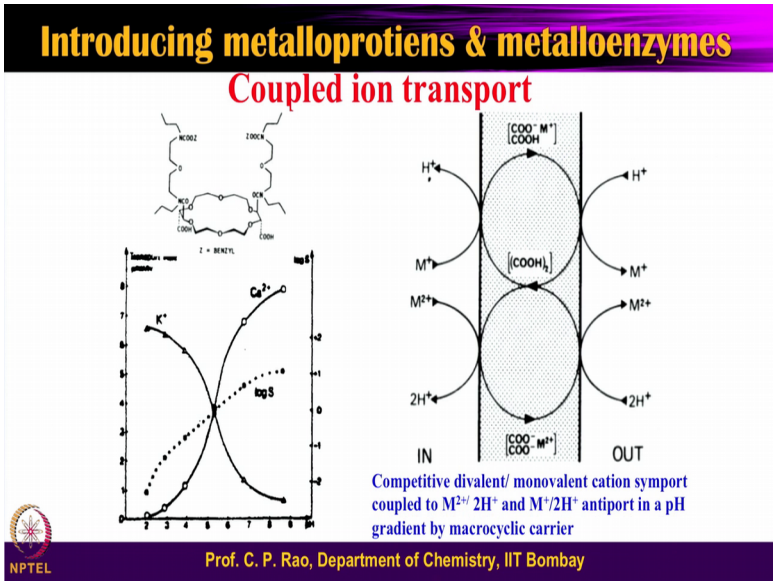

Now, let us try to look at these in terms of an a coupled ion transport, one of the example taken to over here is' this is the molecule. So, in this molecule which is nothing, but a crowd ether which is derivitized and you have a carboxylic at the carboxylic. And you know that the carboxylic group COOH proton, the presence the proton is dependent on the p H that should be kept in mind.

So, here is a transport phenomena are shown and this dotted region is let us say lipid region and at one side inside the cell, other is outside the cell equal to that; so inside and outside. So, in this particular thing as you have the metal ions on this side, the metal ion will interact with the molecule at this interface and picked up by this particular molecule and replaces the proton and the replace proton will be ejected out. So, that is what you can see that; so ejected out.

So, when it reaches the other end, again it will it will release the M plus and picks up the proton. Now it has become the neutral carrier then goes this side and then where it can pick up. So, you can see this is the kind of a direction in which it goes the molecule, this particular molecule inside this. So, picks up the metal ion and knocks out the proton and then transports to the other end, releases the metal ion and then picks up the proton here.

Similarly instead of one and monovalent so you can have a 2 ions coupled with the metal ion. Suppose if you take a divalent metal ion here as shown over here and the divalent metal ion approaches here at the interface, it will kick out the 2 protons of this particular molecule and make a complex with both the carboxylates. This ion is liberated or generated or released at the other end that is in the out of this particular membrane and wherein, you have a input of the 2 or the protons picked up you form a neutral one and then go back to this. So therefore, you have a transport taking place in this particular manner.

So, these are basically coupled the cation coupled with a proton and here divalent cation coupled with a 2 protons and both are in the opposite direction. So, therefore, this is where you have a antiport kind of a mechanism. So, same thing can we can understand that by looking at their log K s values and as a function of pH as I mention the protonation abilities will depend on the pH values. Whether the CO which is fully in the protonated form or CO which is in the COO minus form that will depend on the pH

value that you have here. So, as the x axis has a pH variation going from left to the right increasing the pH.

Now for the same molecule as you increase the p H, the K plus stability goes down C has you go to there. On the other hand if you look at this particular curve and for the calcium 2 plus it goes up. So, initially there is very little binding for calcium and as the p H increases the binding becomes very strong I mean log K s.

And for K plus initially there is a high association and as you increase the pH it goes down this stability goes down. So, exactly reverse that is because at the lower pH you have the molecule in the protonated form with the COOH COOH. As you keep increasing the pH, one of the COOH which loses the proton as we increase further the pH of both the carboxylic groups will lose the proton and becomes both COO minus.

So, since calcium has got a very high affinity towards the carboxylic as we have already studied in the earlier classes, the calcium bond complex becomes much more stable at this particular higher pH. So, it is lower pH potassium plus can make the complex. So, when you have a COOH can still form a complex with the potassium plus, when the COO minus and both the COO minus calcium plus complexes very much favored.

So therefore, a nature tries to utilize various chemical groups which are susceptible even to the pH and help besides the other points which I explained to you earlier, the pore size, the ligating number of ligating atoms, the lipophilicity, hydrophilicity of the molecule as well.

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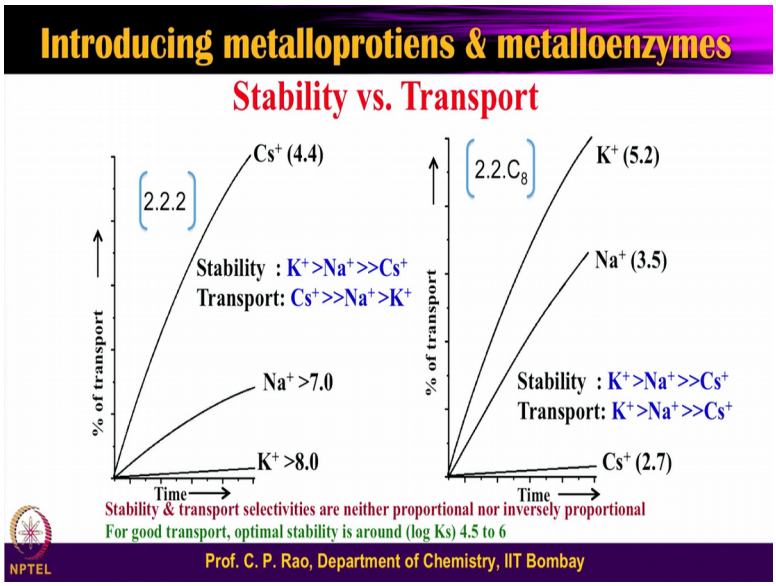

Now, having understood the log K s very well let us look at the next aspect how would we compare the log K s with another transport.

In this particular slide we have picked up 2 molecules, one is the 2 2 2 krypton other is 2 2 C 8 krypton. And you know here you have all 6 oxygen atoms, here you have 4 oxygen atoms, and one of the strands is completely carbon chain. Now in this if you see a time versus percent of transport, transportation is from 0 percent of transport to 100 here, similarly percent of transport 0 to a 100 percent. If you look at taking the 2 2 2 and adding K plus. So, over a period of time as you can see almost do much transport, but if you add potassium plus there is a little better transport percentage and if you add cesium plus will be a great transport you know greater transport or a very high transport property.

So cesium you so if you look at the stabilities which are given in the brackets here the potassium plus log K s is greatest as compared to the sodium plus, as compared to the cesium plus that is what is shown over there. The stability is or the log K s is K plus is greater than sodium plus is much greater than this is C s plus. But in the other hand transport is cesium plus is much greater than sodium plus, which is greater than potassium.

So, what do you conclude here? You conclude the stability and the transport or not are in the inversely related in this particular example. Now come to the right side example 2 2

C 8. So, you would find the transport stability is K plus is greater than sodium plus is greater than cesium plus, you can see 5.2, 3.5, 2.7. On the other hand transport; if you look at the transport part the K plus is greater than the Na plus which is greater than cesium plus.

So, what would be your conclusion? Both the stability order and transport order or are directly proportional whereas, here the stability versus the transporter in directly proportional. So, what does this mean? So, if you take one molecule you getting inversely proportional, if you take the other molecule you getting directly proportional. So, this is a kind of a controversy, which is definitely is not a controversy. If you look at carefully and try to compare wherever you have K plus values in the range of 4 and a half to 6 range, then you get the maximum kind of a transport all other times; even if you have a greater stability transport will be lower than that. And that is what we are trying to find.

So, therefore, the stability order and the transport order have no correlation, neither the direct relation nor the inverse relation at all. It is this value of the log K s which is determining. So, log K s and the range of 4.5 to 6 is the maximum transport that it shows.

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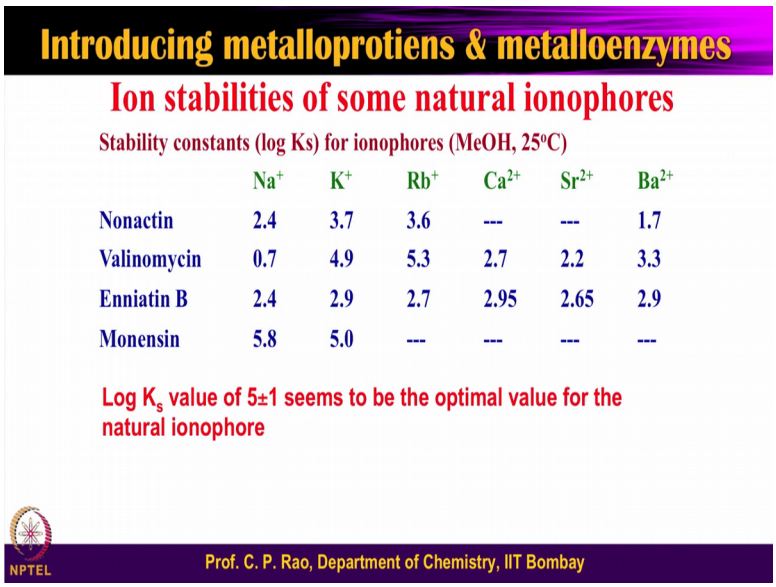

Now, let us try to compare with some natural ionophores, if you look at the natural ionophores the monensin which is for the sodium will shows 5.8 and if you look at the

valinomycin it will show for the calcium 2 plus is the 2 point sorry a potassium 2 plus potassium plus I am sorry potassium plus the 4.9.

So, somewhere around 5, in the vicinity of the 5 you have the greater the affinity of these ones. So the natural valinomycin which is specific for calcium, potassium plus has got around 5, log K s value and for Monessen the sodium plus has got 5.8; so in the range of 5 plus or minus 1 seem to be the optimal value for the natural ionophore and this same thing that we had tried to look for the other ionophore which is the synthetic ionophore.

So, therefore, in fact, what we would like to say is that for the natural ionophore or the synthetic ionophore the main thing that is basically reflecting is the log K s value. If the log K s value is the range of 4.5 to 6 range that is the most preferred one. So, what this means is, the lower the stability constant; the greater the stability constant with respect to 4.5 to 6 both are detrimental, because when it is lower it will make the complex, but the complex transport during the transport itself it will break. When you have a very high log K s beyond 6 what will happen? It will from a very strong complex, it will take across the (Refer Time: 13:05), but will never release.

So, in one case the breakdown of the complexes before the release point, in the other case even with reaches the other side of the membrane, it will still not release the thing. So, this is the kind of a situation that we find there is where the log K s value of 5 plus or minus 1 is the helpful indicator for all this. So, let us look at one another aspect.

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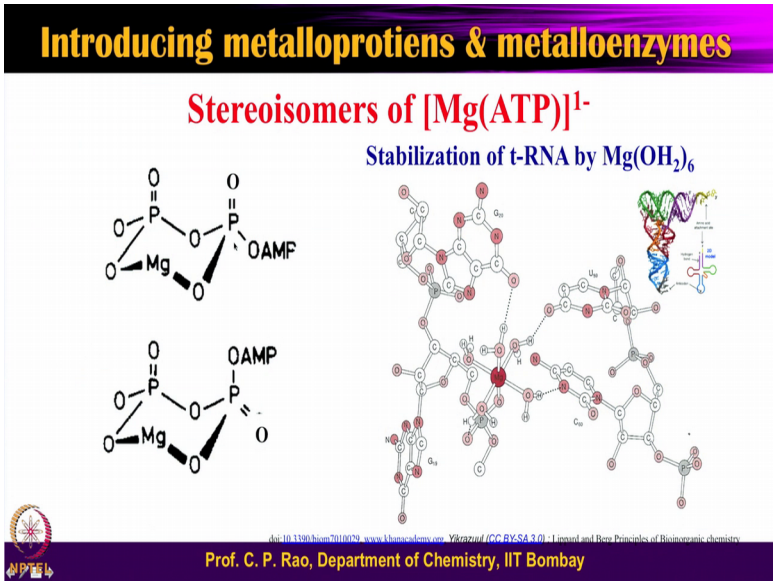

As I mentioned initially the magnesium, forms a complex with ATP in all these enzymes to convert for the hydrolysis of ATP or even for synthesis of ATP from ADP, in both the cases the magnesium 2 plus binds to this.

So, when the magnesium 2 plus binds to ATP you can see here, one of the isomer is a this way other isomer there are 2 possible isomers are there. And so these are the ones which provides the stability to this particular system; this how it basically explains the is the whole thing of the stability of the amp or ATP with respect to the magnesium 2 plus in the process of phosphorylation as well in the process of the dephosphorylation, where it has to add a phosphate group where it has to add remove the phosphate group.

And the other side I have explained some things the magnesium 2 plus ions, in fact stabilize the t-RNA structure. How does it stabilize magnesium? 2 plus ions do not directly bind to the t-RNA. So, what basically binds is magnesium aqua complex Mg OH 2 6 2 plus, and this particular complex is the one which binds to the t-RNA. So that means, it is the water which is bound to the magnesium and in turn interacts with the t-RNA.

So; that means, it is basically a secondary sphere interactions of the magnesium. So, the magnesium first sphere is the water, the water molecule in turn interacts with this t-RNA. So, therefore, these are called the secondary sphere kind of interactions. Because there is no direct interaction between the t-RNA and the magnesium center, but they interactions is between the t-RNA and the water molecule and most of these are by the hydrogen body.

So, magnesium hexa aquo is the ion which stabilizes the structure of the t-RNA through the formation of the hydrogen bonds as you can see the example over here. So, therefore, in this particular lecture what I am talked to you is about, the monovalent versus divalent balancing or selectivity it terms the log K s value that I am explained and first of all the log K s values themselves or dependent on the core size. or the pore size ligating sectors number of ligating atoms present in that, and as well as the life of philicity, hydrophilicity of the molecule. Then we talked about the couple transport the ion versus proton, ion versus proton in the reverse direction which is anti-pore mechanism.

So, I expect to you through an example of dicarboxylic group containing crowd ether. So, for monovalent for divalent for monovalent let us say potassium plus, for divalent it

is for the calcium 2 plus. And we have seen that the divalent calcium 2 plus has got a very high stability constant at a higher pH whereas, it is exactly reverse the for the potassium plus, because at the low pH the carboxylic groups are in COOH form, at a higher pH carboxylic groups are in COO minus form and both the COO minus will be strongly binding to the calcium, whereas the both the COOH positive a COOH groups will be binding to the potassium plus. So, this difference also we looked it.

Then we are looking the stability versus the transport ability. So, I am shown in one case the stability and transport ability or directly proportional, in another case stability versus the transport or are indirectly proportion. So that means, it is there is a controvercity which is not really the aspect, the aspect you need to look at is; look at the log K s, so wherever the log K s is the radio 4.5 to 6 that is the one which is a favor. And this is comparable with the natural ionophores and that is what I have shown at the end.

Thank you very much.