Inorganic Chemistry of Life Principles & Properties
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Lecture - 18
Role of Alkali, Alkaline earth elements in life – continuation

Welcome you to the next class on the Inorganic Chemistry of Life Principles and Perspectives. In the previous class, we have been talking about the ion transport phenomena in terms of variety of things like uniport symport antiport.

We also have seen certain ion, transport will change the potential certain ions transport will not change because one ion is going in one direction, other ion is going in the other direction having the same charge, etcetera, sometimes where it is the H plus, then the pH variation will happen.

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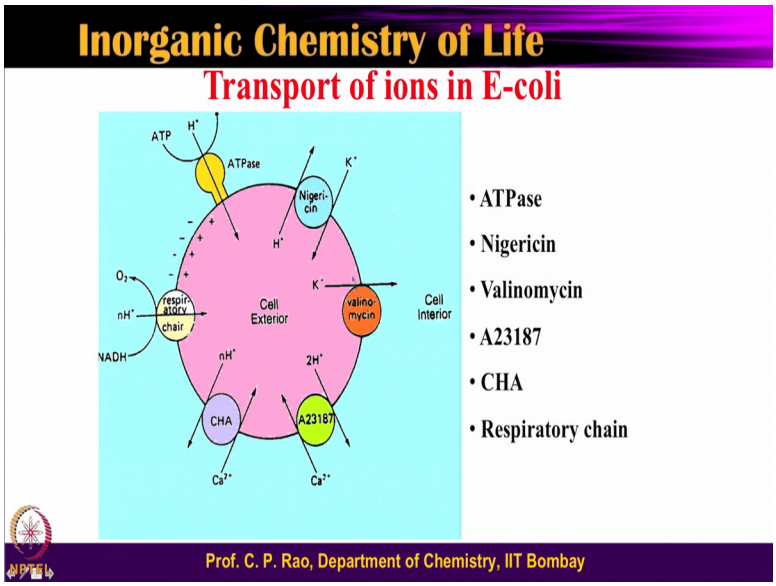

So, these are all and we also have seen an example in E-coli how so many in different kinds of transports are coupled together. So, how complicated is the ion transport process even for a simple being like an E-coli ok.

So, how do we understand such a phenomena by taking an example.

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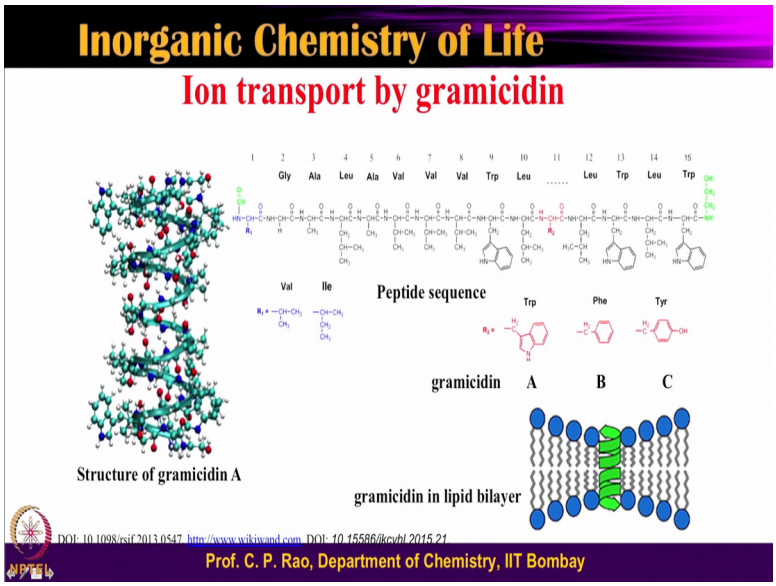

So, take an example of one of the peptides which is involved in ion transport is gramicidin; gramicidin as you can see from this picture, there is 15 amino acids are there, ok, as you can see, some uses some tryptophan, some phenyl only, some tyrosines all kinds of things are there, it is a 15 amino acid residues.

So, it is a kind of a small peptide not a huge protein small peptide even this peptide, I was taught to you earlier primary sequence that is this one secondary structure tertiary structure, etcetera, if you take those things, you consideration; you can see that this particular peptide takes a kind of a turn like this is which is nothing, but the helical turn. So, you form a helix kind of a structure, here you can see that this is the structure of the gramicidin a with a helical structure having the same peptide sequence.

Now, if this goes and sits inside a membrane you see this head portion tail head and tail this is lipid and this is 2; so lipid bilayer; so, lipid bilayers are typically the membranes. So, if you insert this gramicidin into this, you can see that green one with the helical. So, you can nicely see that this is very well very well you know inserted into this.

Now, form a kind of a barrel. So, there is a barrel; it is not of course, this is a simple kind of thing you have lot of residues interacting with various things, etcetera; that will allow the ions to flow through this. So, what is the mechanism a protein will form a kind of helical structure this helical structure will span across the two ends of the membrane on one end which is outside other end which is inside. So, it is spanning across and then

forming this helix is like a kind of a your pushing a tube through a certain kind of a material that is kind of thing.

So, you have so, this is a tube formed by the protein ok. So, therefore, the protein; obviously, is having a amino acid lining. So, therefore, therefore, you have some amino acid base kind of a interactions inside. So, this is used for ion transport. So, now, we got one idea is how these will do it; which we did have earlier, but how peptide.

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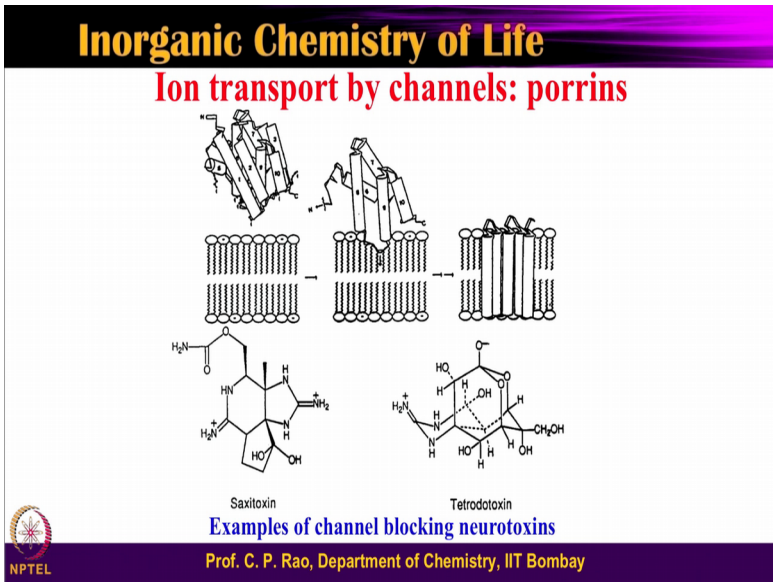

Even proteins there are bigger size proteins there in the peptides what we are seen gramicidin these are called porrins, these are nothing, but transport deform ion transport channels some of these also formed gated ion transport channels, I will tell you just in a while

So, this porrin peptide a polypeptide or a protein, see, it has so many kind of helices other things and this will get basically inserted, you see this and when it is fully inserted you can see all of them, it is not one part, this is one parts, this is another part, this is another part; whole thing coming from this and the gated means that you have allowing in not allowing in and out through a check that kind of things are gated channels; the gate will open under certain conditions gate will close; may closed under certain conditions.

So, keeping that assigned, you can see the porrins also do the same kind of thing as this has done gramicidin in this case only one peptide. So, one barrel only and in case of

porrins not 1 barrel, 1, 2, 3, 4, 5; these may be used for different ion these may be used for same ion different concentrations variety of things we are not taking the details of that at this stage because which is out of focus to that; how do you do that these are following font channels.

So, there are some molecules should over here; these are the molecules and if you add these molecules to this the ion transport will stop and if you remove these molecules ion transport will go so; that means, these barrels having the ion transport property and those barrels are filled by these ones; in other words; blocked by these molecules and these are basically called as the neurotoxins.

So, those which prevent the ion transport is the neurotoxins now we understand. So, ion transport then how a peptide can do how a big protein can do; we have learned on this in very general way.

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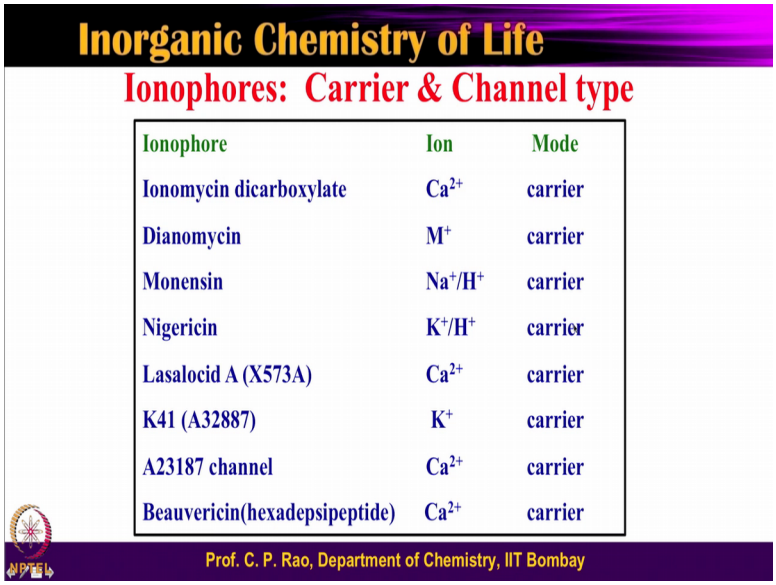

Now, let us come to some Ionophores biological biologically important Ionophores. So, you have seen earlier, in this case, the ions are flowing through this. So, it is called channel type.

If the ion goes in a straight away without such channels; for example, some of these ions here; for example, potassium ion by the nigericin or valinomycin; they are sequestered by this valinomycin taken in, taken out, in this case, it is taken out. So, this kind of thing

is not called a channel, this is the one is a channel kind of mechanism another is the chelation or the carrier kind of a mechanism. So, it chelates binds and takes it out. So, one is carrier type other is the channel type.

Now, so small molecules having different binding sites can bind to the metal ion and wrap around the metal ion and take across the membrane those things are referred as a carrier and if the carrier molecule is a peptide and protein it forms a kind of a channel and channel is placed across the membrane and therefore, the pro ions are transported across the membrane through the channel.

So, that is called channel kind of mechanism is that clear carrier mechanism channel mechanism. So, I hope you understand in the carrier you have an ion you have molecule molecule sequesters at the whole thing as a complex on goes into the cell or out of the cell.

In other case, the molecule forms a spiral and spans across the membrane and then forms a tube like structure through which the ions will flow from in to out to in whatever be the mechanism is these are all called channel mechanism. So, carrier mechanism and channel mechanism.

So, ionophores like ionomycin dicarboxylate. So, this is one a small molecular, but these are all biologically important ones biologically relevant ones to; this is calcium 2 plus; what is the mode; it is a carrier type dianomycin, it is a no selectivity between the potassium and sodium, it will be all right and that is a again carrier mechanism monensin, it will be for sodium plus Na H plus not potassium plus, it is a carrier. So, you can see the selectivity here monensin.

So, that molecule is a natural antibiotic and the nature has synthesizing such a way that it can only bind to sodium plus and not H plus; we will study why is like that in a while as we continue this particular topic on ion transport nigericin potassium and H plus, but not sodium plus.

So, monensin is selective for sodium nigericin selective for potassium in the same can do the H plus in the reverse direction to lasalocid is a calcium carrier. So, the some other antibiotic is as the number, do not worry, it is a potassium another antibiotic, it is a calcium ok, a hexadepsipeptide not a peptide depsipeptide as a calcium which is a

carrier, then valinomycin which is very well known to many people this is a cyclic peptide, it is a potassium, it is a carrier.

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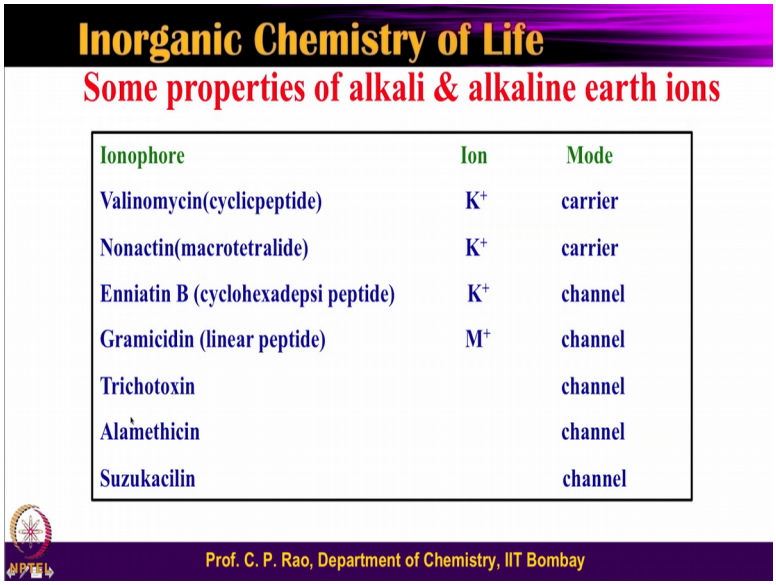

Nonactin is a macro macrotetralide and show some of the structure soon is a carrier and enniatin its another cycle cyclohexadepsi peptide potassium channel gramicidin, it can be K plus; there are some peptides trichotoxin its can form a channel aalamethicin, it can form a channel suzukacilin, it can form a channel. So, these are gramicidin; these are all channel kind of a systems. So, channel mechanism all other words on carrier mechanism in a carrier, the ion is bounded by the ionophore from all directions and take it inside the cell or taken out of the cell.

So, carrier and channel type to get more clarity let us say on the carrier kind of a case cyclic ionophores.

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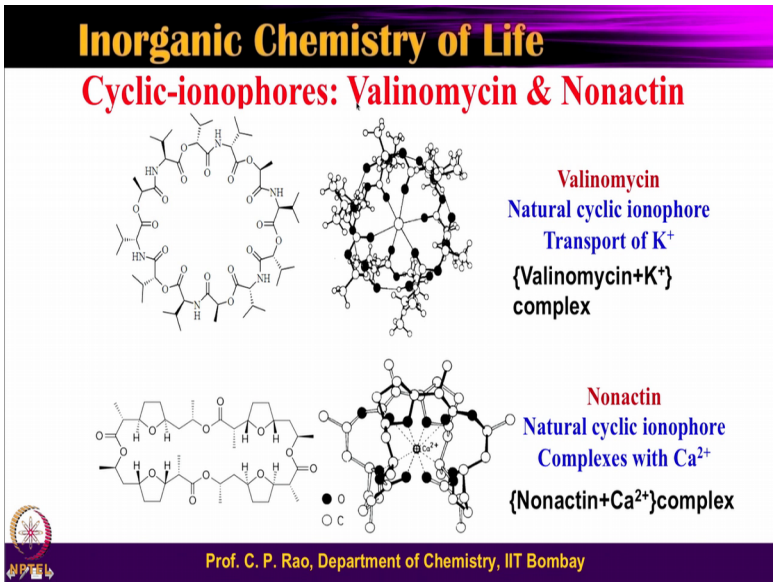

One example is shown is for the valinomycin, another example is shown in these cases nonactin. So, see this valinomycin is nothing, but natural cyclic ionophore cyclic peptide v peptide because CO NH CO NH. So, you have all this kind of thing, you have other liquors also, other liquors are also that it is a cyclic peptide. So, this is a natural the cyclic ionophore and this is very selective for the potassium, you see that how there are carbonyls though in this writing.

They all look towards inside you see the crystal structure, the crystal structure only some of them this one the after two more, then after after after after. So, only 6 have been protruded inside carbonyls. So, these protruded 6 carbonyls inside will form a core like a octahedral core at the metal ion is at the center now you can see this is a metal ion this is your valinomycin. So, this is valinomycin complex and such a complex will go through the membrane straight away by concentration difference diffusion mechanism. So, concentration difference will also be resulted the potential difference.

So, therefore, this is kind of a thing this, you can call it as a carrier, then another molecule should over here this one. So, this is a molecule of for the calcium bond nonactin, you can see the structure over there here and natural cyclic ionophore, it complexes with the calcium 2 plus and this molecule is shown over there.

So, it is not exactly this ways form, it is slum some you know kind of a folding etcetera will come and finally, we will fold like this. So, that it wraps around. So, ion and the

peptide is or the molecule is wrapped the ion and the molecules are the top one is for potassium valinomycin, this is the one below here is for calcium is a nonactin and you can both are carriers.

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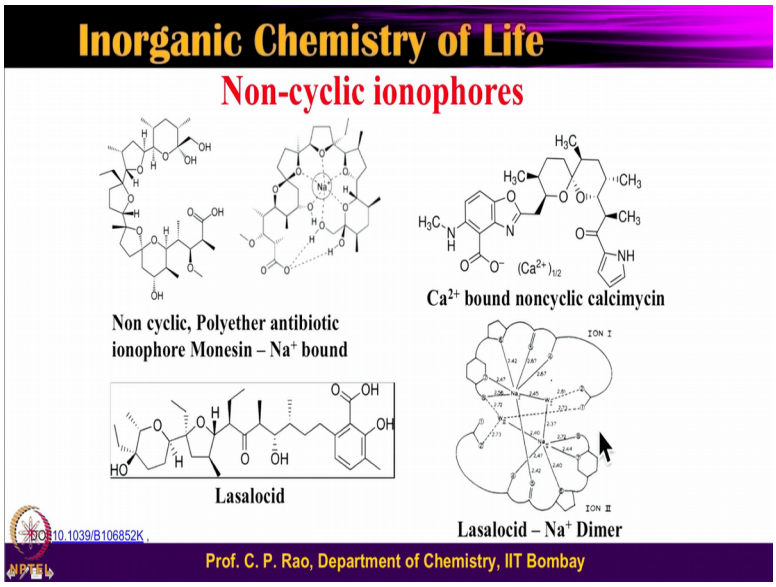

Obviously, it is not only cyclic, you can also see some noncyclic examples, this is an example perfect example for a noncyclic and it is the ionophore called; it is short name is monensin commercial name is monensin. So, you can see some ether like oxygens hydroxyl oxygens ether like oxygen hydroxyl oxygens and at the end carboxylic group.

So, this if you see for the sodium; it is binding to all this ok, but there is a bit of opening here in this part of it is exposed to the exposed to the environment ok, there is another molecule which is shown calcimycin and similarly, this also binds that this is another example which is shown for lasalocid, this is for sodium.

So, such a open molecules; when they bind to the ion, there is always a part of the part of the region is exposed and you know when it has go to the membrane what is membrane property, it is a polar non-polar. So, if the ion is open part of the ion ion sphere is open, ion coordination sphere is open what is that one this is hydrophilic.

So, therefore, hydrophilic part how can it go through the membrane there is no energy is also applied in this case. So, it is only concentration differences. So, what it happens is two such molecules will join together you see here, there is one molecule with one ion

sodium there is another molecule with a sodium ion here. So, you can see centro symmetry between them, this to this, this to this, etcetera.

So, a centro symmetric pair of two ligands and two ions; So, now, this is completely closed this is not open whereas, this part is open. So, it has some hydrophilic region this is does not have. Therefore, this kind of a systems when you have a noncyclic systems most often not necessary 100 percent time most often when there is opening of the coordination sphere it will dimerize and the dimer will pass through the membrane not the monomer ok, in the other case, no dimer is required here the valinomycin monomer itself nonactin monomer itself whereas, the monensin lasalocid monensin all these kind of things you have a the dimer is formed I hope you understand.

Now in the carrier, I have shown you two types one is where the metal ion is completely sequestered by a cyclic ligand. So, therefore, the overall metal ion positive charge or the hydrophilic region is covered by the hydrophobic or exterior therefore, it can go through the membrane.

The second case noncyclic ionophore where the noncyclic ionophore you have the ligand wrapping around, but not hundred percent there are certain region is open up. So, this region of the coordination sphere is a is a hydrophilic therefore, this cannot go through a membrane because it is a hydrophobic therefore, two such half kind of things join together and there go through as a dimer to the things because the dimer is less exposed to the atmosphere O environment having understood the philosophy how these ions are transported one is my carrier other is my channel.

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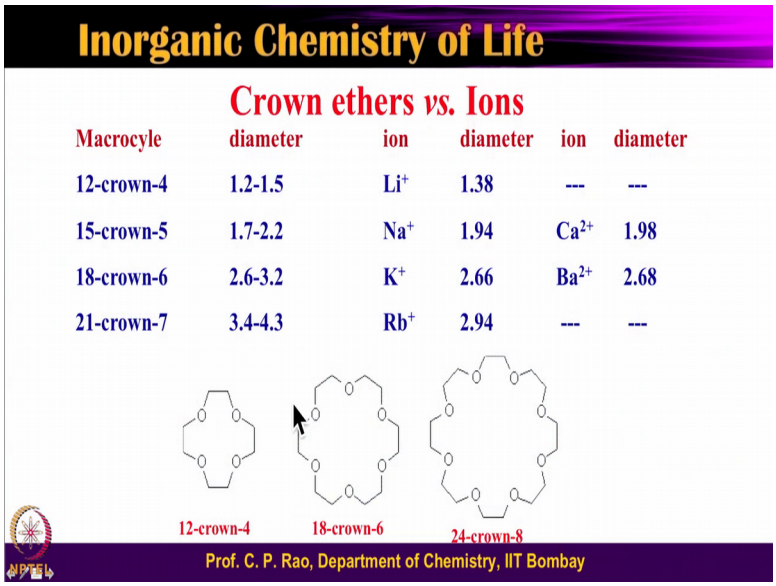

Now, let us look at their affinity is how would we understand at some stage, I said this antibiotic is useful for potassium this antibiotic for sodium, this is for something else, how did we say that how did we understand that we said that because experiment shows that, but how do we understand we have to understand that; we have to study certain level of coordination chemistry of these ions and their transport properties.

So, for that we can semantically break molecule of cyclic type noncyclic type and then study their affinity for monovalent ion divalent ion and they look for their stability constants and compared with the literature compared with the natural ones compared with natural ones. So, our process goes in that direction.

First, we take simple cases is called crowd ether. So, 12 crown 4; crown 4 means there are 4; this oxygens are there and 12 means there are total atoms, periphery is 12, here total atoms are 18, oxygens are 6, total atoms are 24; oxygens are 8. So, you have a 4 atom core 6 atom core and 8 atom core. So, what are these 12 crown 450 crown 5 which is not shown here 18 crowd 620 crown 724 crown 8. So, many things are taken so many kind of a example.

Now, you can see their diameters going from around 1.3 to 2 to 2.8 to 3.8 something like that. So, you can see that they are increasing size of the thing and coordination number is also increasing there are 4 oxygen atoms, 5 oxygen atoms, 6 oxygen atoms, 7 oxygen atoms.

Now, if you try to see among the ions which are of a part of the from the alkali alkaline earth, let us look at the alkali ions lithium ion sodium ion potassium ion and rubidium ion. So, what is the diameter 1.38 is that 1.38 is somewhere in between these two, absolutely 1.2 to 1.5 and it is 1.94; 1.7 to 2.2 is what? It is somewhere in between. So, it is very nice fit 2.66 is absolutely, this 2.94; somewhat bit looser lose to this. So, you will not getting.

So; that means, you are looking for a fit between the diameter of the macro cycle versus the diameter of the ion. So, there is a size fit, this is a ion pore this is a ion size. So, this is a macro cycle this is a ion. So, therefore, you can find in the nice match nice binding. So, lithium 4 oxygens absolutely perfect sodium with 5 oxygens will be good and then potassium with 6 oxygens perfect kind of thing. So, you can see that they have a size of the pore versus the size of the ion have a perfect thing. In fact, these kind of a crown ethers are used for a very selective ion transport or ion reactions in organic synthesis, they will used to as a phase transfer catalyst.

Now, I will do a little bit of exercise regarding their affinities regarding their binding constants, let us look at some binding constant.

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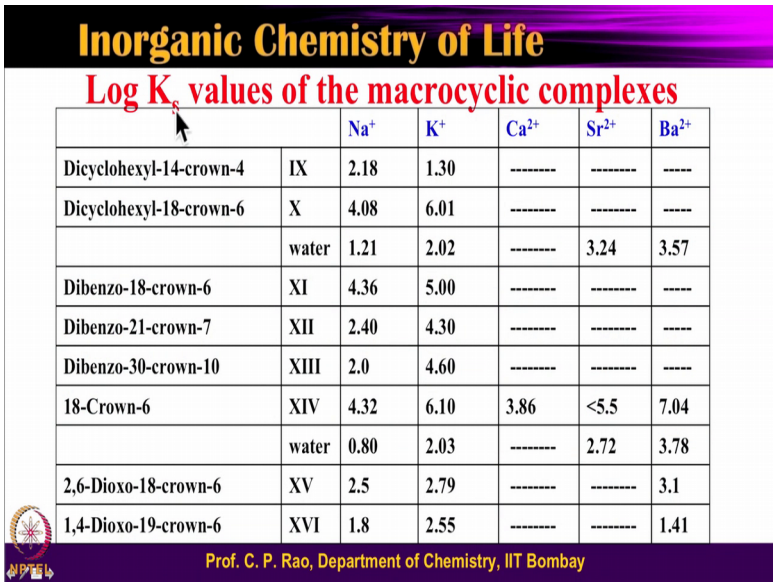

		Na^+	K^+	Ca^{2+}	Sr^{2+}	Ba^{2+}
Dicyclohexyl-14-crown-4	IX	2.18	1.30	--------	--------	-----
Dicyclohexyl-18-crown-6	X	4.08	6.01	--------	--------	-----
	water	1.21	2.02	--------	3.24	3.57
Dibenzo-18-crown-6	XI	4.36	5.00	--------	--------	-----
Dibenzo-21-crown-7	XII	2.40	4.30	--------	--------	-----
Dibenzo-30-crown-10	XIII	2.0	4.60	--------	--------	-----
18-Crown-6	XIV	4.32	6.10	3.86	<5.5	7.04
	water	0.80	2.03	--------	2.72	3.78
2,6-Dioxo-18-crown-6	XV	2.5	2.79	--------	--------	3.1
1,4-Dioxo-19-crown-6	XVI	1.8	2.55	--------	--------	1.41

Ks is the binding constant in the solvent whatever it is a log of this value. So, log 10 K value; that means, this whatever the value have on the decimal side, you have to take antilogarithm and multiplied by 10 power 2 antilogarithm of 0 8 multiplied by 10 power

4 like that. So, you know now you understand what is the K K value is the antilogarithm of this decimal point multiplied by 10 power of the on the side ok, you take dicyclohexyl 14 crown 4, we have seen a good fit for; this is what a good fit for this is lithium and here what we are looking as the sodium sodium shows some binding strength potassium shows much less why because potassium ion is much more bigger than that of the sodium ion, it cannot fit at all sodium also cannot fit, but slightly it can interact.

Now, instead of 14 crown 4, increase the size 18 crown 6. So, the size of the core is increased the number of oxygens are increased. Now, you see that is this molecule will bind instead of 2.18, 4.08; that means, 100 fold greater hundredfold greater. So, the sodium plus is captured by dicyclohexyl 18 crown 6 to an extent of 10 power 4 something a potassium is much more 10 power 6.

So, what do you say now? So, 10 power 4 versus 10 power 600 fold difference. So, what do you say, it is this molecule has affinity to sodium affinity to potassium, but selectivity is more towards the potassium because potassium is binding 100 times better than that is sodium how hundred is coming, it is 10 power 6, this is 10 power 4; of course, when you add water you take in water all these things are taken in the ethanol, if you take it water hydration. So, every stability will go down all these molecules all these ions do bind very give any stable binding.

Now, come to another one. So, cyclohexyl take the benzo. So, 18 crown 6 showing 4 point; let us say 4, this is showing five the difference is not as large as here, here is a hundredfold here, it is not that much much less difference is there. Now that is because you changed from cyclohexyl to benzo and you are not changed 18 crown 6 at all.

So, therefore, it is not only the size of the crown ether not only the number of ligating size, but also the what is there outside. So, dibenzo, you have a more pi system and you have only alkali kind of system that you have. So, therefore, hydrophobicities are also playing a role.

So, therefore, hydrophobicity hydrophilicity of the molecule core size and the number of number of ligating centers all these will play important. Now, go to the dibenzo 21 crown 6. Now, 21 crown 6 becomes too big for sodium. So, 4.4; it become 2.400 times became weaker in binding and whereas, the for potassium also it is bigger, but the it is weak by about 5 times or something not even 10 types ok.

So, that you understand by now; dibenzo 30 crowns 10 because much more bigger. So, all these becomes very weak sodium almost does not bind much at all potassium will bind to much lower extent ok.

So, similarly 18 crown 6 for sodium 4.3 and potassium 6.100 fold as I told you in water is no important dioxo this is like adding oxo groups outside keto groups outside the 18 crown 6 periphery; then what you are doing hydrophilic here dicyclohexyl is hydrophobic dibenzo; you have both the hydrophobic hydrophobic and once you come to the dioxo, you have a hydrophilic is a keto group, it will attract the water therefore, your binding strikes have got down just compare this with 18 crown 6, 18 crown 6, a 4.32. So, two 6 dioxo 18 crown 6; 2.5, similarly this has fallen down ok.

And little not too much worry about these this side of it then one 4 dioxo nineteen crown 6 again the; so, what are we finding the size of the core the number of hetero atoms and the groups present outside whether they are hydrophobic hydrophilic these all these play important role; that means, with the nature has synthesized all these antibiotics it has taken a optimal of all these.

Let us take another system which is referred as a cryptand system.

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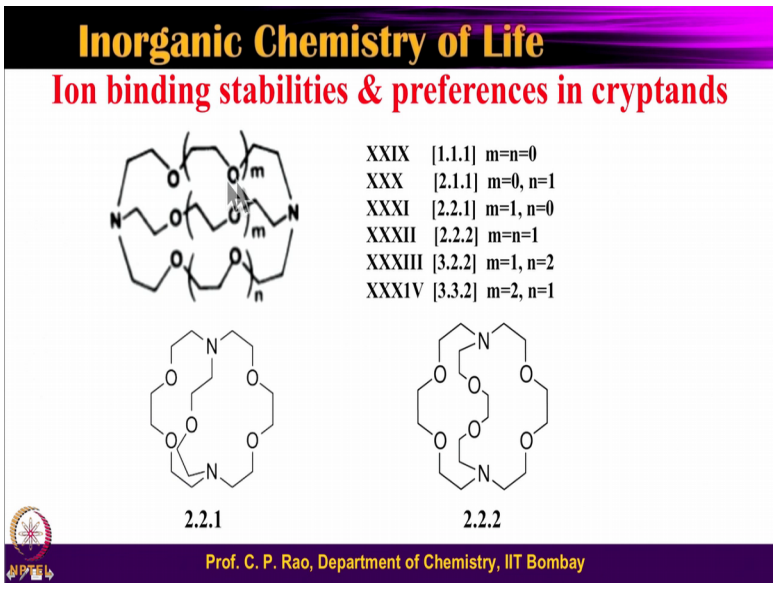

The cryptand system is like this 2 nitrogens connected by these ones. So, you can see 2 2 2 3 1 1 that is the number that you have 2 2 1 2 2 2, etcetera. So, you have the oxygens;

the oxygens are coming from each strand. So, there is a strap between this nitrogen and this nitrogen one there is a second strand third strand there are three strands are connecting between the two nitrogens. So, therefore, it is more or less three dimensionally arranged with respect to this. So, therefore, it will wrap around the any ion from all direction.

So, this you can easily make out from m and N. So, 2, 2, 2; there is a 6; 2, 2, 1 has got 2 plus 2 plus 1. So, that is 5 atoms, etcetera ok. So, ah; so, these are the kinds of things. Now having seen this, let us try to look at this one; this is 1 1 1 will have only 3 atoms, 2 1 1 has got 2 1 1 and you will have 4 atoms; 2, 2, 1, you have got 5 atoms, 2, 2, 2 has got 6 atoms, etcetera, etcetera.

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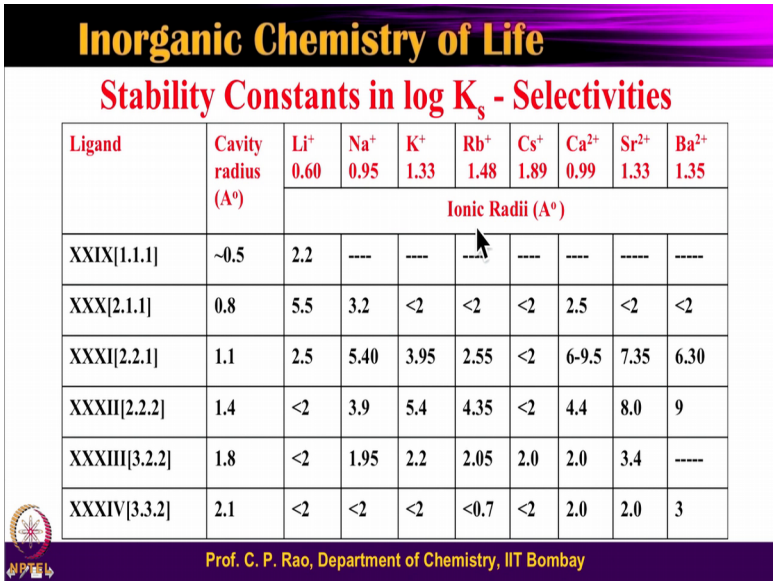

Now, let us look at these ones; this is not important. So, you take 2 1 1, there are 4 oxygen atoms in this, you see that lithium absolutely perfect, we have seen earlier when you have 4 atoms and when you have a crown 4, it is perfect its giving very high binding, then it going to take the sodium not so much fit and all others are not fit at all.

Now, going to 2 2 1; now you have 5 atoms are surrounding 5 oxygen atoms are there. Now once you have the 5 oxygen atoms, the chain length is also increased. So, therefore, pour size increase lithium becomes weak lithium becomes loose rather lithium is now loose fit not a good fit, but whereas, you go to the sodium this becomes a strong fit here

lithium is good fit sodium is not fit here is lithium is not fit, sodium is fit and potassium etcetera is not fit.

Now, go to the 2 2 2, then lithium is not fit sodium is not fit potassium is fit because 10 power 5; 3 2 2 that will have 3 plus 2 plus 2 that is called 7; 7 oxygen atoms not only number of oxygen atoms, even the core size will also increase no binding much no binding much no binding much, even potassium cannot bind that thing so; that means, increasing the number of atoms to 8 7 and so, huge size is no use at all ok; So, since similarly 3 3 2 3 3 2 means 3 plus 3 plus 2; that is 6 plus 2; 8 eight atoms almost nothing.

So, now you can see the 2 2 1 is good for sodium, 2 1 1 is good for lithium; 2 2 2 is good for the potassium. So, lithium sodium potassium; so, like a diagonal here 4 atoms, 5 atom, 6 atoms, the ion the core size is smaller little bigger much bigger. So, now, you can understand how this is really working.

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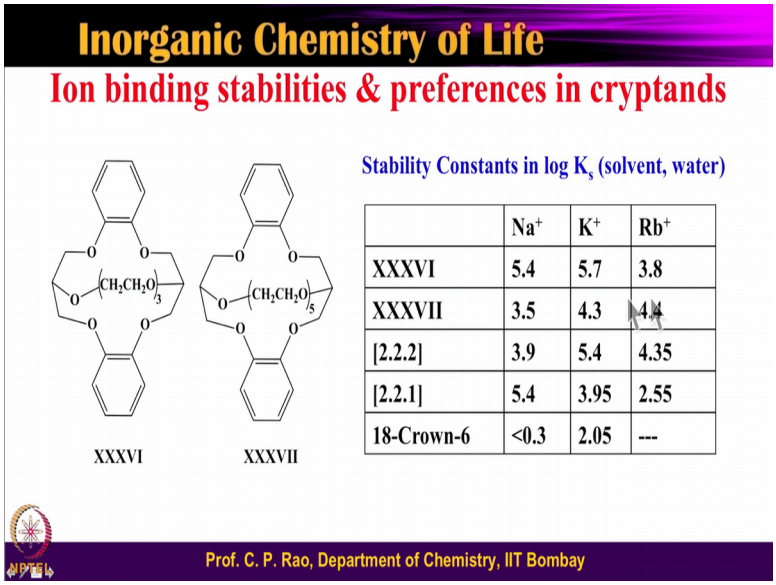

	Na^+	K^+	Rb^+
XXXVI	5.4	5.7	3.8
XXXVII	3.5	4.3	4.4
[2.2.2]	3.9	5.4	4.35
[2.2.1]	5.4	3.95	2.55
18-Crown-6	<0.3	2.05	---

Similarly, one can see the di diionic or bivalent cation 2, I mention to you earlier the changing the periphery with some hydrophobic, etcetera will also influence this ok, this is the thirty seven which is over here 1 2 plus 3 5 6 7 8 kind of thing and this particular thing is showing showing 5.4 for sodium and 5.7 for potassium and 3.8 for rubidium.

Now, if you go to the next one next one you have this is only three and this is 5. So, you increased. So, when you increase this is decreasing basically you can see the values quite

much to going down? So, on the other hand if you take 2 2 2 which you have seen on the previous slide there is a maximum at the potassium and 2 2 1 will have. So, therefore, the size increases.

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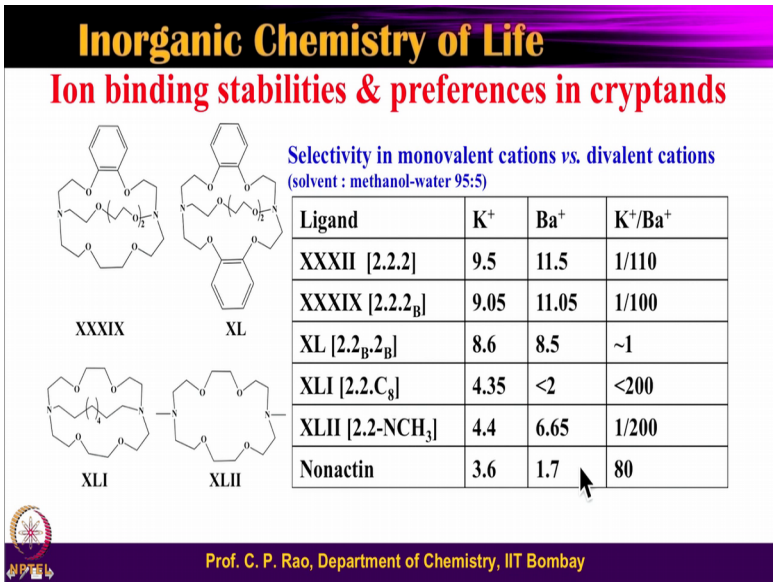

All these or indeed affect a lot so, let us see a case where we have only one benzene ring and there are cases two benzene rings. So, take one benzene ring here 2 2 2 b 2 2 2 2 b 2 b, see the potassium, it does not change much, but barium it changes by three orders of magnitude almost.

So, therefore, sodium to potassium to barium ratio is become one, here 1 is to 100. So, you take instead of that c 8 no oxygens at all only all 8 are carbons; that means, only 4 oxygens and nothing then the potassium will come down barium will come much down. So, it becomes potassium selective as compared to the barium.

Now, instead you put two methyl groups one methyl group here one methyl group here 2 2 NH 3. So, that gives more or less similar for the potassium, but for the barium; it is bigger because its opened up and therefore, again it inwards the monovalent ratio for potassium to barium.

So, these are some of the things which nature has basically balanced in order to get the trans in order to get specificity for the antibiotics that are being naturally synthesized

take an example; non acting for potassium 3.6 barium 1.7 and the ratio is 80. So, therefore, this can take mainly monovalent potassium, but not the barium ion in this case.

So, now what we are trying to look at is that they. So, the ion binding properties preferences are dependent on how many ligating centers are there what is the core size of the molecule and whether the exterior is hydrophobic hydrophilic partially hydrophobic partially hydrophilic and therefore, these all determine the selectivity between the sodium versus the among the among the monovalent cations between the among the monovalent versus divalent as shown in this particular case, you see that this is divalent 2 plus. So, K plus and 2 plus. So, therefore, this becomes almost nothing.

So, this means this is more favored for barium this is more favored for barium; this is neither good for anything, this is more favored for potassium, this is more favored for barium, this is more favored for potassium. So, the numerator greater value is for potassium denominator greater value is for the barium divalent. So, that is how the nature has tried to adjust these things, we will continue with this ion transport in the next class with the by take by looking into certain additional systems.

Thank you very much.