Biological Inorganic Chemistry Professor Debashis Ray Department of Chemistry Indian Institute of Technology, Kharagpur Lecture 55 Chlorine and Iodine

(Refer Slide Time: 00:48)



Hello students, a very good morning to all of you. And we have reached the end of the module 11 where we are discussing about the nonmetallic elements and their biological roles. And today, we will be talking about chlorine, as well as iodine. It is not chlorine and iodine, but it will be chloride ion and iodide ion.

So, we will talk about these two elements in biology whether we need some ion channels for that purpose or not. And why we require some exclusive Li, the chlorine transport or the chloride and transport for a particular point. And that way we can also try to know that whether CL minus and i minus the inorganic anions the way we know them are essential for our life processes also.

Then how we can correlate this? Whether your chloride or your iodide can be correlated to some essential hormone synthesis, and that we also will be able to know or learn about the ordination and deiodination reactions, which are very important organic chemistry reactions.

(Refer Slide Time: 01:29)



So, if we have chlorine, as well as the chloride ion because we know that it will be converting to sodium chloride like salt. So, which is an essential element and sometime we call as a very beautiful or very useful nutrient for us, for our metabolism, because everywhere we need the presence of chloride ion in our system. So, how much you have? When you first time learned the chemistry practical in your school, you know that your chloride sample is given in the form of sodium chloride and you have been asked to identify the salt as sodium chloride, not as sodium chloride, but only the anionic part.

Because it is given that, okay, you have given some chloride salt. It can be sodium chloride, it can be potassium chloride or it can be calcium chloride. So, we have identified that chloride ion by adding silver nitrate solution and we get know that we get the silver correct precipitation. So, the same understanding or same knowledge we can use also if your sample is different, not we have prepared it for you by dissolving sodium chloride or not you can have the biological fluid samples, but how much you have that means the quantitative determination, not only the presence of chloride and in this biological system or the fluid, but you should know how much is there which is important, because the concentration plays a very important and vital role for our life processes.

So, in the seawater, we all know that potassium chloride in Chile saltpeter we know the sources and all these. So, the geological point of view or the biogeological point of view here from we are getting all these things. So, highly concentrated seawater can have the chloride concentration of 2.55 millimolar. It is easy to remember also. We know sometime we ask

what is the concentration of water in water, that figure is also 55 molar concentration, and it is 0.55 millimolar so it 0.55 millimolar concentration what we can have in seawater.

So, if some standard reference you have that means, this much chloride ion is present in seawater, and how much they are in our drinking water we talk we talk in terms of the PPM level of the chloride ion, as well as the other ions like sodium and other ions. So, we can have the cell, and outside cell you have some fluid and inside cell we have some fluid and we have the barrier the lipid barrier or the phospholipid barrier we know, which is encasing your cell.

So, what should be or the outside environment concentration, which is nothing but is 103 milliequivalent per liter. I am not talking in terms of your millimolar concentration because I am giving you some confusion. So, you should be confused a little bit such that you understand nicely, how much these equivalences are. Millimolar concentration, milliequivalents per liter as well as the PPM concentration what do you drink as your water.

So, it is 103, the figure is compared to that of 142 for sodium ion and 27 for bicarbonate ion. So, all these will come and compete with the chloride concentration. Then compared to your outside concentration to the inside concentration, which is very low. So, which is only 2 milliequivalent per liter compared to your bicarbonate concentration which high. So, we should know about the balancing of all these concentrations, how much sodium concentration we have in the sodium ion concentration in the extracellular fluid, and how much inside, similarly, the potassium concentration.

We know the relationship when we have learned about the corresponding ion channels of sodium, as well as the potassium in biological inorganic chemistry. So, there we have seen that you can have some reverse thing, that means, you can have one particular point your sodium is concentrated and in other part the potassium ion is concentrated. So, that gives all these informations and all these activities and the functions.

(Refer Slide Time: 05:34)



So, we have the typical significance. And from physiological origin what you can have, what basically the corresponding chloride ion can do? We know the person suffering from hypertension, we always best guide that you do not take much of your sodium chloride, so our sodium intake as well as the sodium chloride intake should be reduced. So, what is controlling that osmotic pressure? You have to know that, you little bit you try to understand it that what is being balanced. The osmotic pressure due to sodium ion or osmotic pressure due to chloride ion?

So, here we have the answer that, the osmotic pressure is being controlled by the chloride ion also. What about the sodium ion? So, already we have learnt it, but we can fix these questions or we can give these questions in that particular form that you compare the roll of Na plus role of Cl minus in controlling the osmotic pressure in our body.

It can also go for very useful electrolyte balance because the common thing is that we can have the chloride ion with respect to Na plus and K plus an acid-based homeostasis because Cl minus we know is basically the corresponding part what we get from HCL. And we know in our body also the stomach acidity goes down to 2.8 pH is due to that of the formation of HCL. So, chloride can definitely play some acid-based homeostasis, that means, the environment.

So, it is basically therefore essential electrolyte, that means, the anionic part of that electrolyte playing a key role in maintaining the cell homeostasis and transmitting action potential in neurons. So, the transfer of sodium ions from the cell membrane or the neuron basically neuron will get the signal so, it is basically the concentration difference you have

the barrier, it is a cell barrier or the membrane barrier. You have one highly concentrated part and another is low concentrated part so we will have the movement so that movement will generate a corresponding ionic potential along that particular membrane.

So, how this can be transferred? Already we have seen that we can have the proton channel, we can have the sodium ion channel, we can have the potassium ion channel. Similarly, for the first time we are knowing that, for the typical inorganic anions the chloride ion, we can have also the channels, which occur basically in all cell types, in plants in animals in bacteria and everywhere. And basically, it can permit the transmembrane movement, you have the membrane which is the barrier and you have to cross that barrier otherwise you will not have the corresponding differences in the concentrations.

Because we are talking about that you have a highly concentrated one part and you have the low concentration in the other part. So, if you go for that particular movement and sometime it can so happen that you can have the transfer also from the lower end to the higher end against the corresponding natural process the osmotic pressure or osmotic flow. So, along their concentration gradient so rightly we can think of highly considered area and too low concentration area you can move, but otherwise the reverse can be true, if your motor or if you're that particular channel and the pump.

We know that proton pump similarly if we can have a typical pump for chloride ions also, so we can deliver so we can lift like water from lower to the upper part that means low concentration to the high concentration region also. So, CIC channels is basically the chloride ion channels so is a huge group of channels is a huge thing is there. So, we are not going to cover all these things but only you know what are the CIC channels.

It is basically a large family of chloride channels. Because depending upon its working thing or depending upon its working percent potential, you can have many sub channels. They are basically giving us idea that you can have those channels for the transfer of chloride ions in all forms of life.

(Refer Slide Time: 09:52)



So, basically what do we get? Earlier we have learned about the sodium and the potassium ion, that you can have the corresponding cationic channel, similarly, you can have the anionic channel. So, how these anionic channels can be developed, which basically allow the movement of the chloride, that the channel itself tells that you have the channel, that means, you have the passage. And you have the plasma membrane of cells, so plasma is enclosed. So, those cells basically either it is getting chloride ion or it will be losing some amount of chloride ion concentration.

So, we call them, as you have the transport proteins, which are taking care of these ions are faced with an relatively modest challenge of selecting chloride ions because they are charged. So, if it is control by only the potential, the charge and the charge neutralization. Suppose some positively charged species is responsible for trapping the chloride ion like your sodium ion. So, if you have the sodium ion, as well as potassium ion, you do not know, if you are asked to crystallize the sodium chloride as well as the potassium chloride you should know the corresponding ionic product and the solubility of the individual salts.

Similarly, some selectivity whether we can develop that such that it can discriminate this anon with respect to the other anion. Because the phosphate we know that charge is more size is big sulfate also your charge is more size is also big, and the bicarbonate also the charge is less, but the overall charge is a very big one HCO3 minus is a big one, but chloride is only single ionic species, one atom is there, one analysis there is a Cl minus and we know the charge relative to that of your corresponding Cl minus ionic radius.

And if you have some ionic proteins. Because sometimes we can go for the transfer or the transport of those ionic proteins also which are anionic in charge. So, all these things, very small molecule to the big molecule you must have some selectivity for that particular process. So, what is the difference? We know already, that you have the cation channels the potassium ion channels, and which goes for the selective moment or the gating moment, and which is basically mediated by to things where we can have the separate structural elements. We know that we can have innoforce.

An innoforce we have seen that they are basically crown ethers type of thing. So, those crow ethers type of thing can bind your sodium ion or the potassium ions, so you can have some structural unit, which can take care of these sodium ion or the potassium ion. But what about the CIC chloride ion channels? The selectivity and gating seems to be intimately related. So, if one is affected the other will definitely be affected. So, the selection of the ion from a pool of other anions is also responsible for the gating process whether you have a voltage-gated process or a ligand-gated process for your movement of the chloride ion.

So, in the muscle basically. The vertebrate skeletal muscle CIC Cl-minus channels stabilize the resting potential and regulate the electrical excitability, that means, the corresponding electrical pulse the signal a signal in the form of electrical pulse we can generate from our muscle movement or muscle contraction or muscle relaxation, so the movement of chloride things can be there even for your muscle contraction and relaxation.

(Refer Slide Time: 13:26)



So, when you have huge amount of all these things, we know, that we go for urination and we remove all these chlorides from our body the excess amount of these things during our

metabolic process. So, we call as a huge subject has been developed also the metabolomics. So, metabolomics will tell you that in kidney again another vital organ in our body, which can function basically through the transepithelial fluid and electrolyte transport.

So, whatever amount of that particular chloride we want to discard from our body which is not necessary, which is not required and is basically going from the downstream when you take intake in our food, the food material it should be discarded from your body. So, it can flow through then again, these chloride channels including one important receptor, we call it, we only know about that what is GABA, GABA A receptor.

So, the GABA A receptor is there and can be transported by these are the abbreviated names also such that people can understand and know that it is only attached to the chloride transportation is KCC2 to and NKCC2 so N is attached to that transporter only, so it is one type of that particular thing.

So, GABA is nothing but gamma aminobutyric acid. So, A type of that transporter is an ionotropic receptor is not ionophoric or ionophor is ionotropic, and is a ligand-gated ion channel. That means, it is not a voltage-gated one. So, the presence of GABA is important. So, when GABA is present it can take care of the chloride thing, that means, it is gamma aminobutyric acid, so that butyric acid can so some function or some relationships.

So, what is there? So, you have the corresponding ligand so endogenous ligand will come and that endogenous ligand is your GABA, the gamma aminobutyric acid, which is nothing but a major inhibitory neurotransmitter in the central nervous system. So, we are basically correlating these things very important functions.

We know that CNS the Central Nervous System for us is important, and the corresponding muscle movement and all these. And we know that the corresponding knowledge for your different availability of the neurotransmitter. So, if neurotransmitter is available so neurotransmitter giving signals, so the GABA basically can inhibit the function of those neurotransmitters, and that can also affect the corresponding passage or the movement of the chloride ions in our body.

So, it is basically nothing, but what we know is a very simplified form or the simplified understanding is that you have the opening up of the thing and the closing of the thing. So, GABA A receptor, A is your superscript. So, GABA A receptor is selectively permeable to Cl-minus and to a lesser extent to HCO3 minus that is why it basically go for the discrimination that it can selectively choose Cl-minus to pass and the bicarbonate anion to block. So that is the important thing, why we need GABA?

(Refer Slide Time: 16:31)



So, the structure of this Cl-minus selectivity filter. We all know, why we use the filter paper, what is called filter, because you have to block something and you have to allow something to pass, that is the corresponding gating function also. What is gate therefore? The gate for your Cl-minus ion is the same thing that you will filter it out, but is a different fashion not that your filter is there, ports are there and some ions will pass and some will be blocked.

It is not that you cannot have the corresponding filtration where you use the filter paper and chloride will be filtered out and your bicarbonate will be blocked it is not that, because the mechanism that filtration is basically depending upon the size of the molecule, size of the neutral species or size of the cation or the size of the anime if it is aligned some passage like that of your ion selective electrodes.

So, it is basically filtering the CLC-Kas as determined by the cryo-electron microscopy. So, how do you determine it? So, one particular substrate or material people identified it, they have published in some paper, that material has been written in the book that is why what book we are following the latest information of all these things. But what instrument they have used basically is a very sophisticated one. So, it is the cryotemperature that means liquid nitrogen temperature or liquid helium temperature, so cryo-electron microscopy gives as the figure or the picture.

So, you have one diagonal arrow, the corresponding arrow for the arrow giving pointing towards the extracellular thing. That means, the moment of the chloride basically, the movement is basically taking place from there, and that movement is basically going from that particular part. This you can have the extracellular thing, that means, how we can passage. So, if you have the, you are blocking this particular part, so you would know about the corresponding protein chain or the peptide chains and the corresponding amino acid residues.

Because the pendant part of these amino acids say B16 is the valine or the tyrosine. So, these amino acid residues basically can allow the movement basically, so the amino acid residues you see the way it is placed over there, so is basically the head of these, head of this and head in the lower side.

So, these three basically when we are talking about these basically so is valine166, tyrosine 520 and serine 121. So, serine residues is all you should know is a hydroxyl function, alcohol type of function, the phenol type of function and the corresponding valine type of function is there. So, these functions are basically properly oriented within that particular channel. So, not only you should know about the structure, the cartoon diagram of the corresponding polypeptide chain, but also the relative orientations of these three amino acid residues. So, they have sown also in the ball-stick degree presentation, and basically that basically showing where you have the arrow, so that is why the passage is there, so which is basically indicating by your gray arrows.

(Refer Slide Time: 19:40)



So, how we therefore have the corresponding CLC the chloride ion transporter. So, the chloride ion transporter is like this, so you have the shortened thing of this passage. So, you have the corresponding external chloride ion or the central chloride ion in S E S and S external. So, you have the extracellular side on the top and the cytosolic side on the lower part. So, arrow movement will tell you from left to right you go there. So, we see that you have the passage, so is the passage of the chloride ions, so greens are all your chloride. So, basically when E is out that means E is there, so you look at the E the positioning of the E, one of the amino acid residues that once is basically pushing.

So, when it is covering and the pushing of the ion to pass through that particular channel. So, one is basically coming out so, that one is basically coming out, and there is some pump is also there which is also controlling that particular serine residue, so that OH so the channel bump is important. Because once it is there, so bump is there, so only one of the thing that means, one is passing out, but one is still within the above that particular bump.

So, what do you see now that you can have the corresponding entry of the proton, so the proton is then entered and proton will come to that particular corresponding acid end of the corresponding amino acid residue, and basically it can go for the neutralization of that particular part. So, if you have this particular part, so, the protonation of that particular point, the serine residue is still there, will allow the movement of the second chloride ion, so your second chloride ion will move.

So, basically it is passage. So, it is one way movement so it is not a catalytic cycle or catalytic loop, the loop is basically for your cycle, where you have moved that thing then again, new chloride ions will come from the top again and the cycle will be repeated through that particular passage.

So, it is basically is going for the swinging motion, and we can have the corresponding glutamate gate and glutamate gate color code everything is written over there, so you read it nicely and understand it nicely what I have explained just now, because these languages are for your knowledge sake only such that you can preserve it and read n times until and unless you understand it nicely. So, it is basically the gray dashed area so the binding site is still there, so you will basically reaching so this is the gray binding side and so the gray binding side is located for your chloride ions to catch over there.

(Refer Slide Time: 22:07)



So, cystic fibrosis is a transmembrane conduction regulator, which is a complicated one, but you read a little bit about that which is dependent on your chloride channel, and is responsible for transepithelial salt and fluid transport. So, it is very complex one but is there. But there are people then even for the newborn babies also you can have the genetic defect, which can cause a CFTR hypo-functioning that means lower functioning not hyperfunctioning, it is a hypo-functioning lead to cystic fibrosis is a diseased condition.

Sometimes a newborn baby out of 2500 or so, one died. The most common lethal genetic disease. So, how you can correlate a disease a genetic disease even to that of your malfunctioning or the hypo-functioning of a particular regulator, which is dependent on your chloride channel. If we have also the intestinal colonization of the microorganisms, the pathogenic, which are harmful for us for hyper functioning of CFTR.

So, these two conditions have been demonstrated over here one is hypo and another is hyper function of the all these things which provokes the secretary diarrhea is the leading cause of mortality in early childhood. So, another disease can also be identified, which has some relationship with CFTR and which has some relationship with your chloride ions.

(Refer Slide Time: 23:32)



So, the next part we will just talk about, quickly about the iodine, because the iodine is the most simplest one, and we also know very much about why we take the iodized salt in our food. So, it is basically extensively utilized by the marine organisms because as we have discussed the corresponding Source of the chloride concentration in seawater, similarly, you should also know about the amount what you can have as your source from again the seawater. Because I iodine always we know, compared to your potassium iodide like your potassium chloride is a costly salt.

So, the algae basically so brown algal kelp, some part algal kelp species are there and which are most efficient iodine accumulator. So, there have specified mechanism where the bigger iodide ion it can accumulate or some time the free iodine also can be stored, because the reactivity of free iodine because the i2 has a solid brown, black brown solid we know it has some different property compared to all other halogens.

So, among all living systems is basically it can accumulate and with an average content of point 1 percent of dry weight, representing 30,000-fold accumulation of the element from the seawater, so it has a huge capacity to trap that particular iodine. So, if we can see or if we can find out that particular algae, you can have a good amount of iodine what you can accumulate from the seawater.

So, basically what you find that it is not deposited at the free iodine so we are not getting that particular thing, but you have to control. You have to know some geochemistry you have to know some biogeochemistry because these two things are coming into the picture together. Once you know that the salt water, the sea salt water basically you can have the

corresponding iodine or the iodide ion and the corresponding algae are taking care of all these things and but it is basically accumulating somewhere some sea nodules we can find and those noodles if we can take out, we can have a plenty of this particular source.

So, what do we get therefore that is a required component for your corresponding thyroid hormone. So, how we can correlate, why you take the iodized salt because we have to go for or produce for your corresponding thyroid hormone. What is that thyroid hormone? So, it is basically a phenyl ring which is iodized. So, iodide derivative or iodine derivative of that particular one for the biosynthesis of thyroid hormone basically. And two types of thyroid hormones are required one is T4 that mean four positions our T3 is three positions are iodized based on that hormone thyronine. So, triiodo species and tetraiodo species that is why 3, 3 prime 5, 5 prime and another is 3, 3.5 triiodo species with us.

(Refer Slide Time: 26:27)



So, you see, you try to know about the corresponding structure of these, what is T3, and what is T4 and what is DT and MIT? And looking at the structure immediately you can see that these are something, some other products, but related to T3 and T4. So, how it can be related to one of the very well-known amino acid tyrosine. So, thyroxin hormone is related to the tyrosine residue because if you know, if you see, that this particular part if you protonate it this is your corresponding tyrosine the corresponding amino acid.

So, the tyrosine amino acid basically when you can have the further phenyl ring and you can have two other positions that is why the two ortho positions with respect to the O or OH you have all the iodized positions. So, the DT and MIT is our diiodotyrosine residue and monoiodotyrosine residue. So, when you have the corresponding full form of the hormone you do not have that thing, but if you have get this particular part before that iodination, you have the corresponding tyrosine which is your Tyr. So, the tyrosine is your amine acid residue. So, even for that particular process is not the corresponding form that means another phenyl ring will come, the actual hormone you are getting, but you can go for the corresponding iodination.

(Refer Slide Time: 27:52)



So, you have the first generated in the thyroid and then circulated throughout the body to regulate many metabolic processes, very important metabolic process is basically control. So, basal rate of metabolism how we go for the metabolism, temperature regulation of your body and expression of numerous other proteins, in the protein synthesis it is dependent. So, this iodide is transported and concentrated in the thyroid gland, we have the thyroid gland here and here attaining a level of iodine within the cell 40-fold greater which is found in your plasma.

So, you have to have the corresponding accumulation of these iodide ions, that is why we have the shortage of iodine from our food material that is why you take through your sodium chloride, iodized salt of the sodium chloride we take that is your iodized salt, and then it basically going for the bound to the tyrosine residue of that thyroglobulin.

So, thyroid hormone and the globulin is a protein we know that globin protein like hemoglobin says the globulin in protein one form of protein as mono and di-iodinated in a tyrosyl residues in reactions, which are catalyzed by thyroid peroxidase, which then serve as the intermediate. So, these monoiodospecies and the diiodospecies is basically the intermediate that means what we have shown just now that means the two side products are forming always they are basically required for the final production of your T3 and T4.

(Refer Slide Time: 29:19)



And the proximal diiodotyrosine residue form an iodothyroninyl residue product catalyzed by the same thyroid peroxide is responsible for the preceding iodination reaction. So, basically, what do you get? We have many types of these iodination reaction. So, 7 of them MIT and 6 of them DIT are there, and one T4 are formed in that particular that thyroglobulin molecule.

And some are therefore can contain T3, so T3 and T4 and sometimes we not only know about the amount of T3 and T4 but also you should know about the corresponding ratio. So, what is that ratio? Because the hydrolysis can take place, and to release the corresponding T3, T4 into the plasma is also required for the proper functioning of your thyroid cells.

(Refer Slide Time: 30:09)



So, in conclusion, what we have seen now that your chloride channels may conduct many different ions, can take care but are named for chloride because its concentration in vivo is much higher than other anions. So, if your concentration is higher, so, it will only be transported nicely through proper selectivity.

And the deiodination part, the reverse part. The deiodination of T4 to keep primarily active T3 process via selenium deiodinase is also. Already we have studied selenium so that selenium bearing deiodinase enzymes are also available, which can selectively remove the iodine, not only the ordination, but deiodination is also important for our life. So, chloride channel and the iodine in biology you read it from the Wikipedia page and the book. Thank you very much for your kind attention.