Circular Dichroism and Mossbauer Spectroscopy for Chemists
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Lecture - 14
Chirality and biology - IV

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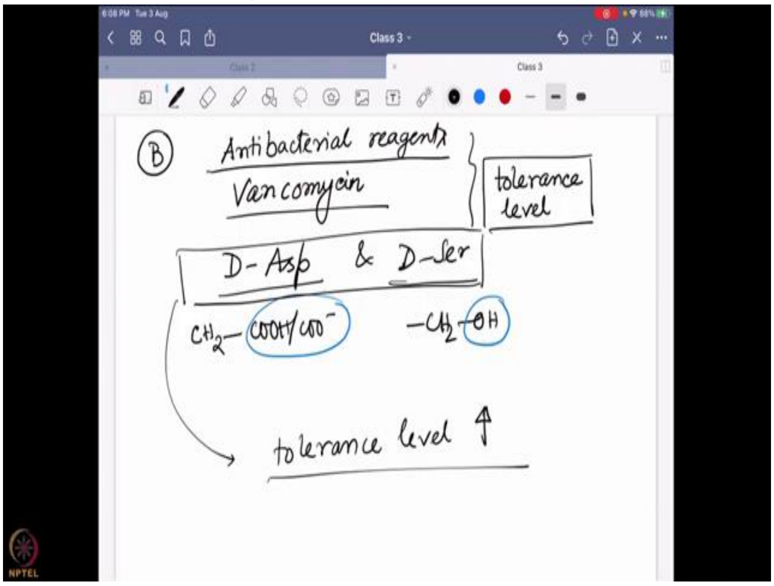

The second example come into this picture it is not only the protease sometimes, some of the organic molecules can also directly bind to this bacteria cell wall or their vulnerable parts and break it down So, they are also known as antibacterial reagents and from the time of Alexander Fleming we actually started producing a huge number of them and one of them which I am more interested to discuss here today is known as vancomycin.

Those who are very much interested in the organic chemistry can go back and look into the structure of vancomycin, I am not going into there. So, the important thing was that this vancomycin was a very strong antibacterial reagent and most of the bacteria are actually failing to it. In the terms of bacteria pharmacology itself the tolerance level. The tolerance level was so important over there that even with a very small amount of this vancomycin.

The bacteria were dying and then they figured it out that the bacteria are not willing to let the fight go. They are trying to give a fight such a way that they can still survive in the presence of this strong antibacterial disease and during a study what some of the researchers found that this started changing some of the amino acids, especially D aspartate or aspartic acid and D serine these two amino acids they actually started changing.

So, you can remember the aspartic acid, it is actually having CH_2, COOH or COO minus group present over there and serine is CH_2, OH group. So, you can easily see they are actually having some polar groups present over there which is obviously going to play a huge role during the molecular recognition of this vancomycin to the particular position of the cell wall.

And what bacteria are doing? They are actually changing it to the L to D amino acid and as they are changing to L to D amino acid they are changing the overall three dimensional orientation of the molecule with respect to the vancomycin. So, the vancomycin still comes and it knows like which of the distances or which of the bonds I have to interconnect with they cannot find all the groups in the proper position and once it cannot find all the groups in the proper position.

It cannot affect the antibacterial reactivity and by that it is antibacterial reactivity actually goes down and that is has been found that this tolerance level. Tolerance level means if your tolerance level is high that means you can survive even with a high concentration of active bacterial reagent and it is found that once the bacteria has evolved with this D amino acids that tolerance level actually goes up.

So that is one of the very unique finding from this particular system that the tolerance level actually goes up over there. So that is two different ways, one is the protease, one is organic molecule and both of them can wreck habok on the bacterial cell wall and kill them but the bacteria are fighting back by L to D amino acid orientation change. So that is how it has been done and that is showing that one of the important part like how important it is to have the particular amino acid as a D or R state.

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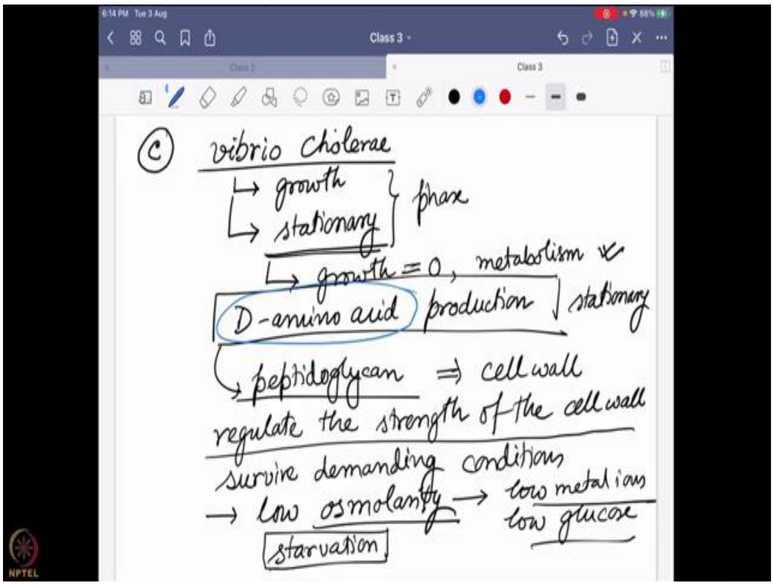

Now, coming the third example and this particular name you most of you probably heard vibrio cholerae. So, this is actually the bacteria which actually triggers the cholerae among us so, this is the bacteria and this bacteria has two different phases. In one phase it is actually the growth of these bacteria happens so, they have two different phases growth phase. So, where the bacteria multiplies in numbers and just spread around.

But that is actually a very short span of their lifetime most of their lifetime if you try to take a look into we found they actually remain in a phase called stationary phase so, these are the two phases of their life. What is the stationary phase? Stationary phase is that where the growth is stopped growth is basically close to 0 but the metabolism in the system is on that means the system is live but it is not actually growing.

So, in this phase it is very important because in this particular condition they are very vulnerable. Because they are not increasing a lot so that means if I give a drug and try to kill them, if I kill it over here because they are not increasing, I can kill it and over there it is very interestingly found as vibrio cholerae and just probably a little bit scary that they started producing a lot of D amino acid in this stationary state.

Generally, they do not produce a huge amount of D amino acid in the growth phase but in the stationary phase they started producing a huge amount of D amino acid. Why it is important? Because this D amino acid again goes to this peptidoglycan which is again the forms that bacterial cell wall and over there it actually helps it to regulate the strength of that cell wall. So, if you put a D amino acid instead of L so, there is a change in the overall arrangement and that actually strengthens the overall cell wall for this particular vibrio cholerae system.

So that has been formed and it has been found that when the vibrio cholerae has having a good amount of D amino acid present over there they can survive demanding condition. So, what is the demanding conditions we are talking about or we are interested in the demanding conditions we are more interested over here is called low osmolarity. So, what is osmolarity? Osmolarity does not generally means that when you have a particular ion or a molecule present in a solution.

So, it is kind of an idea or a parameter that actually gives you an idea how much concentration it is actually present. okay So, it is somehow connected to this molality, molarity all those things. So, take a look into what is osmolarity, it is actually a biological term but it is derived from a physical chemistry point of view. So, in very Layman's term the low osmolarity means that you have very low amount of metal ions that means a very low amount of glucose and both the things are very important glucose metal ions.

Because they are the metabolite by which a living system can survive and what has been found that this bacteria when they actually goes to kind of you can say in a stationary phase where it is not growing, just munching up whatever it is available around it. So, for that they actually change it to D amino acids so that they can even survive at a much lower availability of the metabolites.

So, their survival instinct is actually kicks in and they can survive this particular kind of I would say this starvation period. Even at a very low food for them the metal ants and glucose at the food for them they can survive and one of the factor that is actually affecting it one of the critical factor is the presence of this D amino acid because through this D amino acid one they actually controls the cell wall strength and will come into little bit later.

How it can also controls the pickup of the different meta lines and glucose from the surrounding solution? okay So that is how the bacteria try to exchange themselves and that is how it survives with the presence of D amino acid.

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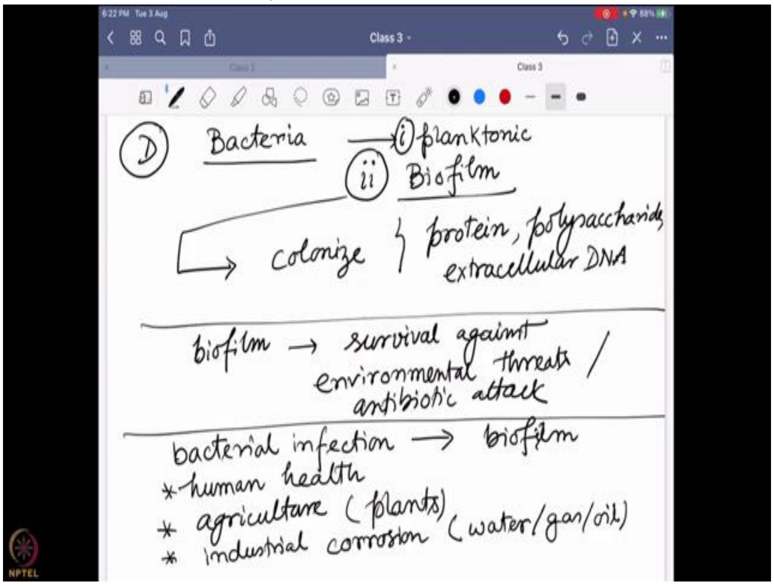

Now, we go to the next example, example D fourth example. So, we are talking about bacteria so we will continue that do not worry that is the last time we are talking about bacteria. It is not a biology class we will come back to chemistry very soon but some fun facts about bacteria. So, when we talk about bacteria as bacteria not only can have two different phases that is the growth phase and stationary phase but it can also have two different lifestyle that you can survive.

One of them you already probably learned this term called planktonic, you all heard about that like what is planktonic? So, you have all heard about plankton they are like very small amount of bacterial especially the blue, green algae that is surviving on the surface of the water and produce the huge amount of oxygen through photosynthesis. So, most of the oxygen coming to the earth or most of the carbon dioxide that is getting bound in the glucose is actually done by this planktons and mostly which is known as the phytoplanktons.

If it is doing this kind of photosynthesis and zooplanktons if it is having more of like a animal kind of behaviour. Anyways, so plankton behaviour mostly is that they are surviving in very small families. So, like not more than a few number of bacterial cells are sticking together, so that is called the planktonic. So, what is the advantage of that? That means they can move around very easily.

However, the problem is in this particular lifestyle that you are much vulnerable anything can come and kill you because there is no other thing present around you to save you. So, all of you probably heard the story that you stick together to fight together and that is what exactly also the case for biology and bacteria they follow up another system which is known as the biofilm. What is biofilm? No nothing to connect it with the bollywood movies.

Biofilm is that they actually colonize they colonize in such a way that it creates a layer of bacteria around them and that is comes like a film structure and that is known as the biofilm. And what is the major ingredient of this bio film formation? Again, the common ones that you can expect protein the polysaccharide that means, the carbohydrates basically and even something called extracellular DNA.

That means the DNA that can be surviving outside the cellular system and all these three things and some other molecules also come together and create this film which actually gives an extra protective layer outside the cell wall for the survival of the bacterial and this is very crucial this bacterial biofilm. Because that actually very important for the survival of the bacterial against what it is called environmental threats or antibiotic attack.

So that is what the biofilm is very important about. So, this biofilm is also very critical for our day to day life. Why? Because when we are talking about any bacterial infection because this is a season when we have some sore throat and all those things and we generally say oh you have a bacterial infection. So, if we look back and find out what is actually happening in our throat, we will find it is nothing but we created a biofilm over there and that biofilm is creating issues over there.

So, most of the bacterial infection that we face it is actually inflicted by these biofilms so that is why the biofilms are not a good thing. It is good thing for the survival of the batteries but not good thing for the host like us. So, human health care is going to take a huge hit for that. This biofilms are also very bad for agriculture because the plants when they are getting affected by this kind of biofilms that is affecting their metabolism that is affecting their growth and that has a direct effect on the produce of the agriculture.

Because we are giving so much of different substituents for a good growth of plants and this bacteria is actually hitting them up through these biofilms. So that is why it is not very good with respect to that so that is why it is not very good to have this kind of thing is happening there. So, again coming back to this bio flame the bacterial infection is infected by that the human health is getting affected.

The agriculture where the plants are actually getting affected for this and our agricultural produce get a hit and not only that even in industrial scale industrial corrosion can also happen through this biofilm. So, these bacteria can survive in water, gas or oil pipes. So, water gas is fine because that actually provides a very nice niche for it to survive and gas and oil generally their hydrocarbons on which they can chew upon because they reduce source of carbon for them instead of glucose.

So, they can eat on those things and when they start eating on those things they started to colonize and when they start colonized they form these biofilms which actually corrodes the pipes and that actually creates a lot of leakage around it. So that is why biofilms are not very good. So, so far we are talking about that how the D amino acids are actually improvising and strengthening the overall cellular structure? Over here the example.

Is that biofilm is bad and we can use D amino acid cocktail to degrade the biofilm and destabilize the biofilm and people have found that if you use particular cocktail.

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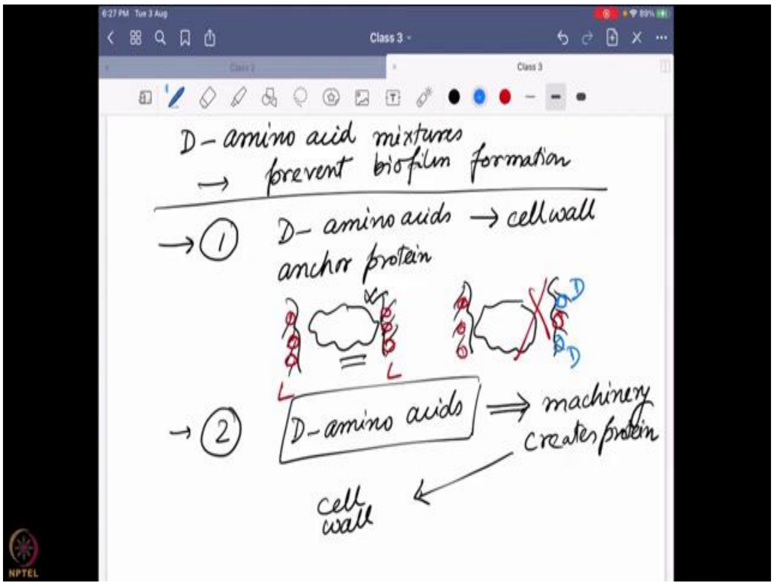

That means D amino acid mixtures and depending on which particular bacteria you are talking about you need different amino acid mixture they can actually prevent this kind of biofilm formation and there is a huge controversy actually how it actually happens? Because okay I give a D amino acid and magic. It stops the biofilm formation but as a chemist it comes to our mind like okay it works but how?

And that how it actually has two different answers so I will give you one by one. First answer was this D amino acids actually goes through the system and forms as an integral part of the biofilm whatever the biofilm is there so, it tried to form that thing. So, it is going to sorry So, it should not say biofilm, I should say cell wall. So, it start to form this cell wall on the outside and then the two different cells from two different bacterial is going to combine together and for that they need something called anchor protein which is going to bind two different cell walls from two sides.

Now, what happens once you have an L amino acid over here that is binding fine. So, these are all L amino acids but at the same time if you able to inflict a few more D amino acid over there then what happens? So, again the same cell wall we have a lot of L amino acid and then say I have a few of the D amino acids and as it becomes a D amino acid this anchor protein this anchor protein cannot come and bind pretty well. Why? Because over here look into that this is another protein this is cell while interacting with a glycoprotein structure.

So, they need some molecular recognition over here and because you change some of the L to D amino acid now, it cannot recognize it properly and that is why this anchoring part does not work very well and unless you put the anchoring this anchor putting is kind of like the adhesive which actually binds everything together. It is not working properly and that actually shuts down the biofilm formation that is explanation number one.

The second one is actually almost having the similar idea so that this D amino acid are actually playing a role over there but the D amino acid how they are coming into their that is actually debated. So, they said the D amino acids when they put there they actually even affect the machinery which actually creates protein and by that it actually affects the overall structure of the cell wall and then the same story follows that anchoring protein does not work.

Yes Rajdeep, you have a question. Sir, uh just for my question? Sir are you sharing the screen? Because I cannot see anything sharing. Okay Is it true for everyone? No Sir, your screen is visible. okay So, Rajdeep if you can please uh log out and log in back again that probably. okay okay thank you. Yeah. okay So, this is how it is actually working over here that how the D amino acid getting incorporated. So, there are two different ways it can possible.
One is that the D amino acid directly go and bind to the system and the other system is the amino acid affects the machinery, machinery means the ribosomes they are affecting and affecting the how the different proteins are actually formed and that is how it is affected. But anyways whatever the matter is what we found that if you have some D amino acid present over here the blue ones.

It is going to hamper the overall interaction and that is how the biofilm formation can be stopped. So, D amino acid is not always bad. It is not always harming us but if you can use it smartly you can even prevent the biofilms and attack back on the bacterias.

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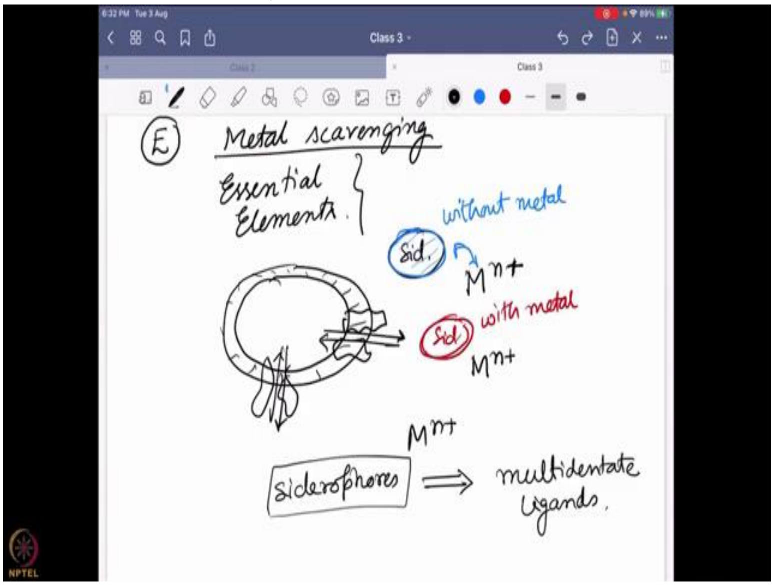

So, again our ODC on this particular bacterial lifestyle will continue with this particular example this is the last example we are discussing about. It is about metals say okay we come back to this inorganic slowly so, metal scavenging. So, as you all know every living entity requires metal for function in the binary organic chemistry you have probably learned that each and every metal have their own role to play and there are certain elements which are very critical for our survival which are known as the essential elements they are very critical.

Now, bacteria also survive on that now when a bacteria actually requires some essential elements to be cobbled upon how it actually does so, it does in this following way. So, I am just drawing a very simple cartoon. So, say this is your bacteria inside and this is the cell wall and this cell wall is not totally dead. They have some proteins present here and there which actually act as the gateway for controlling system going back and forth. Okay

So, those kind of systems are present. So, through that protons, metal ions all those things go back and forth. Now, what happens the bacteria say does not have a lot of metal lines to play with in the beginning? So, it has to get it somewhere now bacteria are not human beings that I can take a iron supplement and get my iron. So, biology has to fight for that where it fights? So, in a bacteria in a system when it is surviving outside there is water or environment and there present a huge amount of say metal lines.

So, they have to grab that metal and and bring it inside. Now, it cannot directly always take the metal end on Is it possible? It is possible for like sodium, potassium this kind of ions because they are so, huge in amount present outside that it can just get it through simple even osmosis system. However, if you try to find a faster transition element it is not that straightforward because of two reason first the concentration is low, second there may be different metal is present.

For example, iron is present, cobalt is present, nickel is present and say you will be required at that moment only iron but not nickel or cobalt so, you have to differentiate it so, how I can differentiate? So, for that biology come out with a very unique idea known as siderophores force. So, what is siderophores? Siderophores is nothing but multidentate ligands. So, what biology does the bacteria does they kick out this kind of siderophores outside and this siderophores it is very similar you can say as an edta.

Once it sees a metal and it just grabs it because it is a multi-dented ligand so, it is entropically favourable for it to bind this metal ions. So, once it binds it, it changes a little bit the overall property of the ligand obviously ligand without metal with the metal the properties will be different and this bacterial at that time cobbles that siderophores with the metal inside it. So, first it sends the siderophores without any metal.

So, I am putting it say in blue so, siderophores without metal and once it interacts and bind with that metal, it creates siderophores with metal this red one. So, this is with metal and this is without metal and then it gobbles it up and that is how the biology survives. Now, the problem is that biology, the biology bacteria is not the only player over there. So, there are some other bacterial are also present there who also try to get this siderophores out.

It is kind of like a parasitic parasitic environment over there. So, they are just waiting someone giving their siderophores outside and grabbing the metals and they are patiently waiting. Once it binds the metal they just grab the siderophores bound with the metal. So, there is like a real dog fight going on over there for the metal ions. So, if a biology has to survive they have to work in such a way that they can actually not only get the metal but they can also take the metal without notifying the other living systems around it.

Even the plants sometimes also use siderophores to grate the nutrients so, it has to fight with a lot of things. So that is how the siderophores are important and it is very much important for the life. So, over here D amino acid can have a huge role to play and for that I am going to give you an example how it is going to happen?

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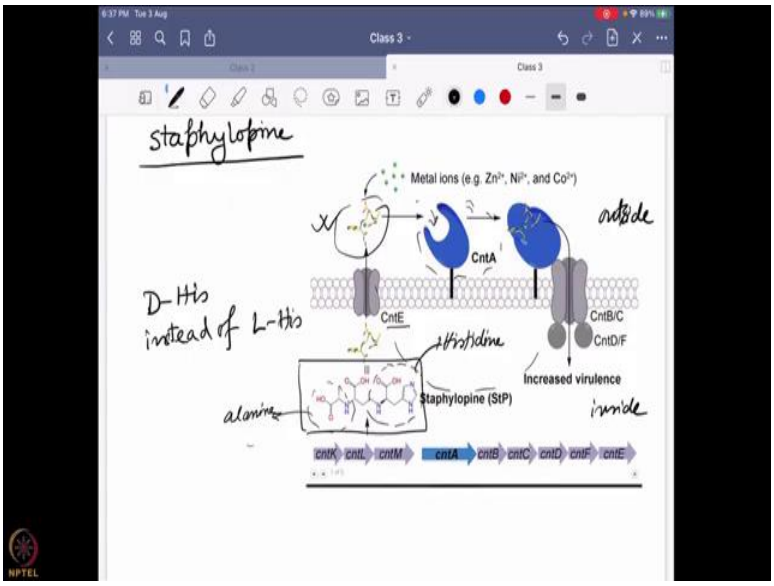

So, over there I am going to show you an example of a particular siderophores known as staphylopine. What is a staphylopine? Staphylopine let me show you if I can have the picture. So, this is staphylopine this molecule present over here so, you can see to it. It is actually a multitude of ligand with a lot of carboxylic acid groups and all those things present and if I ask you what are those things actually you can see it is actually derived by amino acids for example this portion over here.

This is derived from histidine this amino acid over here you can see it is derived from alanine so, this kind of staphylopine which is actually nothing but a siderophores which is made out of amino acid resistance. So, what some of the bacterial does and over here I am showing you the kind of the lifestyle of it. So, it is actually created inside the system it is inside and this is outside and it created, it is created inside the cell and through this particular gateway which is known as CntA do not worry about the name.

So, through this it actually leaves outside and over there you can see once it gets outside the metallic comes and binds. It combines different metals zinc, nickel, cobalt and once it binds to it then it can get recognized by this binding pocket of CntA and then it actually comes inside the cell and inside the cell when it comes the metal ions get released and this particular siderophores can get recycled back back to the outside to grab metal.

Now, how the D amino acid is playing a role? So, over there you can see this system is made out of two amino acid alanine and histidine. Some of the bacterial what they do, during the formation of this staphylopine inside their cell they use D histidine instead of L and how it is going to help it? Because when it release, the D histidine system it binds to the metal and up to that part is fine but then this recognition part recognition of this metal bound staphylopine.

It is very much dependent on this overall structure now, if you change from L to D it is not recognized by the other bacterial or the other place present and this bacteria which is smart enough to change it only it has the molecular recognition system which can detect even the D histidine bound better lines and by that it swiftly smuggles the metal ions by putting the other bacterial or other competitors out of the rest.

And that is how the bacteria are using this D amino acid, L amino acid mixture very specifically to play out different orientations and that is how it controls the metal ion scavenging and surviving in very demanding conditions. So, these are the five examples we have gone through today. So, I hope that you probably recognize that how important the D amino acid is and that is mostly coming from the molecular recognition part.

It is not only helping it to fight against the protease. It helps it to fight against the antibacterial reagents sometimes, it also helps it to form a very strong cell wall to survive especially in the which is called the stationary phase of the of the bacterial line and we also found that it is not only the bacteria are using it. It is also the human beings also learn and use it against the bacterial by disrupting the biofilms.

Because biofilm formation is very much dependent on which amino acids are you are using and if you use particular cocktail of D amino acids that you can actually degrade the particular biofilms. And also, we learned how the metal scavenging can be also controlled by this important use of D amino acid. So, later today I will share a paper with you where you can look into and find out how the different roles of the D amino acids have been revealed by the scientists all over the year and how many different interesting roles it actually plays.