**Inorganic Chemistry of Life Principles & Properties**
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**Lecture - 52**
**Inorganics in medicine - Titanium in biomedical**

Welcome you all to the next class on Inorganic Chemistry of Life Principles and Perspectives. In a previous class we have been looking at several therapeutic approaches particularly those based on let us say anti-cancer. For example, we have looked at the details of apoptosis, we also have looked at the microscopy pictures confocal microscopy pictures etcetera, when the drug is loaded and when the cells die all these kinds of things we have looked at. Followed by that we also looked at the photo dynamic therapy, where you have a molecule which is a nothing but a photosensitizer and the photosensitizer leading to the activation of the oxygen to singlet oxygen other hydroxy based radicals or oxo based radicals or reactive oxygen based radicals, which in turn choose away the tissue.

So, this is all we have looked at and let us in this class, let us look at some more items of this photodynamic we have looked at then MRI also we have looked at MRI contrasting agents etcetera.

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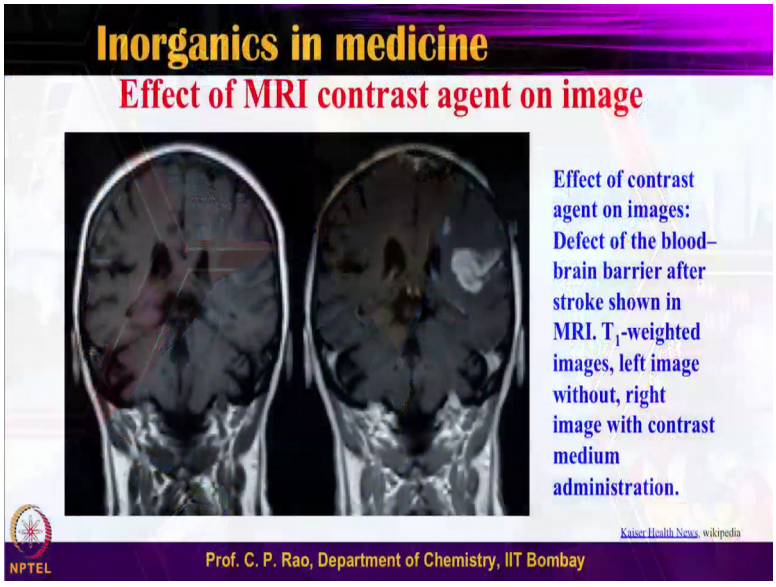


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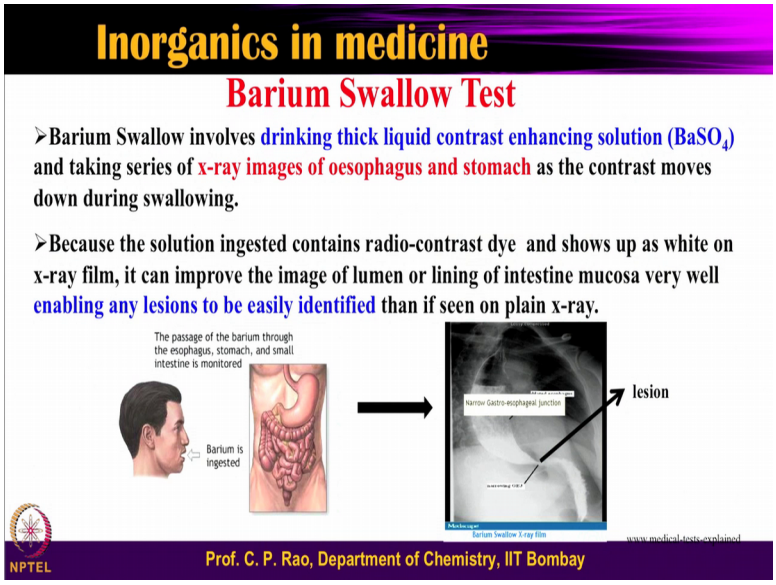


Now let us look at some kind of a implant kind of things.

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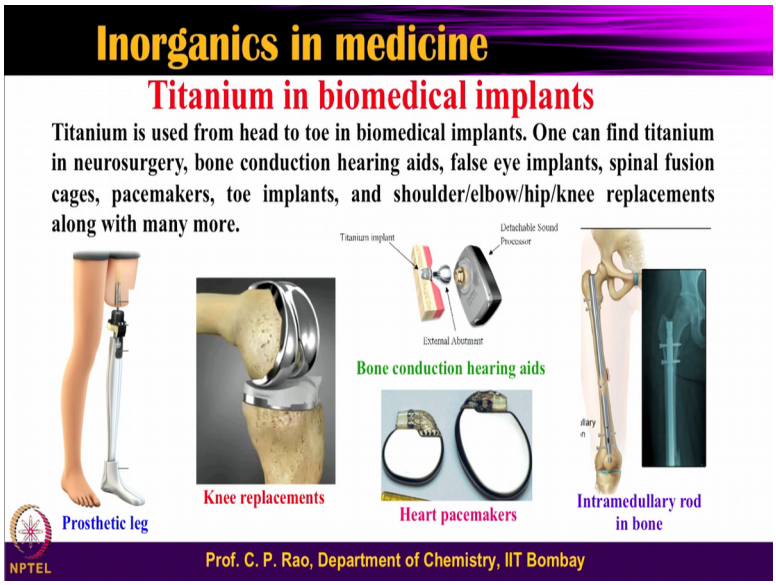


See for example, everyone I am sure knows that the titanium is used as implants everywhere in the body from toe to head everywhere. So, this is used for the bones you know very well, it is also used for the hearing aids, it is used in the eye implants, it is used in the of course, spinal, it is used in the a kind of a joints knee joints etcetera neurosurgery.

So, almost every aspect every facet of human life there is a role of implants and even in the pay pacemakers. So, pacemakers which are used to support the heart beats in this ok.

Here is a slide where it shows a lot of examples of this for example, the one which you are seeing here is the prosthetic leg, where they use the titanium rods to put into this, and here is a knee joints and knee joint can be replaced by these titanium, you know a material things.

So, one can do knee replacement this has become most common thing today among a large number of patients in various countries its nothing to do with one particular country or the other. Hearing aids of these and the pacemakers and also intramedullary rod in bone. So, everywhere the titanium based materials titanium rods, titanium chip, calves all these things are put into the into the human organ implant system. So, therefore, this is quite well acceptable by the tissue. So, therefore, that has been used.

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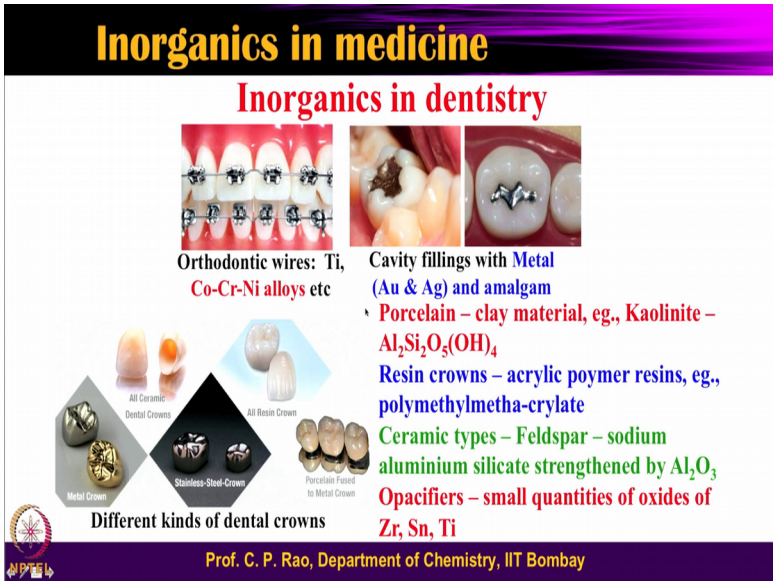


Now, let us look at another example where inorganic compounds inorganic metals inorganic items play a great or important role. So, when coming to the dental treatment, we know very well people use the wires to control the growth, to control the protrusion of their teeth and you know that that kind of thing. So, these wise people use caps for this for the teeths. So, these are also made of the metal.

So, the metals like titanium, they are mostly of alloys cobalt, chromium, nickel alloys in different combinations. These are used mainly for making the orthodontic wires, they are also used in making a large number of caps etcetera, cap pot we will come in a while and. So, you can also use a fill as fillers cavity; as a fillers in the cavity in the dental

cavities are filled with metal you know melt like gold, a silver or amalgam kind of things these things can be used ok.

So, use to protect these ones you have caps, the caps can be made of the porcelain. So, porcelain is nothing but a clay material kaolinite this is nothing but Al 2 S i 2 O 5 OH 4. So, these are all called composites. So, these are all composites. So, the variety of composite materials are used in the dental part either for filling or as a caps. In fact, we can treat these things and then make into a cap shipping. You can also use the resin crowns. So, acrylic polymer resins example poly methyl methacrylate.

So, these kinds of things are also used for making the caps, there are ceramic kind of a types are also there feldspar, sodium, aluminum, silicate which is strengthened by the alumina. So, these kinds of things are also used. So, pacifiers a small quantities of oxides, say zirconium oxides say tin and titanium all these things are also used. As you can see a variety of these things are shown is shown over there ok. So, therefore, here you have the resin kind of a thing, here you have a porcelain kind of a caps you have a ceramic kind of a caps. So, all these kinds of a metal based crowns caps etcetera.

So, there are different kinds of crowns and caps are being used in the inorganic chemistry, in the inorganic materials into the dentistry aspect of it ok. So, also there are many other things that is done even for the dental part, the other part what is the other part important? The other important part is the root canal treatment ok.

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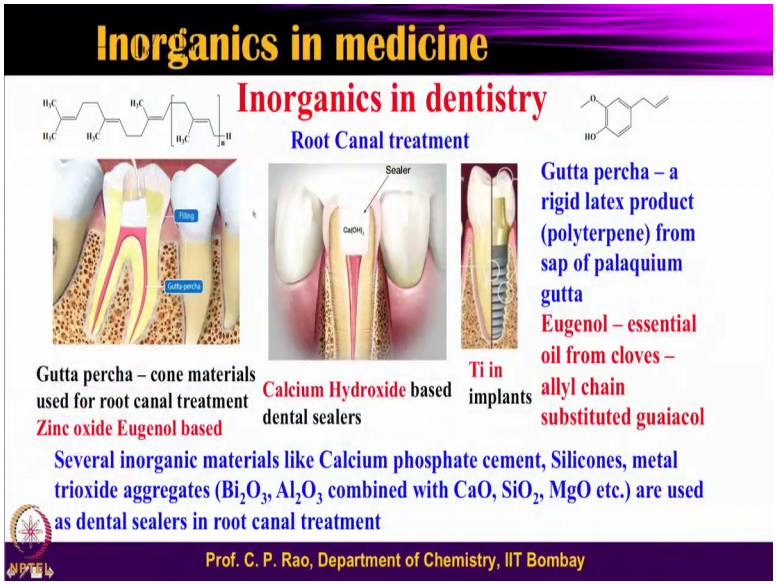

So, root canal treatment once it is done this requires to be protected. So, so how to one protected by various materials for example, Gutta-percha. So, is a cone material used for the root canal treatment what is Gutta percha? Gutta-percha is a rigid latex product is a basically a polyterpene a material, which is obtained from sap of a palaquium gutta. And this structure can be seen over here from the top and the slide as you can see this whole thing is nothing but you have a terpene material you have ok. You also have you also have other kinds of molecules that you are using, so the Eugenol essential oil from cloves.

So, the allyl chain you can see the allyl chain in these ones, the allyl chains are basically the ones which gives the oil kind of a property. So, you can use a zinc oxide with a Eugenol based. Zinc oxide with Eugenol based is the Eugenol is the essential oil which is I obtained from the clove as you can see this one. So, if this has got a allyled chain, which is a substituted guaiacol. So, use these things or Gutta-percha or Eugenol zinc oxide with a Eugenol all these things can be used for filling the root canals.

Also you can see calcium hydroxide based dental sealers. So, you can seal these one by using the calcium hydroxide material as you can see that. So that means, inorganic materials are used in multiple ways in dental treatment as a caps, as a fillers, as a root canal treatment all kinds of things. Also used nowadays a lot of a dental surgeries are going through or dental treatments are going through mainly as the implants. In the implant you need a screws, the screws are made up of the tin titanium and other metals.

So, therefore, again one can use in the dental implants too. So, several inorganic materials like calcium phosphate cement. A cement with the calcium phosphate, a silicones, a metal trioxide aggregates like Bi 2 O 3 Al 2 O 3 which are combined with calcium oxides silicon dioxide magnesium oxide etcetera all of these are used as a dental sealers in root canal treatment. So, almost everything is inorganic, you cannot use organic materials for any filler or for getting the strength. Because they do decree degrade very easily at the body conditions, at their physiological conditions, the human you know physiology.

So, therefore, it is always preferred the inorganic kind of materials, whose solubility is much lower and their deteriorations are also much lower. In fact, most of these caps will stay on alter 10 to 20 years or so that is the kind of a strength that is provided by the

inorganic materials; so inorganic materials in filling inorganic materials, in the implants inorganic materials in fitting the body bones, in pacemakers, in the eye contact, even then ear for hearing aid etcetera. So, these are some of the things that I have been talking in the last couple of classes about the inorganic chemistry in therapy, in organic chemistry in medicines etcetera.

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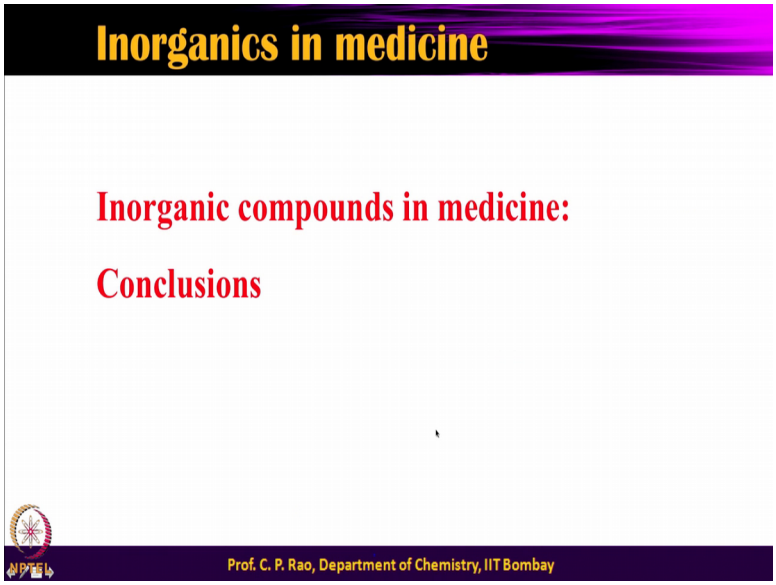


So, let us try to look at the whole thing what I talked in the last two a couple of lectures. So let us take you back to the where we started with the inorganic compounds and medicine, look at as like a concluding kind of remarks.

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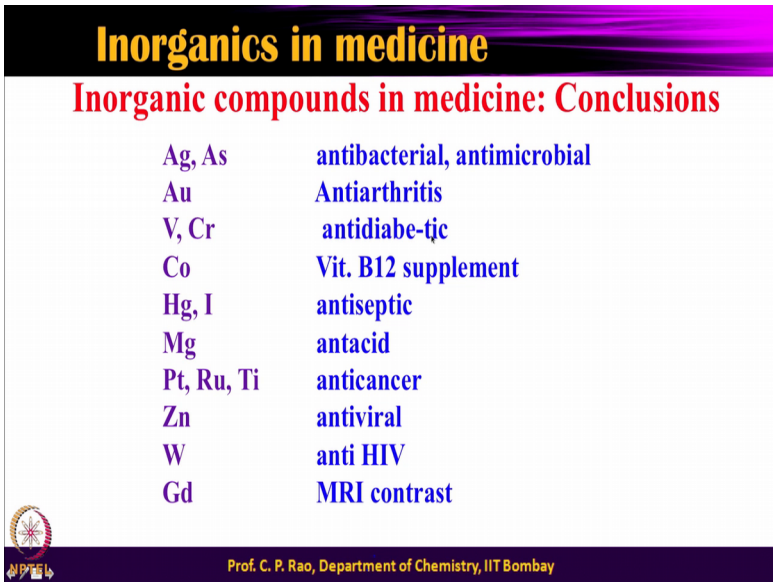


I have shown you there are at least 30, 40, 50 different elements, whose salts ions as well as the complexes are used you know a as a medicine. A few of them I would like to remind you by giving you this particular slide, which I have given earlier when I was giving the main lecture for this.

So, this is just will help you just to recap the things. For example, silver and arsenic they are like antibacterial and anti microbial arsenic, there is where the arsenic salts are used for you know spraying even in the agriculture, where the microbial killing is required. Gold is used very famously an anti arthritis is basically gold thiolate complexes, gold maleate complexes etcetera etcetera. Vanadium chromium can be used for anti diabetic aspects of it, only thing is that they are not basically in the market, but they have been shown to some extent.

In this cobalt as the vitamin B 12 supplement and for example, mercury iodide can be used as a antiseptic magnesium as a anti acid of course, also can be used magnesium salts as a laxative etcetera. Platinum, ruthenium, titanium, anti cancer of which we know very well platinum compounds are been very well demonstrated, very well accepted they are already in the market. Whereas, the ruthenium and titanium are not hit the market yet.

And so, therefore, but they are reasonably well shown for their activity. Zinc is will have effect even antiviral and wound healing many kinds of aspects people use, and a tungsten is a anti HIV and gadolinium as the as the MRI contrast agent. Because when you are

taking an MRI you need a contrast, between the healthy part of the tissue versus the tissue, which is which is affected by that ok. So, while teaching that I have also given a compilation of the inorganic most commonly found in organic compounds in medicine.

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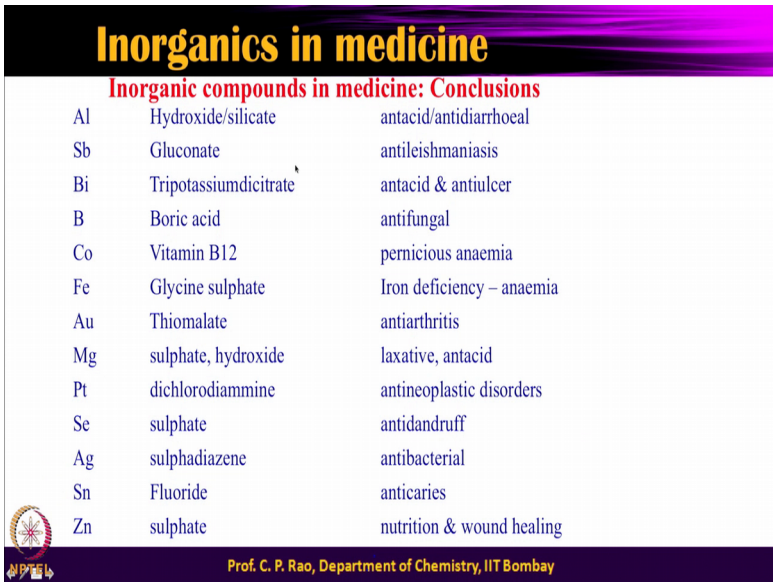


So, you can see aluminum as a hydroxide, silicate is a antacid anti diarrhoeal, antimony, gluconate can be used anti leishmaniasis, bismuth this is the tripotassium dichromate can be used as a antacid, anti also boron or boric as in the form of boric acid can be used as a antifungal, cobalt in the form of vitamin B 12 can be used as the for the anemia, perinicious anemia, iron mythical glycine sulfate can also be used for iron deficiency or anemia, gold thiomalate can be used for the antiarthritis.

These are all quite available ones magnesium sulfate magnesium hydroxide laxative antacid and platinum dichlorodiammine, is basically used as a antineoplastic or a or anti cancer. Selenium sulphate as a antidandruff silver, sulfad is diazene is a antibacterial, tin fluoride is of course, used for the dental for the anti caries, zinc sulfate can be used as a nutrition for zinc as well as a wound healing. So, these are all actually available once through the medicines people are taking and the previous slide shows the previous slide shows the potential for all of these. So, these are all. So, if you look at all of these there is a lot of a role of inorganic compounds and in the medicine.

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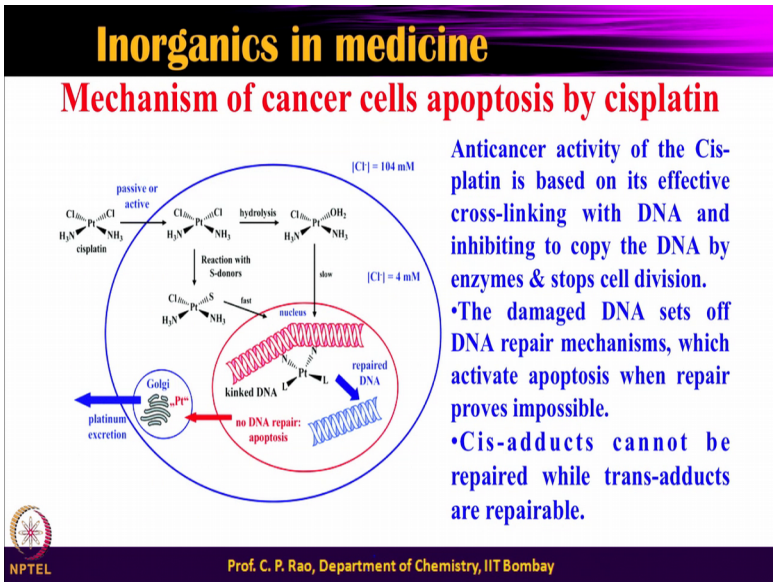


So, here I have brought another aspect of course, I have shown a lot of compounds in the regular lecture that, lot of the platinum based compounds, as anti a cancer agents also I have shown a ruthenium based etcetera. Now and also I have explained how a platinum based or compound will act on the tumor cells. There are two things here one is the cis geometry containing platon, other is trans geometry kind of a flattened cis platin trans platin. See the composition of these is exactly the same while the cisplatin acts on the on the tumor cells, transplatin does not act. And this also I have brought to your notice let me let me again bring a recapitulation of this. Both binds cisplatin binds to DNA trans platin binds to DNA.

Cisplatin binds like a kind of a interest strand and trans platin binds between the inter strand, where the always such kind of things can be repaired by the enzymes in the body and assess platin based complexes are not repairable whereas, the transplantin based DNA complexes those kind of things are repairable by system. Therefore, cis products a cisplatin acts as a anti cancer and trans platin does not act as a anti cancer does not have any use as a drug at all. What is the mechanism you have seen that? The cis platin entering in and the hydrolysis of one by one halides and replacement by water, and the water is knocked out by the nitrogen or n seven of the guanine residues and it will bind to the to the neighbor guanine residues and that is how it takes the thing into this we have looked at all of these.

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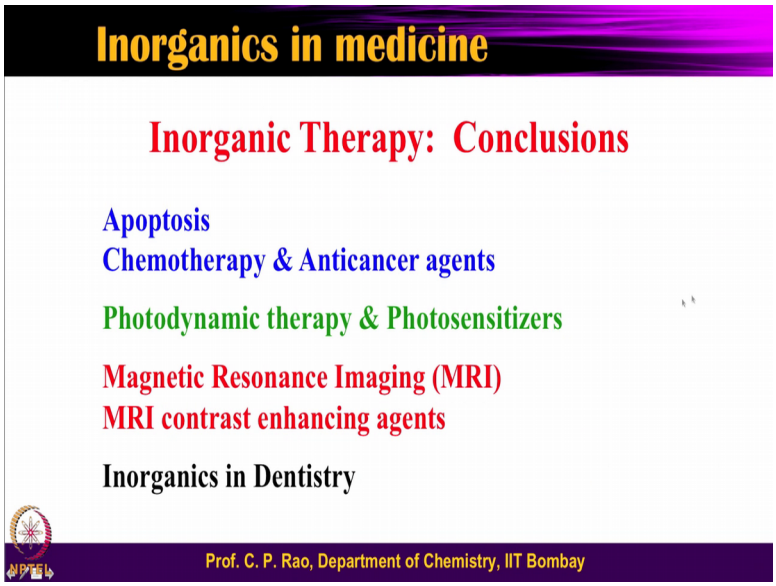


Now, in the in the previous class and partly in this class, I have introduce to you the therapeutic aspects where the inorganic compounds, inorganic molecules, inorganic drugs do play important role. Let us look at the concluding remarks of this, to start with I have explained you apoptosis, I have explained you chemotherapy, I have explained you anticancer agents. I have also explained you for dynamic therapy and photosensitizers, I have explained you magnetic resonance imaging and how this is obtained better by using MRI contrast enhancing agents and also just a while ago I have talked to you inorganic in dentistry.

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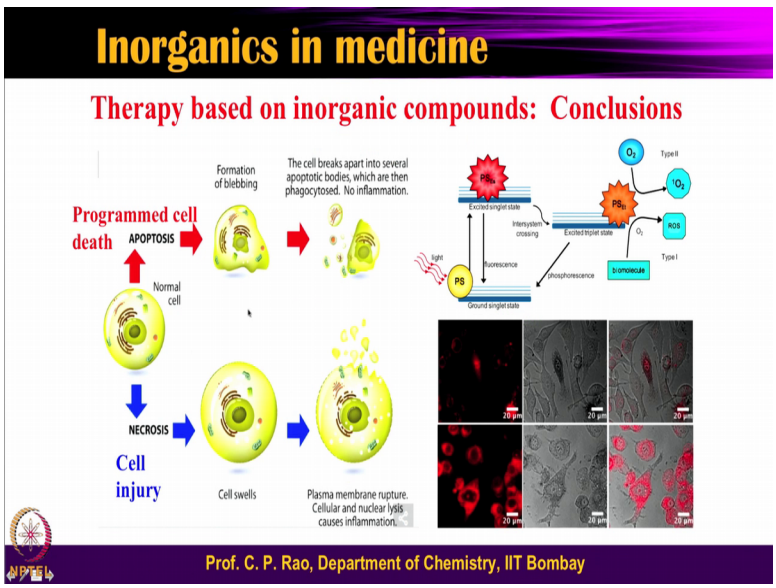

Just to bring a recapitulation back to you, the cells can go through a programmed cell death, where certain other cells have to take the death and that is a programmed one and the best process.

The other one is forcible and unforeseen situations that is called necrosis; so apoptosis and necrosis. So, the normal cell a programmed cell death, it will give the formation of a blebbing and the then finally, breaking into the pieces, where the protein is made into pieces, DNA is made into pieces, all this comes by the signals that are given by different proteins and these pieces are basically engulfed and therefore, no kind of the inflammation or any kind of a problems will be created. So, this is a safe way of thing in a cell.

The other side you have a necrosis and the necrosis is it happens by the cell getting assaulted by cell injury, some kind of a external pressure, it could be a chemical kind of an attack, it could be a biochemical or kind of an approach or physical kind of thing. So, physical chemical biological kind of a signal effects can influence the cell for the death and such kind of a cases that you have, the pieces that comes out or not organized not being engulfed therefore, this can lead to inflammation. So, this is a kind of a problem you have and such kind of a the apoptotic conditions can be checked by using a cells, a cells of the normal type as control cells of the cancer type as the regular ones, and then a study the study their entry of the drug as compared to the control, and a study the control at the drug placement in the nucleus by using some kind of a markers etcetera. So, those things can be identified.

So, by microscopy, fluorescence microscopy and come focal microscopy all of these; also I have explained to you was the photodynamic therapy. In the photodynamic therapy initially people have thought it is a only the perfirins, which can show the photodynamic therapy because of their extended conjugation, but now we have hundreds of compounds where you have a ligands, which are quite heavily conjugated in itself and there are metal complexes, and they have some nitrogen ligands which binds to the metal center its complexes.

So, in the form of such kind of complexes also can be useful for the photodynamic therapy. So, the principle is that the compound will act as a photosensitizer and the photosensitizer in its ground electronic state, with a ground vibrational state when you

when you incident with light and this species will get excited, to the excited electronic state probably even excited vibrational state in the excited by the excited electronic state 2. And as we know very well there are different processes by which the energy changes can happen from a excited vibrational level to the ground vibration level of the excited state can happen by internal conversion, and then the species can lose its energy in the form of a light by returning to the ground level by giving the fluorescence emission too.

It can also go through inter system crossing where the singlet excited state will turn into a triplet excited state, and the emission actual emission occurs from the triplet excited state. If the emission occurs from the triplet excited state it is known as phosphorescence as we know very well. And if the emission occurs from the singlet excited state it is known as the fluorescence ok. So, now, you have an excited species in the triplet state coming to the ground state, this particular energy release can activate the some bio molecules, in presence of oxygen, to give a reactive oxygen species or it can even activate the oxygen to give a singlet oxygen.

So, you will have a singlet oxygen, you will have a superoxide, you have a hydroxide, you will have a peroxide all these kinds of species and. So, these species that is generated they are good enough to kill the cancer cell. So, therefore, you are basically using bullets using your gun. So, this is basically a gun and throwing out the bullets at in different directions and with the different speeds and different activities. So, killing all the cell the cancer cells in that ok.

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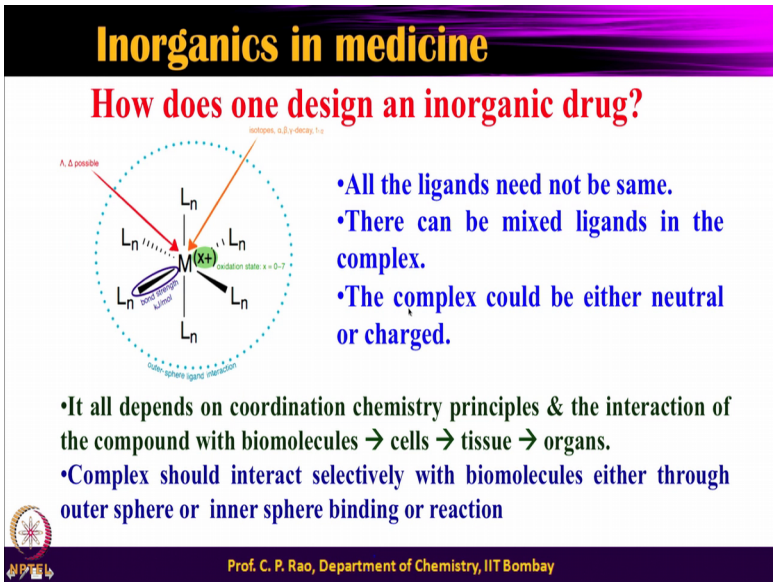


Having studied a couple of a lectures on this inorganic chemistry, inorganic complexes in drugs, inorganic complexes in therapy, I have also introduced to you in the beginning that, one can plan to design an inorganic drug either for a therapy or for a diagnosis or even for some kind of a coating or even for some kind of a protection; so all of these because the inorganic compounds are very much robust in many contexts and they are very widespread.

Why via these inorganic complexes inorganic molecules inorganic compounds or widespread? It is very well known. The in the inorganic complexes or a inorganic compounds the metal ion can undergo a variety of can have verity of oxidation states. When it come to the ligands and these oxidation redox states can be achieved by varying conditions, also these at different oxidation states the metal ion will have different kind of a reactivity. When they combine with the ligands they show different kind of a stability and they can also show different kind of availability depending upon their oxidation state and surrounding.

Coming to the ligands the metals can bind to 1 to 1, 1 to 2, 1 to 3, 1 to 4, 1 to 5, 1 to 6, 1 to 7 most of the a transition metal ions are generally with 6 and 7 of course, lanthanide ions will go much higher and when they bind they can bind from a mono dentate, they can bind from a bidentate, they can bind from a poly dentate they can bind from a cyclic molecule. So, therefore, going from mono dentate to bidentate to tridentate to hexa

dentate to a cyclic molecule, you are increasing the stability by either by the chelation effect or by their micro cyclic effect.

So, therefore, there is a variety of a space in which you can generate the inorganic compounds in organic complexes, you can also have inorganic salts also can be made. Then you can also have different kind of elegance at the same time binding to the metal center or in the same ligand multiple binding sites, one may be nitrogen, another may be sulfur, one may be nitrogen, another may be oxygen all these kinds of one may be oxygen other may be sulphur.

So, a variety of these kinds of things are also possible. So, that is what I have been referring to the inorganic chemistry based on the metal ion the complexes, inorganic salts some oxides, some other kinds of compounds their plethora. They are in fact, much more than the organic chemistry combination, generally people think organic molecule take start derivatizing you can generate halophyte number of molecules.

It is nothing wrong in that in fact correct, but if you take the inorganic case its not one element all elements in the periodic table belong to the in organic chemistry, accepting your carbon and now a chemistry has been developed with the alkali earth ions, chemistry has been developed with the transition metal ions, chemistry has been developed with the with the main group elements therefore, all that one need is a smart guy picking up a problem of making the complex. So, you can make with the 2 coordination, 3 coordination, 4 coordination, 5 coordination, 6 coordination etcetera.

So, this will give. So, all of these just by using the coordination chemistry principles and these will have different kind of interaction with the biological molecules, and they may be immunity of phase interact with the biomolecules to cells to tissues to organs you can take it. So, therefore, it is possible to bring the inorganic chemistry into the re num of the drugs, we service to organic chemistry where we know a lot of drugs are already known.

And I am sure with these couple of lectures, I am sure I am able to convince you that there is a huge amount of inorganic chemistry, which can play a role in a inorganic drugs, in therapy, and in the a prosthetic organ making, and many other device makings also etcetera. I hope I have been able to convince you with the inorganic aspects in the life of these things.

Thank you very much.