Oral Biology
Dr. Jaison Jeevanandam
Centro De Quimica Da Madeira
University of Madeira, Portugal

Lecture - 20
Basics of Biomaterial science and engineering

[FL]. This lecture is about Basics of Biomaterials and Bionanotechnology. And I have mentioned it as small as wonderful as one of the subtitle. Because, it is very interesting to see a large building how it is built? How astonishingly they are built? And everything, but each large building is built by smaller bricks and each smaller bricks have certain smaller atoms, right; so, each atom are clubbed together to form a brick.

So, each brick is aligned in certain way to form a big building. So, it is more astonishing to see the smaller things and if we understand the smaller things, it is easier for us to build a larger building. So, that is why I put small is wonderful. So, that is why today we are going to learn about smaller things, which is nanomaterials and about basics of bionanomaterials, biomaterials, bionanomaterials and bionanotechnology, ok, fine.

So, this lecture series has 3 sessions. So, 1st session I am going to introduce, what is nanomaterials and in the second one, in a 2nd session I am going to mention about, how to synthesize them, how to characterize them and how to functionalize and formulize them and how to utilize them in applications.

And finally, I am going to in the last session, I am going to say about how to what is bio what is biomaterials. What is bionanomaterials. And, how they are helpful in bionanotechnology? So, without further delay, let us move towards the lecture, ok.

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So, the 1st session is introduction to nanomaterials.

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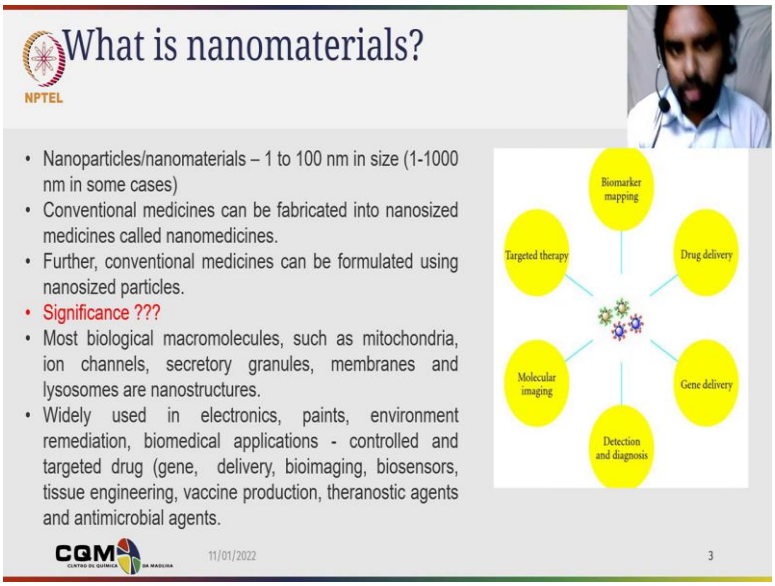

So, what is a nanoparticle? A nanoparticle or nanomaterial, right. So, if you reduce a particle, right. So, if you have a particle with the size of about 1 to 100 nanometer, right. So, it is a nanoparticle, right. So, its size should be 1 to 100 nanometer, right ok. So, what is nanometer? So, 10 to the power of minus 9 of meter, right.

So, if you have a meter so, when you divide them like 10 to the power of minus 9 so, though those small particles are called as nanoparticles. So, and its size should be 1 to

100 nanometer, right. So, if you have 3-dimensions, like at least 1- dimension, right. So, you will have X-axis, Y-axis and Z-axis.

So, if you have 3-dimensions at least 1-dimension should be in 1 to 100 nanometer in size, right. So, in some other cases, right; so, in some other cases, especially in biological materials, bionanomaterials or bio nanoparticles, if you have 1 to 1000 nanometer in sizes, right. So, those particles are also categorized under nanomaterials or nanoparticles. So, what is the actual definition of nanoparticle, right.

So, whatever be its size 1 to 100 nanometer or 1 to 1000 nanometer, below micro particles, right so, below 1 micron, right. So, whatever be its size, but its property should differ, right. So, only if its property is different from of the micro particles, it is called as a nanoparticle, right. So, its size should be 1 to 100 nanometer or 1 to 1000 nanometer in biological in bionanomaterials, but its property should differ.

Those are called as nanoparticles. And if you have building a material with those nanoparticles those are called nanomaterials, right. So, now, what is nanomedicine? Right. So, we have conventional medicines, right. So, like Paracetamol or whatever, right. So, those nano, those materials those conventional medicines, when you combine your when you convert them into a nano size, 1 to 100 nanometer in size it is called as nanomedicine. So, this is one case, right.

So, the second case is, you take those conventional medicines like, Paracetamol and you formulate them inside a nanoparticle, right, you have a nanoparticle 1 to 100 nanometer or 1 to 500 or 600 or 1000, right, below micro, right. So, its property is different. So, inside that nanomaterial, when you are keeping your conventional nanomedicine, when you are formulating them with a nanoparticle that one is also called as nanomedicine, right.

So, these are the two definitions of nanomedicine. So, what is it significance of this nanomedicine? Right. So, this nanomedicine, right so, see because its size is 1 to 100 nanometer in size, right. So, this size is smaller so, because of that they are helpful in bio-marker mapping, drug delivery, gene delivery, detection and diagnosis of where several diseases, molecular imaging, targeted therapy as I showed in this figure, right, ok.

Why they are helpful in these biological applications? Because, most of a biological macromolecules like mitochondria, ion channels, secretory granules, membranes, virus, DNS, and bacterial the inside the bacteria once, right. So, everything is nanostructures, right. So, so for a nanoparticle, it is easier to interact with this nano nanostructure. So, that is why it is highly beneficial in biomedical applications, right.

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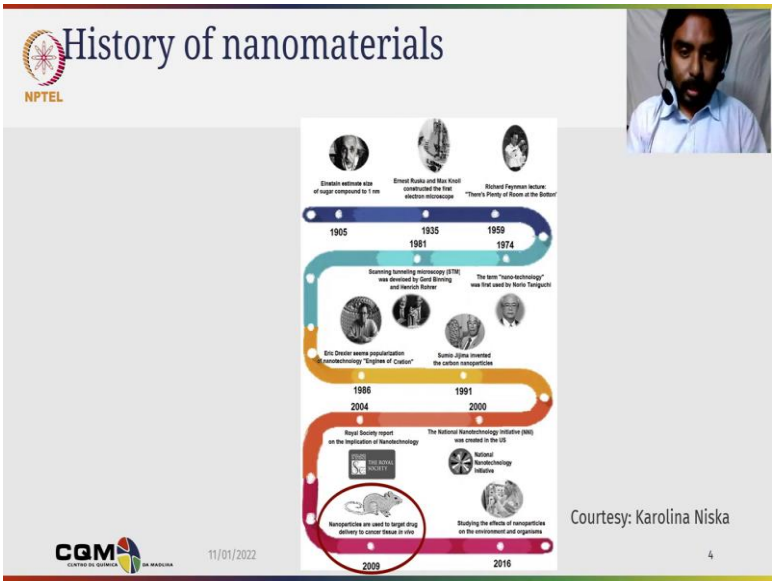

So, now we are going to see about the history of nanomaterials, right. So, in 1905 Einstein first said, the sugar compound is about 1 nanometer, right. So, at that time, he cannot visualize them. So, theoretically he said, a sugar compound will be in the size of 1 nanometer and he also mentioned that and not Einstein, Newton also mentioned that, when you reduce the size of a material its property will differ.

So, for that he mentioned the example of gold. So, gold if it is reduced to smaller size, he does not mention nanomaterial nano-size, but when you reduce the material into smaller size, solid gold will turn into liquid. So, he mentioned that, right. So, they have a theoretical idea of how nanomaterials will behave, right. But later in 1905, Ernst Ruska and Max Knoll they constructed the first electron microscope, after that only we started to visualize nanomaterials, right.

So, we can able to see nanomaterial, but electron microscope at that time is quite premature. So, people cannot be able to see what exactly a nanomaterial, a blurry image is appeared. But still, they cannot actually see the particles, right. So, later in 1959,

Richard Feynman so, he is known as father of nanotechnology. So, he said that There's Plenty of Room at the Bottom. So, the title of the lecture is, There's Plenty of Room at the Bottom.

So, this familiarized the theme of nanotechnology among researchers, right. So, this happened in 1959. Later in 1974, the term nanotechnology was given by Norio Taniguchi, a Japan scientists, right. So, he gave this term non technology, after that only people started to call this technology as nanotechnology and particles as nanoparticles and nanomaterials and everything started to come up.

And later in 1981, scanning tunneling microscope was developed by Gerd Binning and Heinrich Rohrer, right. So, they started to see more clearly how nanomaterials are forming and how their structures are and how they behave, right. Later in 1986, Eric Drexler, write a book called Engines of Engines of Creation. So, this familiarized nanotechnology a more general public, right.

So, now, it is coming it is going from the researchers towards the public, right. And finally, in 1991, Sumio Lijima invented carbon nanoparticles, right. So, these carbon nanoparticle invention is quite interesting and it gained lots of companies interest like industries started to be more interested in nanotechnology, because of the arrival of C 60 fullerene and everything, right.

And in 2000, the National Nanotechnology Foundation, so, initiative was created by in the US. So, after this only, each and every country started to have a department especially for nanotechnology and they started to give research fundings towards nanotechnology, right. And 2004, Royal Society London, so, they started their implication of nanotechnology in their medicinal field.

And in 2009 only, nano-particles are used to target for the targeted drug delivery systems, right. So, it is started in 1905, but in 2009 only people started to use nanotechnology for biological application, especially for drug delivery. But, after even after this also there is a bit of hesitation in providing approval for these types of drugs. So, I will say, why later, right. So, in 2016, studies were moved towards from using the nanoparticles in biomedical application towards toxicity of nanoparticles, right, ok.

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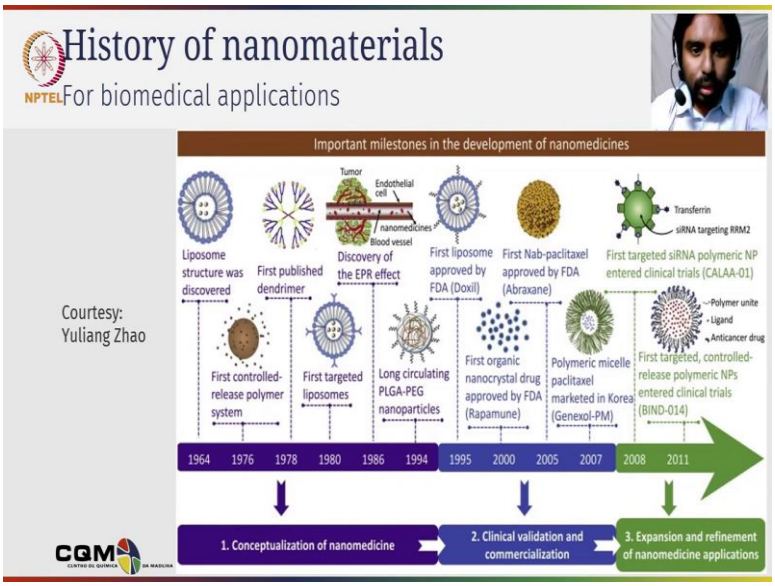

So, now, history of nanomedicines, right; so, now, we move towards a medicinal one. So, from 1964 to 1994 people started to conceptualize nanomedicine. So, around that period, they were like telling liposome's or micro size particles, right. So, liposomes, dendrimers and polymeric nano polymeric materials everything are micro particles.

So, they were conceptualizing like, if you reduce the size, it will be more beneficial. They were saying this and they were trying to trying to utilize reduce their size, right. But from 1995 to 2007 they started to develop nanoparticles like, liposome nanoparticles, nanoliposomes, nano dendrimers and those things and then they started to clinically validate and commercialize them, right.

And now, it is moving towards approvals like they are they started to check their toxicity and also they are sending them to approvals and several particles are getting approved, right. So, FDA is starting to approve, but even though if it started like 2005 and the first approved FDA approved one was Doxil, right; so, which is a liposome formulation of Doxorubicin which is an anti-cancer drug, right.

So, they started to approve, but still now we are checking more towards more more nanomedicines more more nanoparticles are under the Radar of FDA and EPA European Pharmaceutical Agency. So, European medical agencies and pharmaceutical agencies to get more to get approved even more even for more applications more biomedical

applications, right. So, these are the scenarios of nanomedicine. So, until now, we are moving towards the toxicity and approval regulations and those things, right; so, ok.

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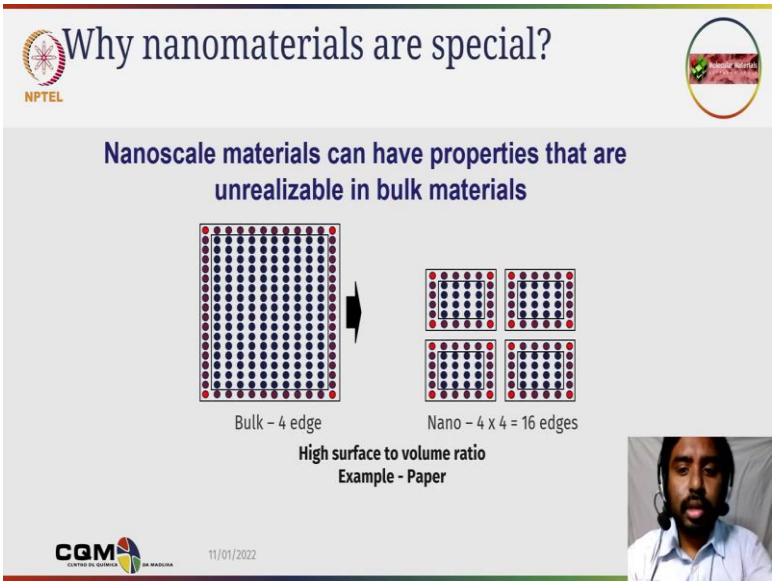

So, now we are going to see about why nanomaterials are special, right. So, as I said before, why in the first slide. So, how I said because of its smaller size they are helpful in biomedical applications, right, because they can easily interact with nanostructures of our body or in the living organisms, right. So, how they are interacting easily with nanostructures, right.

So, how nanostructures are easily interacting with nanostructures, right. So, it is because of why nanomaterials are special? It is because of two things, one is its size and second thing is its shape, right. So, depending of on its size, because of its smaller size, they have high surface to volume ratio. So, what is high surface to volume ratio? Right. So, let us consider this one as a paper, right.

So, when you have this paper and if you want to burn this paper, you are taking a lighter and then you are burning this corner, right. So, first this edge atom, consider this one as an atom, right. So, consider this atom is interacting with the fire first, right. So, for the fire to reach the center, it takes some time, right. So, consider you are having fire on all the 4 sides, right. So, only this 4 edge atoms will interact with the fire first, right, but consider cutting this paper into 4, right.

So, when you cut this paper into 4, instead of four edge atoms you have 16 edge atoms, right. So, instead of 4 you have 16 edge atoms. So, all the 16 will interact with the fire. So, instead of heating, instead of let us say it takes 2 seconds to burn this. So, it takes less than 1 second to burn the whole paper, right. So, you are going to burn the paper anyway, right.

But still, when you cut the paper into 4 and when you are doing it, you are doing it faster, right; so, instead of taking 2 seconds, right. So, the same temperature, same fire, right; so, instead of taking 2 seconds it takes less than 1 second. So, this is what is happening in nanomaterials, right. So, when you reduce the size, their surface is more, right, you have more surface with the given volume, right, so, within the given volume.

So, that is why, nanomaterials are having a enhanced properties, right. So, that is why I said, your bulk property or your microparticles will have property. So, those properties have to differ, when you are changing them into nanoparticles, now only then it is called as nanoparticle, right.

So, when you reduce them their size, so, its surface property differs, they have high surface to volume ratio. So, that is why it is behaving differently, right, you have enhanced properties. So, that is why they have their own properties or exclusive properties, which will be beneficial for biomedical applications, right.

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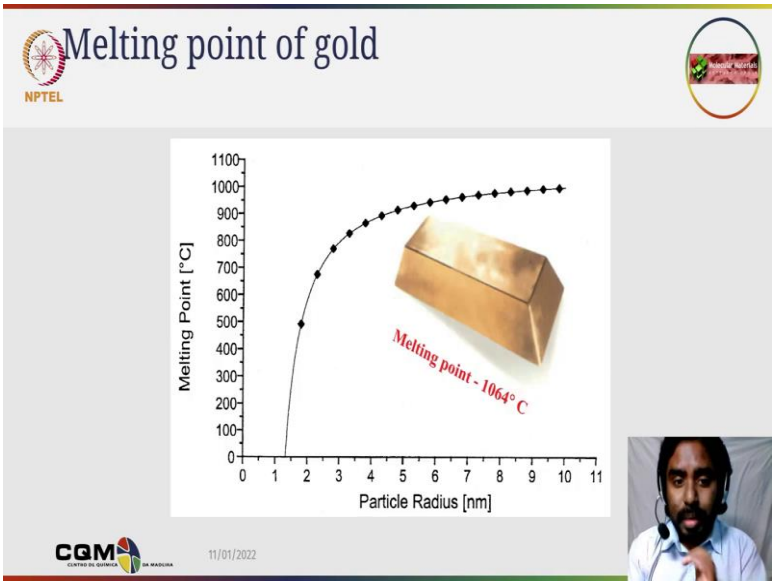

So, the example for this is melting point of gold, right. So, when you have the, a bulk gold which you are using them in jewelries and ornaments and everything. So, the melting point of a gold pure gold is 1064 degree Celsius, right. So, when you reduce the size to nanometer, right; so, for each ones like 50 nanometer and 40 nanometer there is a huge difference, right.

So, the melting point differs from 1064 degree Celsius to, it can be reduced to even 200 degree Celsius, when you have 20 nanometer of gold nanoparticles, right. So, its melting point is around 200 degree Celsius only. So, you can see the drastic change, how it is behaving, right. So, this is because of high surface to volume ratio. So, this property of nanomaterial's, right.

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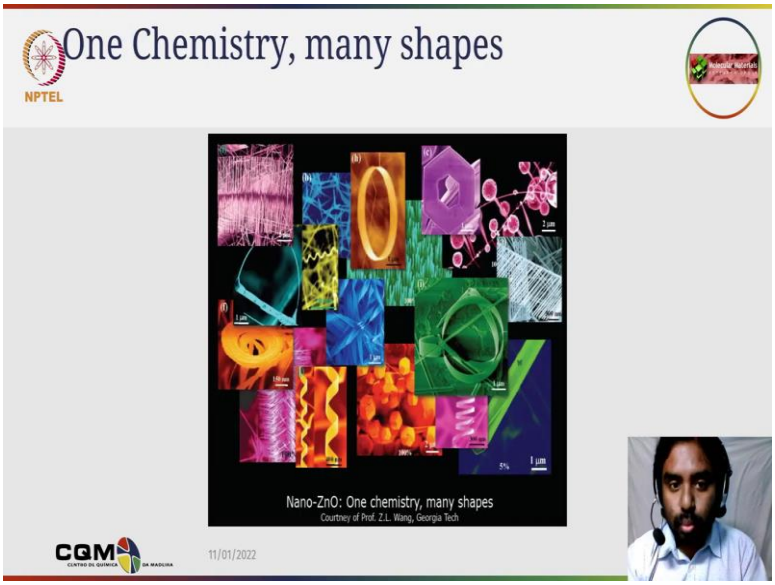

So, the next one is, one chemistry many shapes now. So, as I said before, two things are important in nanomaterials one is size, next one is shape, right. So, just see this image, right. So, you have several different types, several morphologies of one single material, zinc oxide nanoparticle, right.

So, you can fabricate them into rings, fibers, hexagon like ribbon like coils, like fibers, like whatever shapes like nano flowers are there now. So, you can see you can see the crystals, right. So, you can develop them into various types of materials, right. So, various types of morphology so, each morphology behaves differently than the others, right.

So, it differs, a behaves differently with the size and it also behaves differently with the shape. So, that is why each nanomaterial is different. Even if it is from the same material, depending upon its size and shape its property will differ, that is why nano nanomaterials are very special, right.

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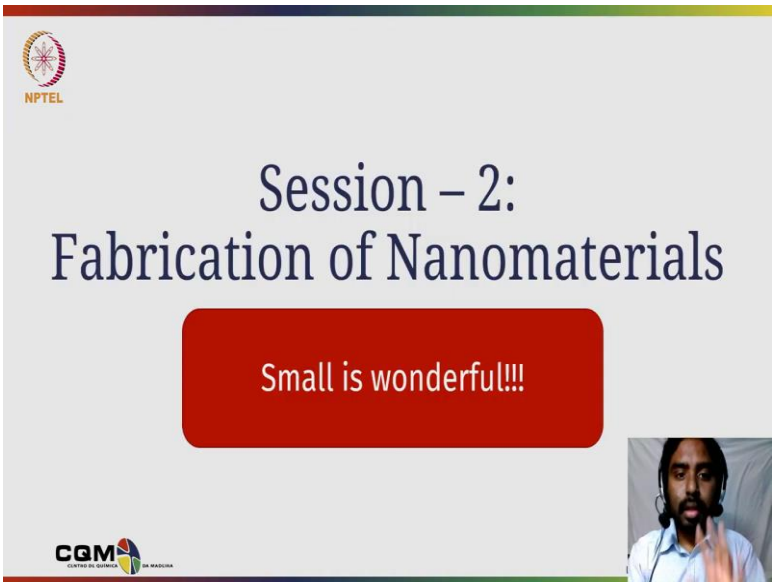

So, now we are moving towards the 2nd session, which is fabrication of nanomaterials, right.

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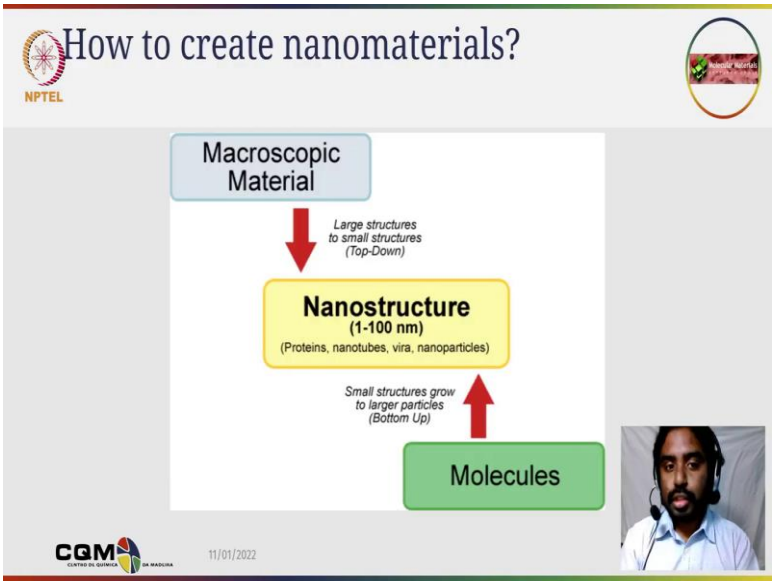

So, for the fabrication of nanomaterial's, two things can be two approaches can be used; one is top-down approach, another one is bottom-up approach, right. So, top-down is you have a bigger material, you are crushing them into smaller size and then you are making a nanomaterial, right. So, that is called as top-down approach. Another one is bottom-up approach.

So, in the bottom-up approach, you arrange atoms you form molecules. So, those molecules form smaller crystals. So, those crystals will form into a nanostructure, right. So, one is from the top, you are reducing their size and then bringing them into nanostructure and second one is they are smaller atoms.

So, they are you are arranging them into molecules and then those molecules you are arranging you are building them, right, from the bottom, right. So, that is why it is called as bottom-up approach. So, this is a broad classification. So, under this you have several types, right

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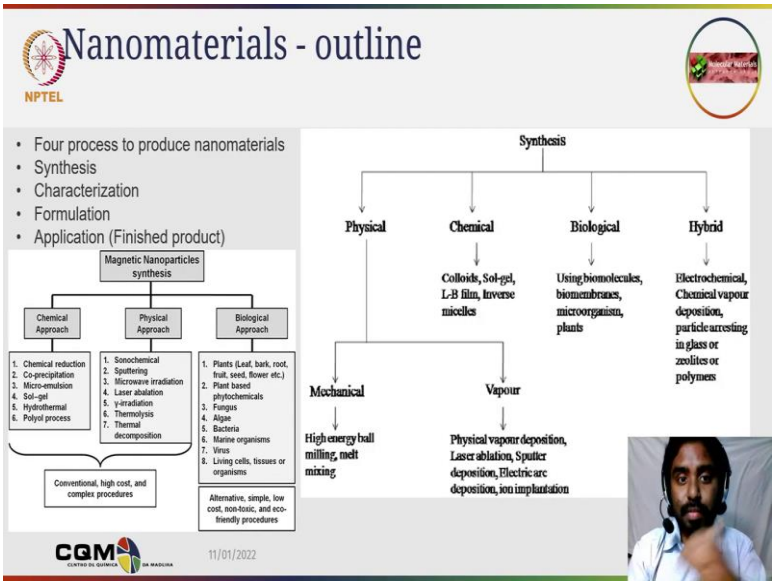

So, for the fabrication of nano-materials, four procedures are followed one is synthesis, you need to have a synthesis procedure. And then you need to characterize, you need to see their optical properties, their magnetic properties, their size, shape, surface properties whatever, right. So, everything you need to study.

And then you need to formulate them, next especially for biomedical applications, you need to formulate them to avoid its toxicity and to interact with other biological structures. And then finally, you have your finished product, which will be useful for application, right. So, in the synthesis, right; so, you have chemical approach, physical approach and biological approach, right.

So, basically physical approach is top-down approach, right. So, physical approach and some of the chemical approaches are top-down approach and many of your chemical methods and biological methods are top or bottom-up, right. So, this is for your general information. So, why we have this chemical approach and physical approach? What are their benefits? Right.

So, you have their benefits are, you can synthesize stable nanoparticles, right. So, you can have stable nanoparticles, but you will use a hazardous materials which is which you cannot use them for biological application. So, that is why we move towards biological approach.

But the problem in biological approach is, even though their toxicity is lesser, the stability is not that much good compared to chemical and physical methods, right. So, that is why now, recently we have hybrid methods. So, those hybrid methods are inter mix of chemical and biochemical biological approach, right. So, we will see that in detail in the next slide, right.

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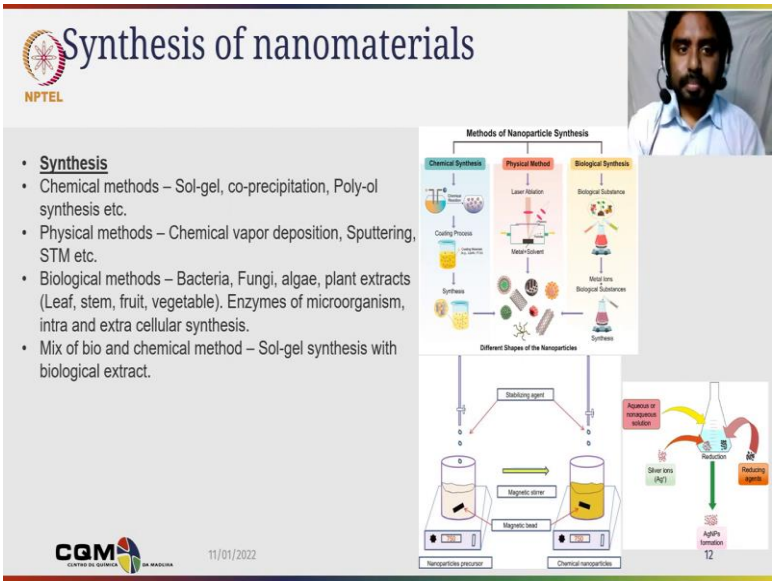

So, synthesis approaches you have chemical approach, Sol-gel, co-precipitation, Poly-ol etcetera, right. So, chemical approach, you have high stability you can synthesize nanoparticle of whatever size you want, whatever shape you want, right. But their stability is also high, but they use a toxic reducing agent, right. So, reducing agent is quite important.

So, in order to reduce the size, right; so, in order to reduce the size, you need reducing agent those reducing agents they use synthetic hazardous chemicals. So, that is why, we cannot use them for biological applications. For electronic applications also, we can use them, but when you are when you are when those electronic things or when you dump them in the environment after their usage, they will also cause toxic reaction in the environment.

So, that is why chemical synthesize once towards the toxicity is quite is not compatible. So, next one is physical methods, right. So, physical methods, you can have stable nanoparticles the you can have whatever size you want, but the cost of those materials like chemical vapor deposition, sputtering, scanning tunnel microscope the cost is very high. So, it cannot be used for large scale applications, ok.

So, in lab scale it is, ok, but for the large-scale commercial applications, it cannot be used. So, that is why, we move towards biological methods, right. So, in this method we are not going to use high-cost materials high-cost equipment's and we are not going to use synthetic hazardous chemicals, right. So, we are going to extract enzymes, extract bio-molecules from bacteria, fungi, algae or plant, right.

So, different parts of the plants you can extract and you can also you can also develop them even like bacteria, inside the bacteria nanoparticles will develop and then we can extract them, extract the nanomaterials from the bacteria. So, this is called intra cellular and extra cellular synthesis, right.

So, that is why we are moving towards this biological methods, but the problem in biological methods is stability, right. So, its stability is very weak, right. So, that is why currently we have mix of biological and chemical methods, which is Sol-gel synthesis, with the helpful with the help of biological extracts. So, now, we are moving towards that era, right.

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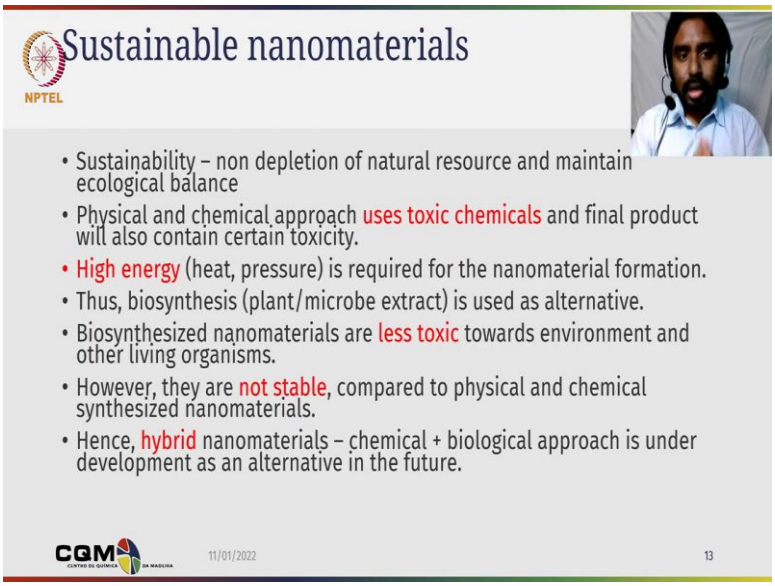

So, what is sustainable nanomaterial's? So, the goal of bringing biological approach or biochemical approach which is a hybrid approach is to develop sustainable nanomaterials, right. So, it should not cause toxic reaction in the living organism, as well as to the environment, right so, that is sustainability. Non-depletion of natural resource and maintain ecological balance, right.

So, you cannot just go there and cut some plants and then utilize them for nanomaterial production. So, it should be a sustainable development, right. So, as I said before physical and chemical approach uses toxic chemicals and final product will also contain certain toxicity, right. So, high and also the another approach is. So, when you are going for physical and chemical methods, high energy you need to use high energy like heat, pressure, right.

So, that is why we move towards biological approach so, which uses less toxic materials so, which is less toxic towards environment and other organisms, right. So; however, these materials are not stable. So, that is why we move towards hybrid nanomaterials, right.

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And there is no regulation until now, to measure sustainability of nanomaterials, right. So, even FDA or European Medical Agency, Indian Nanomedicine Council, they do not have a perfect regulation for the sustainability of nanomaterials to calculate that. So, now we need to focus on producing nanomaterials at low cost, with low toxicity and without any toxic reactions towards humans and the environment for the sustainability in the future, right.

And this sustainability is very important in biomedical applications, right. So, until now, acute sustainability of nanomaterials can be analyzed, right, even though there is no regulation. So, this can be analyzed, but chronic sustainability cannot be analyzed, right. So, we need to think about the future and how to calculate this chronic sustainability and etcetera in the future, right.

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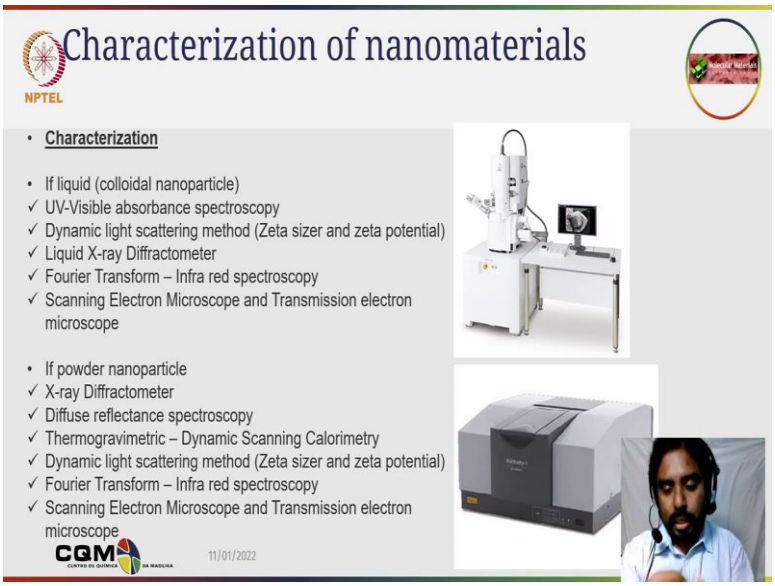

So, what are the ways to characterize nanomaterials, right? So, if you have a material, right. So, if you have a nanomaterial, it can be either in liquid form, like colloidal nanoparticles or powder nanoparticle, right. So, if it is even if it is a whatever be the type of your nanoparticle, either it is liquid or powder, right.

So, you can use all these methods like UV-Visible absorption spectroscopy to study its optical property, dynamic light scattering method to study its particle size distribution and zeta potential in a solvent, right and then liquid X-ray diffractometer or normal X-ray diffractometer to know its crystallinity and Fourier transform infrared spectroscopy to know is surface functional groups.

And finally, to know its scanning electron to know its morphology you can use either Scanning Electron Microscope and Transmission Electron Microscope fine, but if it is a powder nanoparticle to analyze its optical property instead of UV-Visible absorbent spectroscopy you will use, diffusion Diffuse Reflectance Spectroscopy, right. So, this is the only difference, right. So, from all these you can know what are the what are the properties they have, right. What are the initial basic properties they have nanoparticles have, right?

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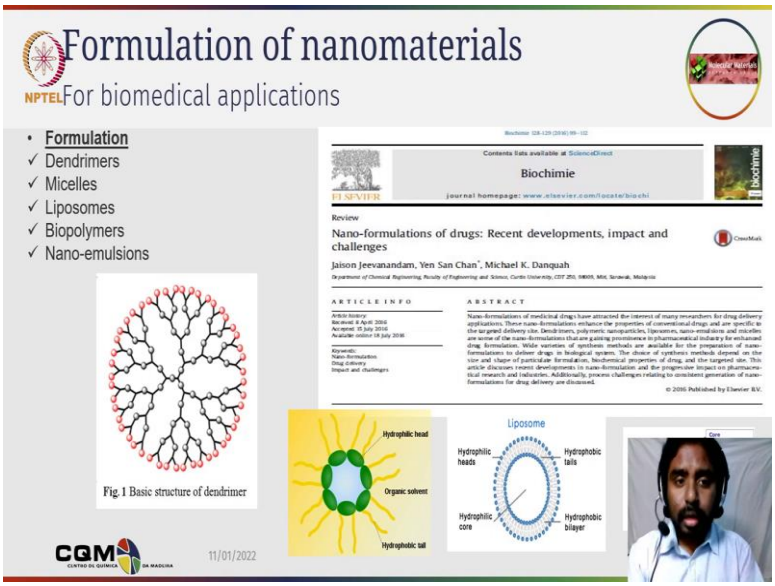

So, for the formulation of nanomaterials, especially for biological materials; so, if you have a nanomedicine or nanoparticle as a medicine, right. So, you need to formulate them, in order to in order to deliver them at the target site, right. If not, other instead of a targeted place. So, it can be degraded by other areas. So, for example, if you need your drug to be in the lungs and you are in your lungs.

So, it would not be going to lungs. So, it will be everywhere in your body because it gets degraded faster, right. So, in order to stop them, you need to formulate them, for the formulation you can use either dendrimer, right. So, dendrimers are here; they are hyper-branch polymers. So, inside these white spaces you can keep your you can keep your medicine or nanoparticle, right.

You can have Micelles. So, here you have micelles. So, inside this micelle you can have organic solvent. So, you have a hydrophilic head and hydrophobic tail. So, inside this you can keep your nanomaterial. And liposome's, you have hydrophobic tails and hydrophobic bilayer and hydrophilic heads. So, inside this you can keep your hydrophilic core hydrophilic nanoparticle, right.

And you have and you also have core shell nanoparticle, right. So, you have a core, right. So, core nanoparticles. So, over that you can also functionalize some biomolecules. So, which is also a core shell nanoparticle, you can also use them, right. So, these are all nano formulations, right.

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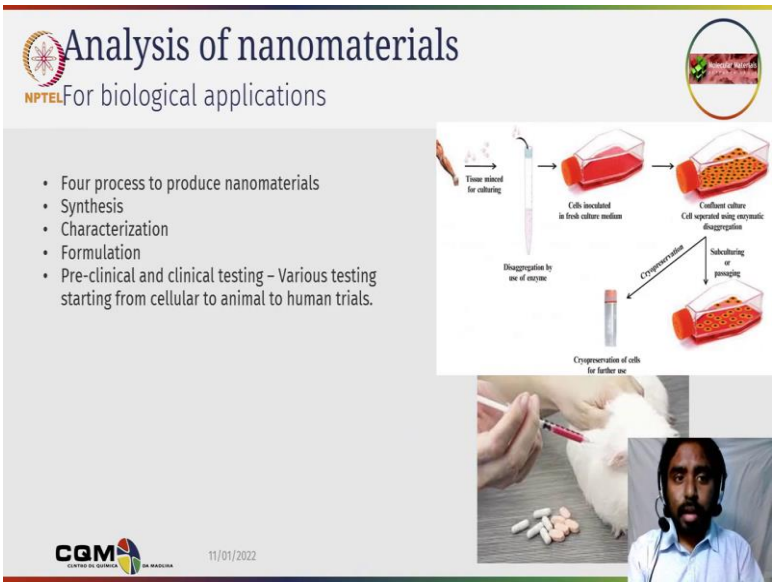

And finally, after all these procedures, you can move towards the final process before your application is pre-clinical and clinical testing. So, for pre-clinical testing's you can use cell cultures and those biomolecular analysis and then it ends in animal to human trials. So, this is how you will develop your nanomaterials for any application and especially for biological applications, right.

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So, now we are moving towards the 3rd session, which is bionanomaterials in bionanotechnology, right.

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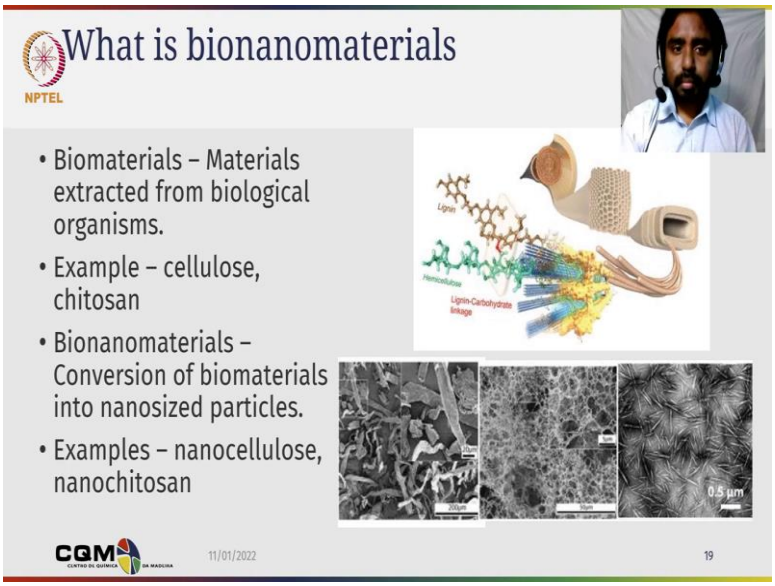

So, what is biomaterial? So, now, until now, we know what is nanomaterials, right. So, what is biomaterials? Say, so materials those are extracted from biological organisms. For example, cellulose, chitosan, right. For example, cellulose so, this is a trunk of a tree. So, from the trunk of the tree, you can extract lignin, hemi-cellulose and cellulose, right, right. So, when you convert this biomaterial into a nanomaterial 1 to 100 nanometer in size, it is called as bionanomaterials, right.

So, just you are converting them. For example, nanocellulose and nano-chitosan as I mentioned here, right. So, you can change them into a nanofiber, you can change them into a nanoparticle whatever, right. So, you can extract them, right. So, the extracted ones are biomaterials and when you are converting these biomaterials into nano size particle it is called as bionanomaterials, right.

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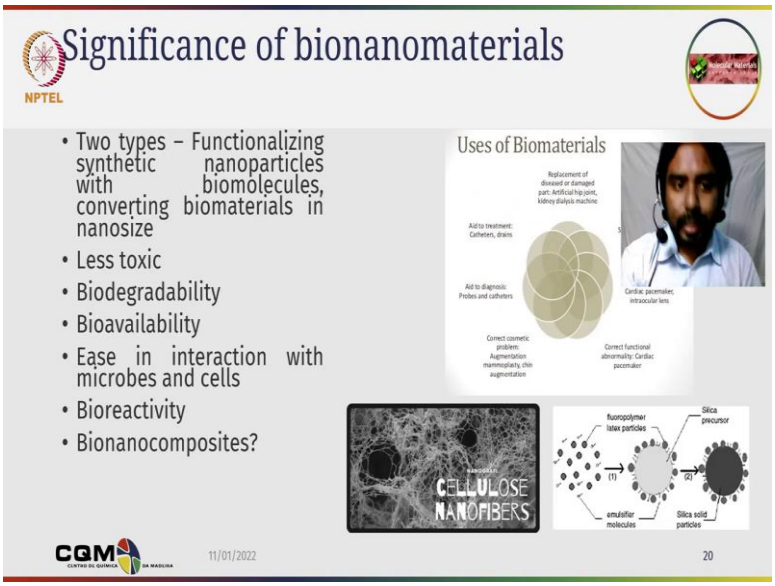

So, significance of bionanomaterials, right, so, they are two types of bio nanomaterials, right. So, the first one is, functionalizing synthetic nanomaterials. So, you have synthetic nanomaterials, right. So, from physical methods or chemical methods, you have your nanomaterial, right. So, in that nanomaterial, you are functionalizing, you are attaching certain biomolecules on their surface, right.

So, it that one is also called as bionanomaterial. And second one is converting bionano biomaterials in nano size. Like for example, as I showed in cellulose and nanocellulose, right. So, these two are also called as nanoparticles, bionanomaterials, right. So, what are its significance? The first significance is less toxic, right. So, they are less toxic, right.

So, they are less toxic, they are biodegradable, their bioavailability is higher and they are easy to interact with microbes and cells as I showed in my first slide, right. So, easy to interact, right because of its smaller size and its bioreactivity is very high. So, because of this reason bionanomaterials are widely used in biomedical applications, right. So, currently there is a development in bio nanocomposites.

Composites are blending of two materials, right. So, for example, you have one material, material A. So, this has one weakness and material B has one weakness, right. So, to have a compatibility, right. So, to have to enhance their weakness, to reduce their weakness and to enhance their positive points you are mixing them together, right. So, this is called as composite.

So, when you have a biological material and a normal material and when you are blending them together it becomes a bio- nanocomposite, right. So, the best example for functionalizing your synthetic nanoparticles is here and for yeah, it is here and for the best example for converting a biomaterial into a bionanomaterial is here, cellulose nanofibers, right.

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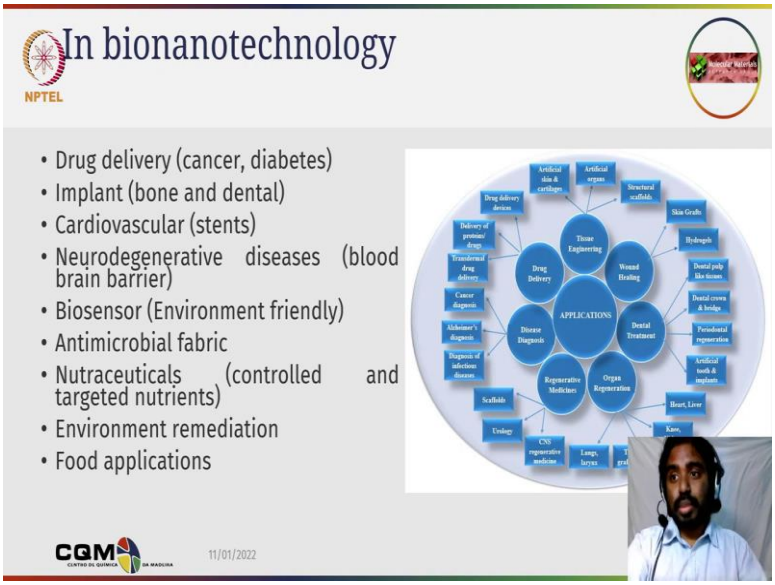

So, in bio nanotechnology, what are the benefits of this bionanomaterials? Right. So, you can see, you can use them for n number of applications, right. The first one which comes to every researcher's mind is drug delivery, right. So, to deliver anti-cancer drug to deliver insulin, you are used it will be helpful for the treatment of cancer and diabetes, right.

And the second one is implant, right. So, either bone implants or dental implants, we are we can use bionanomaterials because of its enhanced properties and application, right. And the third one is cardiovascular to fabricate stents, right. So, drug eluting drug stents are currently gaining more attention among researchers. So, stents, first the stents also now cellulose nanofibers are highly help or highly used, right.

So, next is neurodegenerative diseases, right. So, the main problem in neurodegenerative diseases is when you are having a drug towards your brain, you have something called blood brain barrier, right. So, the there is a barrier which reduces, right, now which

reduces the entry of certain drugs or certain biomolecules from the blood towards the brain, right.

So, those bionanomaterials has the property to bypass this blood brain barrier. So, that is why for to provide drugs towards the brain for Alzheimer's disease for Parkinson's disease. So, now, people are using bio nanomaterials. And biosensors, right. So, biosensors to have even now for SARS COVID 2 from the saliva to detect the presence of the virus, silver nanoparticles are used, right.

So, it is not under it is not still commercially it is not still commercially available. But still, in the future maybe next year it will be coming out in market. So, for the biosensors, we can use because it is highly environment friendly, it can degrade faster, right. And now people are developing antimicrobial fabrics.

So, this fabric will kill the bacteria and viruses since there are lots of variants of viruses how corona viruses are there and several other bacterial infections are also are also developing. So, these antimicrobial fabrics will kill so, which will be beneficial for people who are working in hospitals, and in labs etcetera.

And for nutraceuticals to for the controlled and targeted nutrient delivery for babies and mothers and for the plants, for the animals' people are using bionanomaterials. And for environment revolution, for waste water treatment, for soil remediation people can use bionanomaterials.

Because it has high biodegradable application and also finally, food applications, right for food packaging, because it can degrade faster instead of using plastic bags or plastic one's plastic wrappers. So, now people are developing bionanomaterials, which can degrade faster, right.

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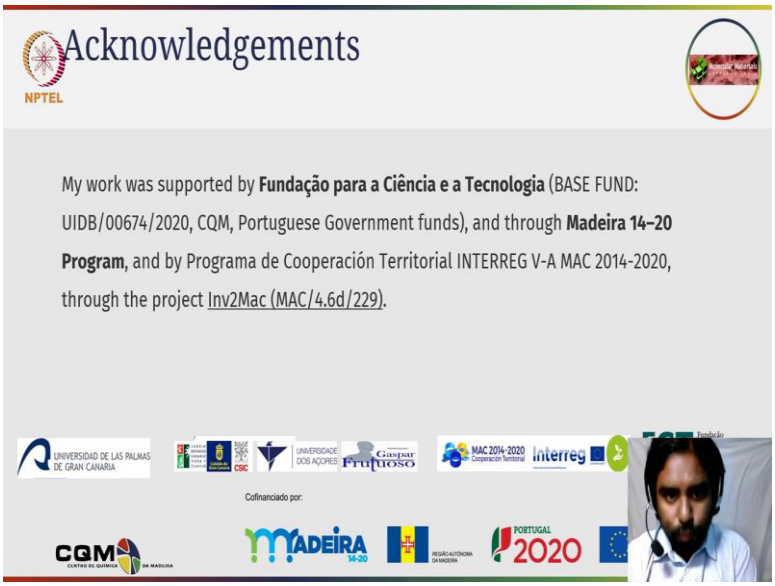

So, that is all about my lecturer so, acknowledgements. So, thanks to FCT Fundacao para Ciencia a Technologia, Foundation for Science and Technology in Portugal, for funding my research and.

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Thank you for your attention.