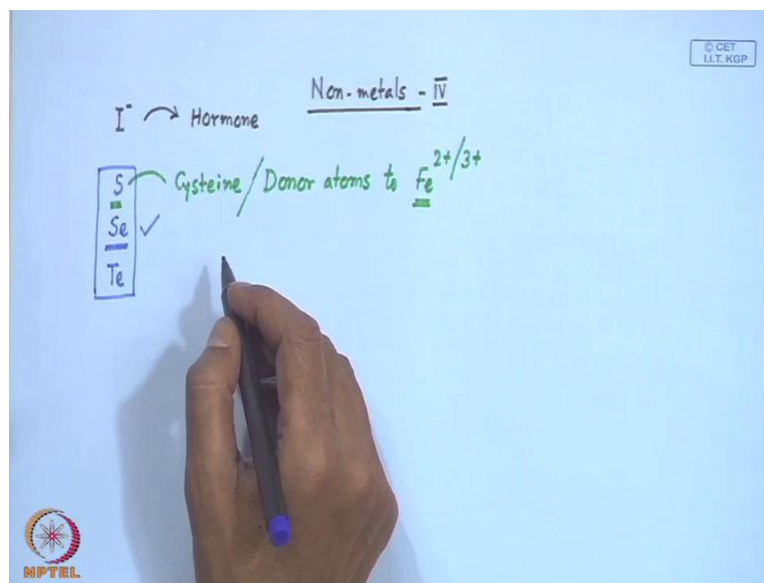


**Bioinorganic Chemistry**  
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**Lecture - 40**  
**Non-metals in Biology-IV**

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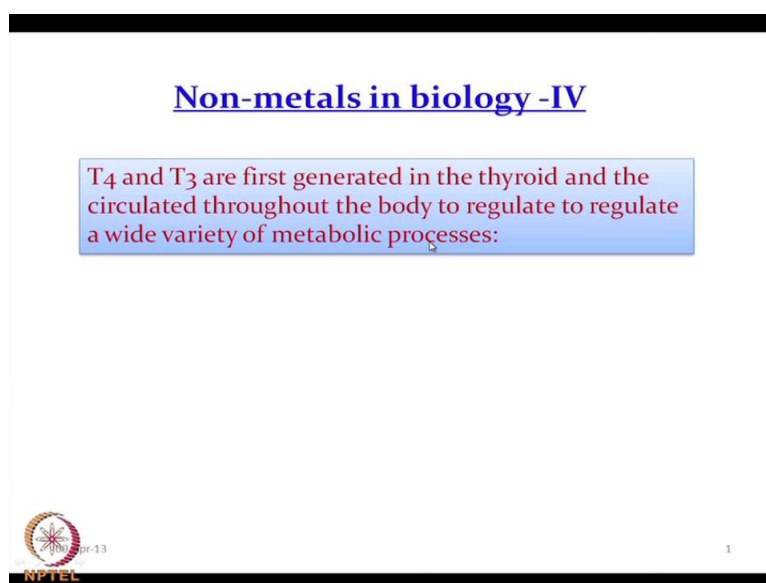


A very good morning to everybody; so today in this concluding class, we will just basically finish off the remaining part on non-metals. And this is basically what we are continuing the 4th part of the present syringe. So, in this particular one, the remaining one what we are talking about how iodide is assimilated, which is a very well-known thing and we say basically, the common knowledge to everybody that this particular one how it is getting inserted into that enzyme system or the hormone system.

So, next we will see also after finishing this remaining part on iodine and thyroid thing. We will just basically another interesting element which is 'selenium'. So, selenium how it is different? So, along the periodic table, how we can compare this with 2 other members of this group? So, we have sulfur, selenium and tellurium. And so far we know much of these developments have already been taken place for the corresponding bio-organic part or the biological chemistry related to the non-metal. Where, this particular sulfur atom from the cysteine so, it can be present in the minus like cysteine, cysteine and mitholine. But, in this particular case this are functioning as simple donor atoms to different metalizes say iron. So, iron in plus 2 or plus 3 when they bind to this sulfur.


So, basically this particular part is not a truly inorganic part related to the non-metal chemistry to the biology, what it is something where, the sulfur is present and which is bound to the iron centre. So, most of the cases it is they hydride thing where, the properties of the donor atoms as well as the properties of the metal centers can take part in controlling all this biological reactions and compare to that the nature of the selenium atom is related to different compare to sulfur. And when selenium is taking control of all this things so, will not talk in terms of its corresponding binding or coordination to any such metal centre like iron in the fears of the ferric state but, the individual thing that means whether this selenium atom how it can control several biological reactions.

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**Non-metals in biology -IV**

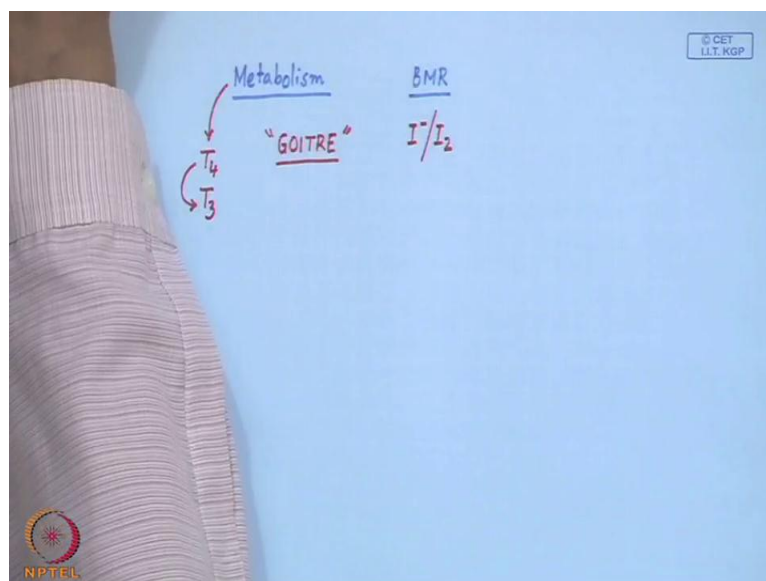
T<sub>4</sub> and T<sub>3</sub> are first generated in the thyroid and the circulated throughout the body to regulate a wide variety of metabolic processes:

 NPTEL

1

So, first will just go back to the remaining part of this non-metal in biology in part 4 where, we are talking about the T<sub>4</sub> and T<sub>3</sub> hormones which are the tetra-hydro form and the tri-hydro form. And already we have seen that they are generated in the thyroid gland and can be circulated throughout the body and regulate wide variety of metabolic processes. So, they are basically required for some metabolic processes.

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So, if we just see that our body metabolism that means, we know the very simple thing that is the BMR which is very important the basal metabolic rate, how we go for the different type of metabolic rate for the anabolism and the catabolism. So, metabolism is definitely depended on these 2 hormones. So, it is the  $T_4$  initially form, who is last life is very high and the active one, the derived one from the  $T_4$  which is the  $T_3$ .

So, it can control the metabolism so is very much depended on notable for the deficiency related disease like 'goiter' but, it can also hamper some of our very important and very basic metabolic reaction pathways. So, if our metabolism is getting affected so, we can consider that not only for the expression of these iodine deficiency interims of the disease goiter but, also the metabolism pathways can also be hampered. So, if we can have some defective metabolism pathways or the defective or the different BMR rate what we are expect then, we can control the corresponding role of the iodine as well as the iodide ion in all this biochemical processes.

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**Non-metals in biology -IV**

T<sub>4</sub> and T<sub>3</sub> are first generated in the thyroid and the circulated throughout the body to regulate to regulate a wide variety of metabolic processes:

- 1) Basal rate of metabolism
- 2) temperature regulation
- 3) expression of numerous proteins.

NPTEL


1

So, these are very important for finding the corresponding basal rate of metabolism. So, how the rate of metabolism is getting effected? It is due to the corresponding concentration and the interaction of this T<sub>4</sub> and T<sub>3</sub> molecules for the metabolic pathways. It is also important for regulating our body temperature because these temperature dependent reactions, rate of the reaction all we know from the thermodynamic and kinetic point of view, we know that the reaction is enhanced when the body temperature is increasing or the reaction temperature is increasing.

Similarly, when all these biochemical reactions are taking part in our system and if we can go off a temperature state from one to other so, for 1 degree or 2 degree rise in temperature the corresponding rate of the reaction or this rate of metabolism reaction in fact is also getting changed. So, for the temperature regulations as well as the rate control for the metabolic pathways are also depended on iodine. And it can also be important for expressing their role in the synthesis of different protein molecules. So, protein molecules are also depended on the corresponding deficiency of iodine and the corresponding related hormone molecules for their synthesis.

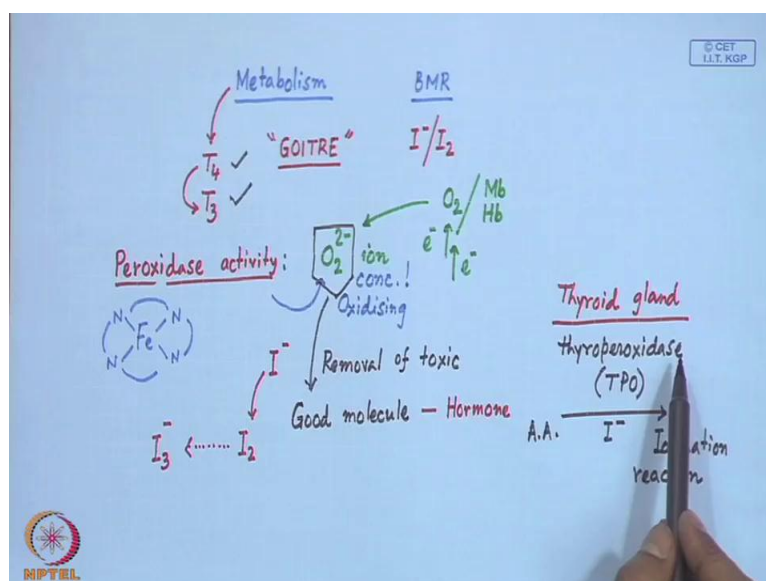
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Through a reaction with the enzyme thyroperoxidase, iodine is bound to tyrosine residues in the thyroglobulin molecules, forming moniodotyrosine (MIT) and diiodotyrosine (DIT).



2

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So, what we see that when we have the reaction we basically bring something that means what we know all the peroxidase activity which is very important. So, whenever we have something that means, the peroxidase activity in taking place that means we are just handling these  $O_2^{2-}$  iron, the peroxide iron and we all know that during our respiration and all we consume this the oxygen molecule which is very important for our very survival and which initially can be taken up by the corresponding myoglobin and the hemoglobin molecule.

The heme proteins, they are basically responding of binding this  $O_2$  and in some process is if we can transfer electrons. So, if we can transfer more than 1 electron so, electron 1 and electron 2 if we can inject into the anti-bonding orbit of the  $O_2$ . That means, if we have the different molecular orbital's also of the  $O_2$  molecule and if we can feed this electrons to those anti-bonding orbitals else will find that we can convert it to the peroxide iron. So, peroxidases are also they are also if can considered this peroxidase activity which can attack on the generation of this peroxide iron and you can responsible for the destruction of the peroxide iron because the accumulation of peroxide iron in leaving organisms in our body, in animals body, in humans body are very important because they are pretty strong oxidizing agents. So, these are oxidizing in nature.

So, if we want to get rid of the accumulation of peroxide iron that means, the concentration, there concentration is important. So, if we want to go for the destruction of the peroxide iron we always take the help of the peroxidases. But, the standard peroxidases what we can have which basically these are based on iron parafiring micro-cycle. So, iron parafiring micro-cycle is there that means, the heme proteins are there and heme proteins are responsible for both peroxidase and the catalyst activity. So, this iron centre peroxidase activity was known to us and we have studied earlier for this peroxidase activity but, this particular activity is very much required for the destruction of peroxide iron.

So, it is a very important pathway for the destruction of this peroxide iron and if that particular destruction we can utilize for some useful function we can utilize for some useful function that means not only the removal path, the removal of toxic peroxides form the system, from the leaving organisms is important and at the same time if we are able to see some peroxidase activity for the synthesis of some good molecule to our system. So, if we are able to synthesize some good molecule at the expense of peroxidation.

So, will find that some molecule. So, in this particular case if we are able to make the hormone, the  $T_3$  and  $T_4$  molecules if we are able to make with the help of this peroxide. So, what we take? We just basically take the iodide ion, iodide ion through its reaction with hydrogen peroxide is basically liberating or ((ins)) to generating the iodine molecule and sometime like our laboratory process is also this iodide oxidation while

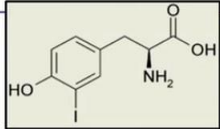
producing the iodine molecule can also be trapped within this particular species forming tri-iodide ion.

So, all these things will be equilibrium concentrations than relative ratios will be there for the iodide, iodine, tri-iodide depending upon the individual concentration of all these species and depending on the starting iodide concentration into the medium, how much iodide you are getting through the food material or through the salt intake what we are utilizing for our intake along with that of our sodium chloride. So, this particular peroxidase activity can be very useful if we just relate it to the thyroid gland. So, in thyroid gland if we can have the corresponding molecule which is available, which is readily going for the corresponding oxidation of  $I^-$  to  $I_2$ , we get the corresponding molecule as thyro peroxidase.

So, the thyroid gland which bears and which shows the corresponding peroxidase activity is the corresponding thyroperoxidase. So, this particular thyroperoxidase so, thyroperoxidase is there so, which is TPO the thyroperoxidase. So, any such conversion so, if we have the amine acid on the left and we have iodine as iodide ion so, we can go for the corresponding iodination reaction. So, iodination reaction can take place with the help of these TPO molecules. So, the generation of these  $T_4$  and  $T_3$  molecules are therefore, dependent on the availability of these thyroperoxidase.


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Through a reaction with the enzyme thyroperoxidase, iodine is bound to tyrosine residues in the thyroglobulin molecules, forming moniodotyrosine (MIT) and diiodotyrosine (DIT).



Coupling of two DIT units produces thyroxine.  
Combining one MIT with one DIT produces  $T_3$ .

Proteases digest iodinated thyroglobulin, releasing the hormones  $T_4$  and  $T_3$ , the biologically active agents central to metabolic regulation.



2

So, when we see that the enzyme which is available now to us is a thyroperoxidase and we have to attach the iodine to the tyrosine residues of the long amine acid based protein chain or the polypeptide chain which is present in thyroglobulin molecules in thyroid gland. So, the iodination can take place if the corresponding phenol range of the tyrosine amino acid is going for the corresponding iodination reaction at one position we get moniodotyrosine molecule and if it goes for the corresponding substitution of hydrogen atom by 2 iodine atoms on the ortho-positions of the hydroxyl group of the phenol range we get the diiodotyrosine molecule.

So, the effect of these reactions for the thyroperoxidase on iodine or iodide ion is basically generating the MIT and the DIT molecules. So, we just produce the MIT and the DIT molecules to us and this is the corresponding moniodotyrosine reaction on the thyroxine residue and if we can go for this particular substitution also we get the corresponding di-iodination molecule. So, tyrosine is basically now is giving for the MIT molecule and the DIT molecule.

So these MIT and DIT molecule in turn can go for the synthesis of the T<sub>4</sub> and the T<sub>3</sub> molecules in the reaction medium. So, when we have these DIT units and 2 such DIT units when they couple together they produce thyroxine. So, thyroxine molecule what we know that it has 4, basically 4 positions which are occupied so, this is the bis-phenol unit. Thyroxine as we have discussed in our previous class that it is a bis-phenol unit. So, we will have 4 phenol positions which are ortho to the OH group or the O group as they either.

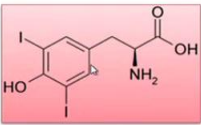
So, all these four position can be iodinated to produce the T<sub>4</sub> molecule and when we combine 1 MIT with 1 DIT it can produce the T<sub>3</sub> molecule, which is much more effective molecule in terms of the corresponding thyroid activity compared to the corresponding T<sub>4</sub> analog because we always get the T<sub>3</sub> molecule from T<sub>4</sub> through di-iodination reaction. So, there also we should take the help of diiodinases, is a selenium based molecule that we will discuss in this class today only.

So, these particular cases we just get than some proteases which are responsible for the hydrolysis of the long protein molecule. So, they digest the iodinated thyroglobulin. So, thyroglobulin is getting iodinated through the use of thyroperoxidase molecule and this iodinated thyroglobulin molecule when we have the corresponding formation of the bis-



phenol unit of the thyroxine residue. We have already formed T<sub>4</sub> and T<sub>3</sub> units through coupling of 2 DIT and 1 MIT. So, both T<sub>4</sub> and T<sub>3</sub> molecules are already found. They are already present in the thyroglobulin molecule as colloid and these 2 both are biologically important molecule, biologically important agents to central metabolic regulation that means, it can control the corresponding metabolic pathways and metabolic rate also. So, when they are formed inside within the thyroglobulin, they can be eliminated to the blood stream.

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DIT is a modulator of thyroid peroxidase. When combined with monoiodotyrosine in the colloid of the thyroid follicle, triiodothyronine is formed.

The chemical structure of Diiodotyrosine (DIT) is shown, featuring a benzene ring with two iodine atoms at the 3 and 5 positions, a hydroxyl group at the 4 position, and a side chain at the 1 position consisting of a methylene group, a chiral center with an amino group (NH<sub>2</sub>), and a carboxylic acid group (COOH).

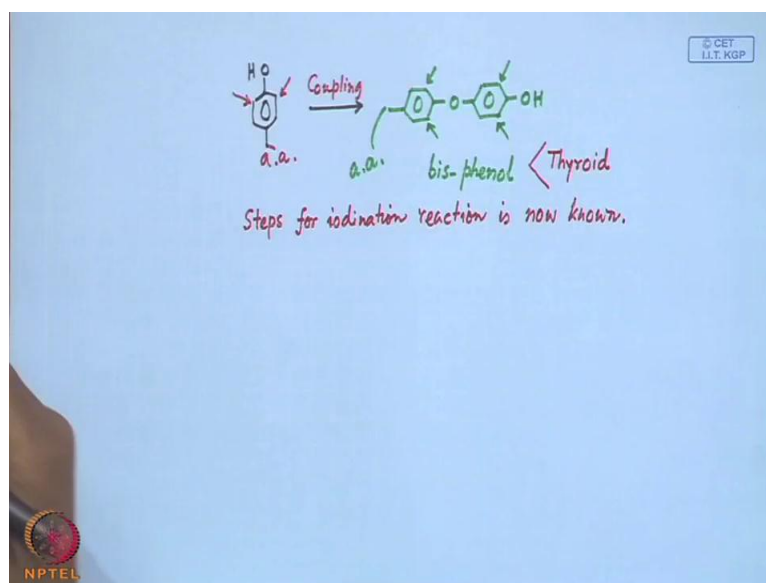
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So, this is the second molecule which is the DIT molecule. So, the previous one was this is mono-iodinated one and the second one is basically that di-iodinated product. So, when they are forming inside the thyroglobulin molecule they go for the corresponding condensation. So, what we see is a very simple reaction like that of our phenol is dependent phenol unit only because this is the glysin part. So, glysin part which is the aminose part. So, aminose part which is substituted the para-position of the phenol. So, these 2 groups are basically responsible for the iodination reaction simple iodination reaction of the phenol unit.

The way we are discussing that the bromination reaction also if we can have the corresponding mixture of bromide and bromate or the elemental bromine we can go for the corresponding bromination reaction of simple unit in the laboratory to give us the corresponding tri-bromo phenol or picric acid. So, this DIT molecule can bind with

another DIT molecule giving us the T<sub>4</sub> molecule. So, the roots are well known and well established so this DIT molecules are also known as the modulator of thyroid period oxidize because they are basically combined with itself or another MIT molecule in the collide of the thyroid follicle and triiodothyronine is formed when this DIT molecule is attaching with another MIT molecule. So, once these are formed and then only we can go for the corresponding coupling.

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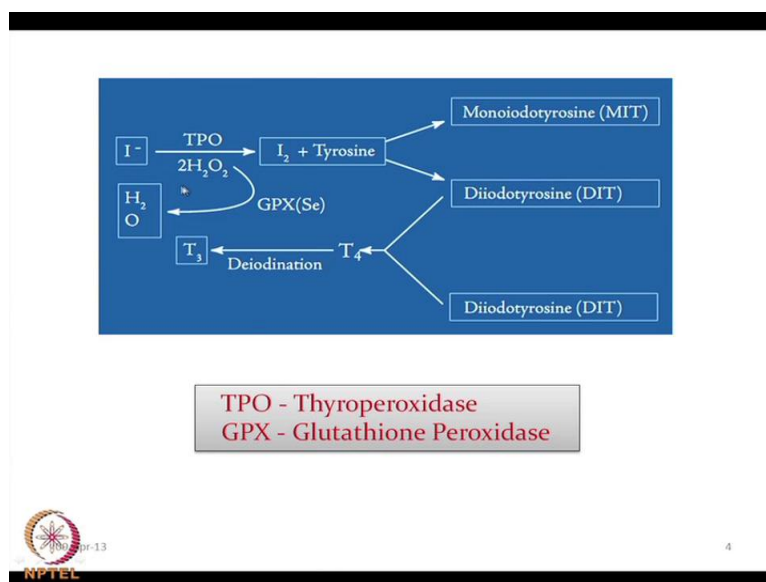


So, this is basically some kind of very simple and well known reaction for this is a substituted one. So, if you have the phenol so, formation of T<sub>3</sub> and T<sub>4</sub> is mainly responsible for the formation of the corresponding bis-phenol unit. Like in the polymer chemistry what we see that it is possible to go for the corresponding bis-phenol molecule. so, this is basically the simple backbone where, we have the amino acid fragment at the para-position, we can have the positions for iodination. These are the positions for the different iodination. So, this entire molecule what we get is the corresponding bis-phenol molecule. So, basically we have like the polymer formation, we have the corresponding bis-phenol unit and the formation of these bis-phenol unit is interestingly taking place in our typical body in our some active gland which is the corresponding thyroid gland.

So, the thyroid gland is therefore, responsible for this particular phenol phenol coupling reaction to give us the bis-phenol unit. So, this phenol phenol coupling reaction is taking

place when we have the iodinated form on this is the amino acid substituted part. It is not that this phenol is forming then we go for the iodination. So, the step for the iodination is well known and well established now. So, the corresponding steps for iodination reaction are now known. This is therefore, known to us.

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So, what we get if we just consider the entire picture that we have some iodide ion which we are taking as a salt or as the food material and for these we want to produce the corresponding iodine molecule and this iodine molecule is produced only with thyroperoxidase activity. So, this thyroperoxidase activity is giving us because we have some accumulated hydrogen peroxide in the system.

So, always we depend on some amount of hydrogen peroxide and in some way it is also beneficial to us. Also, it is showing the corresponding peroxide activity destroying the accumulated concentration of hydrogen peroxide in the leaving organism. So, we have thyroxin and iodine is there. So, these can give rise to two such molecule that is diiodotyrosine and monoiodotyrosine. So, these are completely different from the T 3 and T 4 molecules, that the first step is typically that the tyrosine molecule is iodinated and when we go for the binding of these 2 DIT molecules we get the T 4 molecule and when 1 DIT and 1 MIT is attacking so, when these two basically the MIT and the DIT molecule that the monohydrotyrosine and diiodotyrosine are reacting to each other we

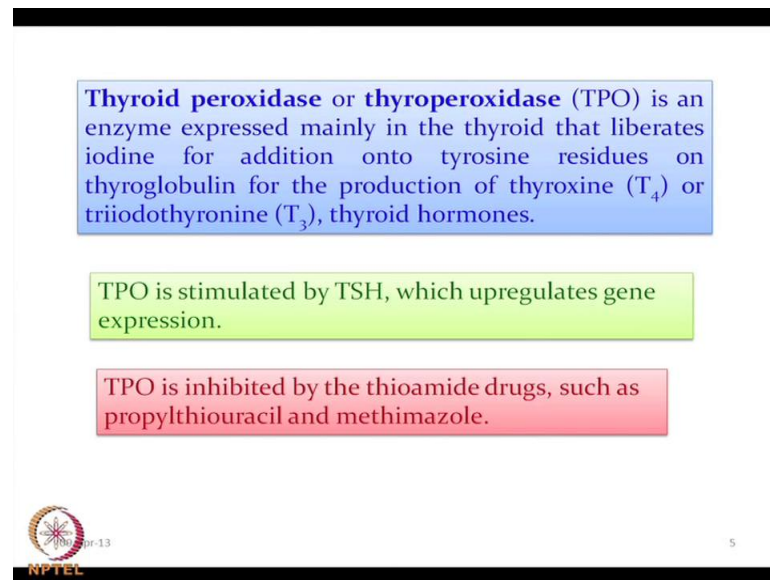
get T<sub>3</sub> directly. But, that also can be controlled by the leaving organism but, the most stable species what we have seen what we are discussing from our previous class.

The T<sub>4</sub> is the most stable thing and when the concentrations of these DITs are higher compared to MITs because the formation of T<sub>3</sub> is dependent on the formation of the corresponding amount of the MITs in the system. But, if the concentration of these MITs is less compared to the DITs we will only go for the corresponding formation of the T<sub>4</sub> species and T<sub>3</sub> is more active. So, this T<sub>4</sub> can we consider some time as the pro-hormone. So, parathyroid hormone which can be activated if we know that the corresponding T<sub>3</sub> through once step deiodination reaction can give rise to T<sub>3</sub> and T<sub>3</sub> is much more active than T<sub>4</sub> than selenium containing enzyme which is deiodinase. So, deiodinase is there operating on T<sub>4</sub> to give rise to the required amount of T<sub>3</sub> molecules.

So, we are basically handling on some of these molecules where, we are talking in terms of 2 peroxidases. So, apart from the iron bearing peroxides also so, studies on iodine and biology. So, what we are studying so far is the corresponding reaction of this iodine in biology and we find that not only we are studying the corresponding incorporation iodine in the biological molecule but, also we are talking some amount of its corresponding peroxides activity. So, when we have the TPO molecule the thyroperoxidase molecule we see that the corresponding TPO is responsible for its corresponding enzymatic reaction for the generation of MIT and DIT molecules.

And in other case because we see that selenium bearing peroxides is also there which is responsible for another interesting anion in base species which is glutathione. So, sulfur oxidation can take place so, we can have the corresponding glutathione peroxides. Since, we are talking in terms of the corresponding peroxides activity we see that whenever we have this H<sub>2</sub>O<sub>2</sub> the peroxides can operate or act on this hydrogen peroxides to form water molecules. So, if it is thyroperoxidase which is utilize for the hormone production and if it is glutathione peroxide it will basically go for the destruction of the corresponding simple peroxide molecule. So, both the peroxides are basically working or destroying the corresponding accumulation of hydrogen peroxide H<sub>2</sub>O<sub>2</sub> within the system.

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**Thyroid peroxidase or thyroperoxidase (TPO)** is an enzyme expressed mainly in the thyroid that liberates iodine for addition onto tyrosine residues on thyroglobulin for the production of thyroxine ( $T_4$ ) or triiodothyronine ( $T_3$ ), thyroid hormones.

TPO is stimulated by TSH, which upregulates gene expression.

TPO is inhibited by the thioamide drugs, such as propylthiouracil and methimazole.

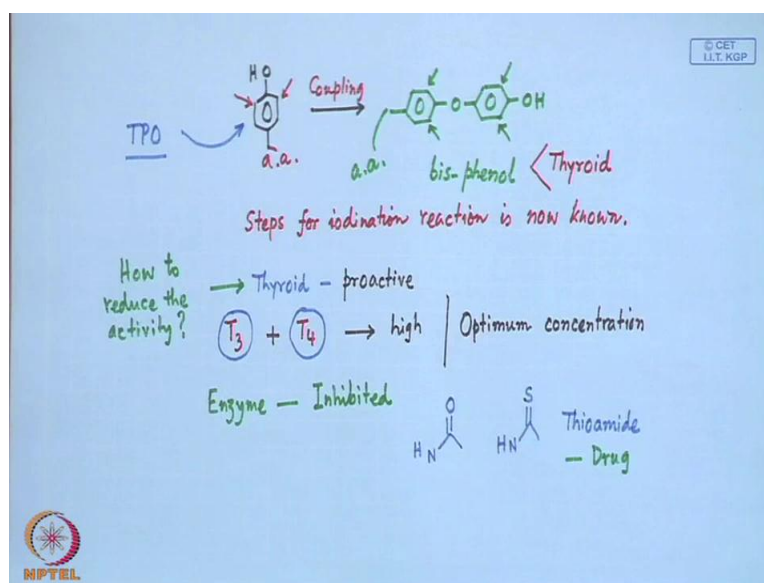
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So, this TPO is also known as thyroxidase, the thyroid peroxidase or thyroperoxidase. Therefore, is an enzyme it is expressed mainly in the thyroid that liberates iodine what we have seen just now; For the addition onto tyrosine residues on thyroglobulin for the production of thyroxin and triiodothyronine that means the 2 thyroid hormones the T 3 and T 4 and formation of their individual component that means the formation of the T 3 and T 4 are typically dependent on the corresponding TPO molecule that means the thyroperoxides molecule.

And sometimes this TPO molecule is also is stimulated by TSH, the thyroide stimulating hormone one such hormone is also there. That thyroid stimulating hormone which is basically activating the TPO and TPO can inturn act on the iodide ion for the production of iodine for the thyroxin synthesis. And this particular upregulates the corresponding gene expression so, TPO has some inter relationship that of thyroid stimulating hormones TSH for the production and for the corresponding gene expression as that we can produce the required quantities or required amount of TPO as well as TSH molecules. So, we see that it sometimes is required that means if we can have something that means our thyroid gland is proactive, is activity, is more and which is producing more amount of the corresponding thyroid hormone thyroxin and triiodothyronine.

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So, if the production of T<sub>3</sub> and T<sub>4</sub> as we have seen, it can control the corresponding metabolic rate of our body. So, if the corresponding production if they are producing in higher concentration that means the gland, the thyroid gland the thyroid gland we have and if the thyroid gland is proactive, activity is more and both these 2 that means, the T<sub>3</sub> and T<sub>4</sub> concentration is high.

So, what in that particular case what we can do because the production of hormone in our system in our body should be balanced it must have some optimum concentration. If the concentration is less we have some symptoms, some corresponding disease symptom and if the concentration is high we can have another type of diseased condition. So, both are not good for our system that means, high concentration of T<sub>3</sub> and T<sub>4</sub> on the low concentration of T<sub>3</sub> and T<sub>4</sub>. We must have some optimum concentration for all these molecules.

So, if it is a proactive and it is producing more and more the corresponding T<sub>3</sub> and T<sub>4</sub> molecules so, what we can do is we just can go for the reducing the activity of these thyroid gland. So, how to reduce the corresponding activity of the thyroid gland? Such that we want to produce less amount of T<sub>3</sub> and T<sub>4</sub> molecules in our blood strength. So, if we know the entire mechanism of formation of this corresponding T<sub>3</sub> and T<sub>4</sub> molecules and which particular molecule is very important for the synthesis and how the

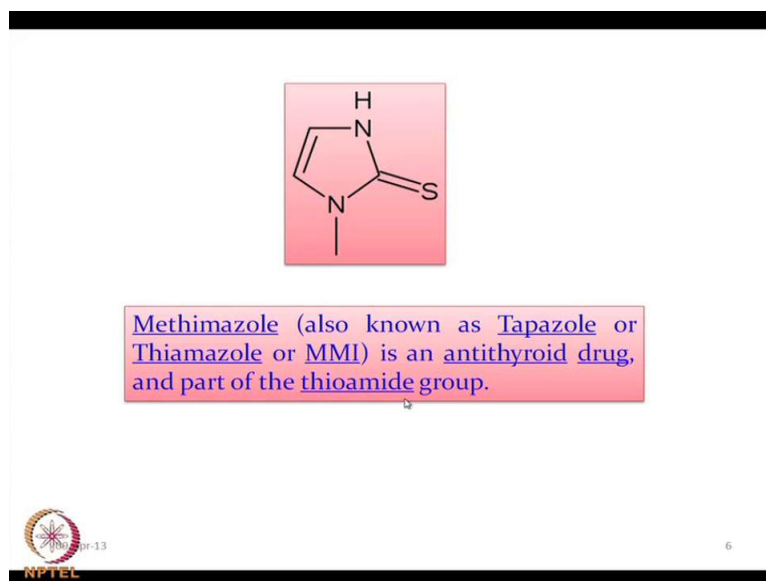
enzymatic reaction is taking place. So, for us it is therefore, is very important pathway that we can control the corresponding enzymatic path.

That means, the enzyme which is there and which is available for the production of T 3 and T 4 molecule should be inhibited that means, if we can go for the corresponding inhibition of the enzyme activity we can reduce the corresponding production of T 3 and T 4 molecule. For the typical adulation reaction on these 2, 4 positions we see that the corresponding tyrosine amino acid it can be iodinated and we can go for the corresponding thyroperoxidase TPO and this TPO is acting on this corresponding, corresponding tyrosine residue and this (( )).

So, if we go for something the mechanism where we can reduce the activity of these TPO only. So, how to slow down the corresponding reaction for this TPO molecule we can have some mechanism for that and we can go for the corresponding inhibition reaction. So, the inhibition of TPO is therefore, can be done by the use of some thioamide drugs. So, we can have some position where, these groups are available and these thioamide drugs can be considered as the corresponding binding of these TPO units. And what are those thioamide drugs? These are basically the corresponding propylthiouracil and methimazole units.

So, these are very small molecules and in some thioamide backbone. So, the enzyme inhibition can be taken place if we can have we all know that amide function is C O N H. This is our typical amide function and thioamide will have sulphur group because this oxygen cannot react so nicely with all these enzymes active sides but, the sulphur can interact and bind inside the corresponding enzyme active side. So, this thioamide type of molecules it can be small ring molecule also. So, thioamide, thioamide tiresome molecules can be utilized for the corresponding high activity the thyroid gland and those gland be used as the corresponding drug molecule. So, they are basically good inviter molecule. So, thioamide type of design is important for inhibit in the corresponding TPO activity.

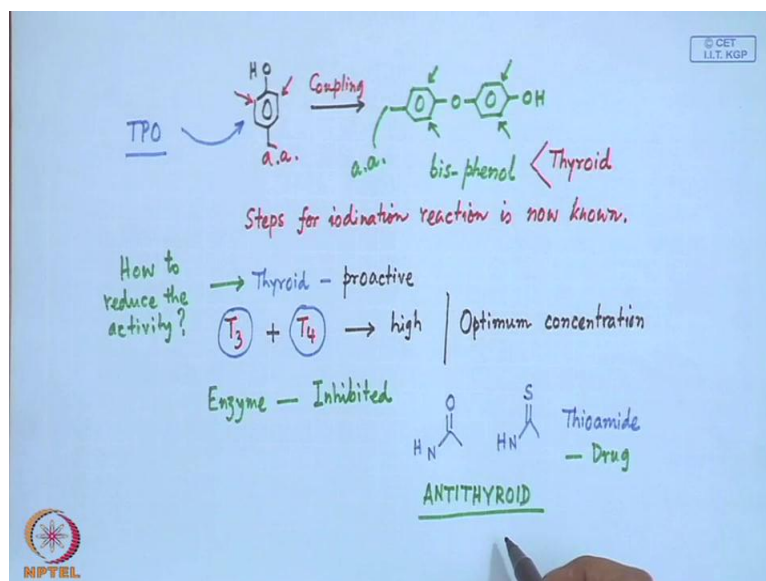
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So, what is that particular molecule? So, one such example is that this is the corresponding molecule where, we have can see the double bond S N H function. This particular part is the thioamide part and they basically go inside the corresponding enzyme the TPO enzyme. And basically what happens that this particular sulphur is a very good unit it can go for some hydrogen bond in interaction or it can bind the some other group. So, through sulphur it is starting inter acting with their and through this N H because this N H can also be a very good hydrogen bonding donor. So, if within the enzyme structure some hydrogen bonding acceptor is present. So, this hydrogen can go for inter acting that particular side through hydrogen bonding. So, both sulphur and this N H function can go and interact with that of our TPO molecule and it is no longer available for it is activity for iodide oxidation. So, thioperoxide activity can be inhibited by this sort of small molecule which is known as the corresponding MMI type where, the basic backbone should have always the thioamide group.

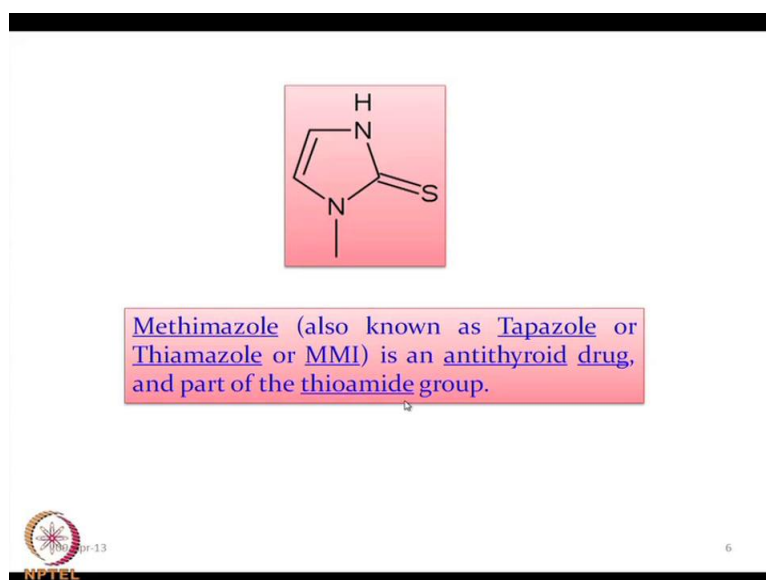


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So, this thioamide drugs are therefore, known as a very important type of drug molecule which is known as anti thyroid drug is a known as anti thyroid drug. So, if we want to reduce the corresponding activity of the thyroid gland for the production of thyroxine and triiodo thyronine, we should have some thioamide base drugs which are known as the corresponding anti thyroid drug.

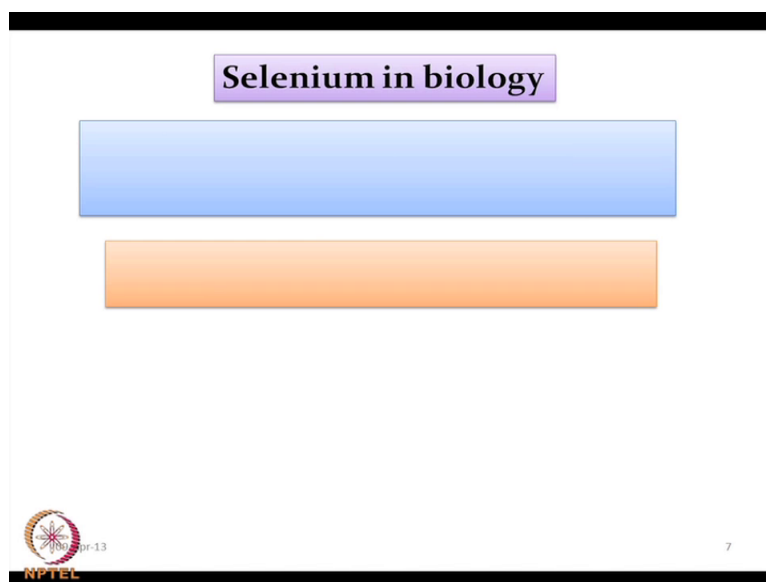
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So, one is known as methimazole is also known as tapazole or thiamazole. So, sulphur bearing thiamazole type of bearing is because this is the nitrogen nitrogen bearing 5

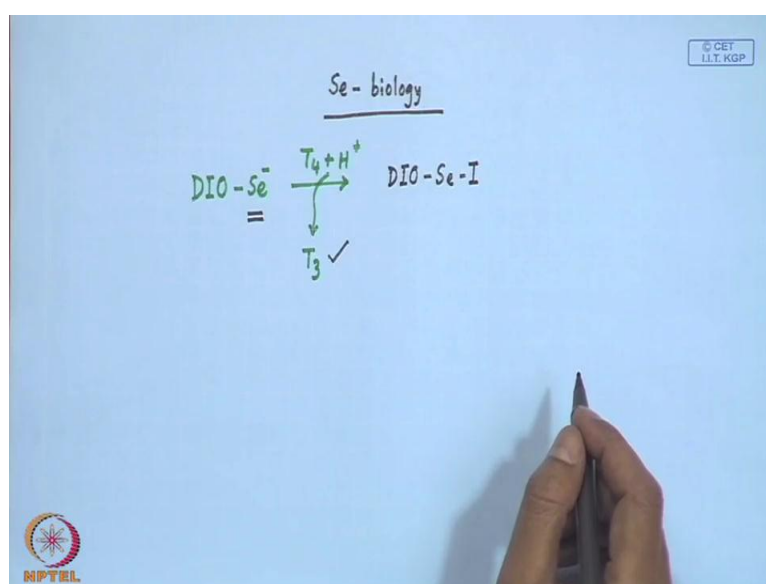
members bearing without this sulphur we know that these are known as the imidazole and if we see that double bond S group is present between these 2 nitrogen atoms we can considered these are thiamazole. So, thiomazole is the corresponding drug and this drug can inhibit the corresponding TPO activity.

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Next, we will just go for the remaining part before we just conclude this class for all these activity for the metal ion activity for the non-metal centers also.

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So, in this particular case we will find their how we can go for the involvement of selenium in the biological systems. So, selenium biology. So, for we have seen for the different deiodinase reactions and all the reactions that will in case of the corresponding production of T 3 from T 4 we have seen in our previous class. That means, we can go for diiodinase activity and that diiodinase activity is basically responsible for the presence of selenium in the group.

So, when selenium is present over there and if it reacts with T 4 plus proton it basically go for the production of T 3. So, diiodine is basically is a selenium bearing molecules that is why it is very interesting group of molecules which are present their so, we should have selenium in our food intakes. Selenium is therefore, essential micro nutrients for our body for the right production of the T 3. So, the formation of T 3 is dependent upon iodine, formation of T 3 dependent on TPO molecule and also this formation of T 3 is dependent on the selenium. So, if the selenium groups are not present that much, we can go for the shortage of the corresponding deiodinised molecule and we cannot get the corresponding right amount of T 3 from the system. So, diiodine is we can have the selenium and which basically is trapping the corresponding iodized group for the corresponding redox reactions for the formation of T 3 from T 4.

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**Selenium in biology**

Se is an essential micronutrient for animals. In plants, it sometimes occurs in amounts toxic as forage, e.g. locoweed.

Selenium is a component of the amino acids selenocysteine and selenomethionine.

In humans, selenium is a trace element nutrient that functions as cofactor for glutathione peroxidases (GPx) and certain forms of thioredoxin reductase (Trx).

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So, this particular one therefore, we can considered as a very useful micro nutrients for animals, for human being, in some plants. It is basically occurs in amounts which are

toxic as forage or locoweed. But, it is very important component for the amino acids selenocysteine and selenomethionine. We know the cysteine molecule, we know the methionine molecule and the cysteine molecule and the methionine molecule when they are attaching to the corresponding selenium atom we get the corresponding selenocysteine and the selenomethionine molecule.

And we have been discussing very much about the corresponding other peroxidases that means, the TPO and we have also discussed the corresponding consumption of the hydrogen peroxide by glutathione peroxidase. But, in our body if selenium, what we can have as trace elements from the food material may mostly and it functions co-factor for glutathione peroxidases that means, the selenium is present in glutathione peroxidase and in certain forms of thioredoxin reductase. This is redox reaction like ubiquinol and ubiquinone molecule and is sulphur bearing redox reactions can take place so, a very group of molecules are known as thioredoxin reductase molecule.

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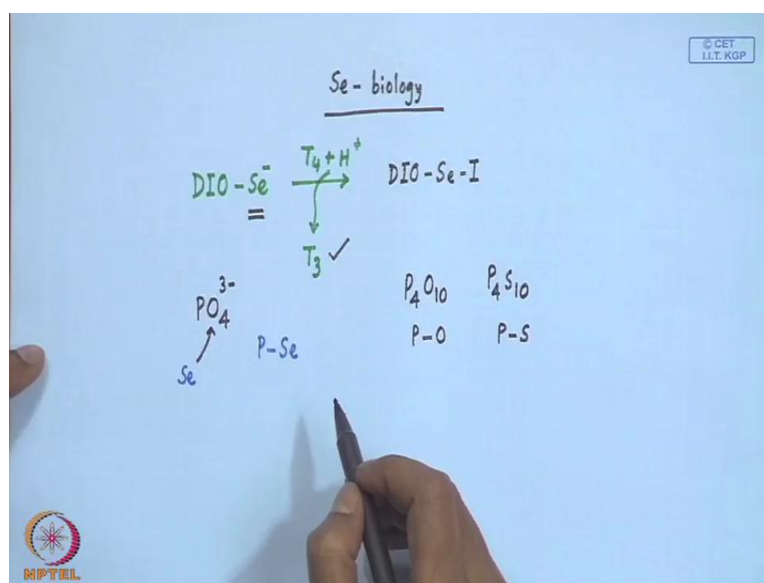
Selenium-containing proteins are produced from inorganic selenium via the intermediacy of selenophosphate ( $\text{PSeO}_3^{3-}$ ).

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NPTEL logo and 'pr-13' are visible in the bottom left corner. A small number '8' is in the bottom right corner.

So, selenium what we can have, selenium containing proteins we all get also can be produced from inorganic selenium salts like that of sulphur bearing salts through the involvement of selenophosphate.

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So, we see that if we have the phosphate groups we all know which is  $\text{P O}_4^{3-}$  and if we are able to go for the substitution of 1 oxygen by sulphur we get the corresponding thiophosphate groups for the inorganic one also because if we all know that  $\text{P}_4\text{O}_{10}$ , the corresponding phosphorous pentoxide, dimeric form of phosphorous pentoxide is there. Similarly,  $\text{P}_4\text{S}_{10}$  is also possible that means, oxygen atoms can be very nicely be substituted by sulphur groups. Here, we have phosphorous oxygen bonds here, we have phosphorous sulphur bonds. So, in the same fashion if we are able to go for the substitution of one of the oxygen atom by selenium we get the corresponding selenophosphate. That means, we have phosphorus attach to selenium and 1 oxygen less that means the 3 oxygen atom but, though all charge on the of species would be 3 minus till. Therefore, you see that in this particular case in this selenophosphate we have the relevant phosphorus selenium bound.

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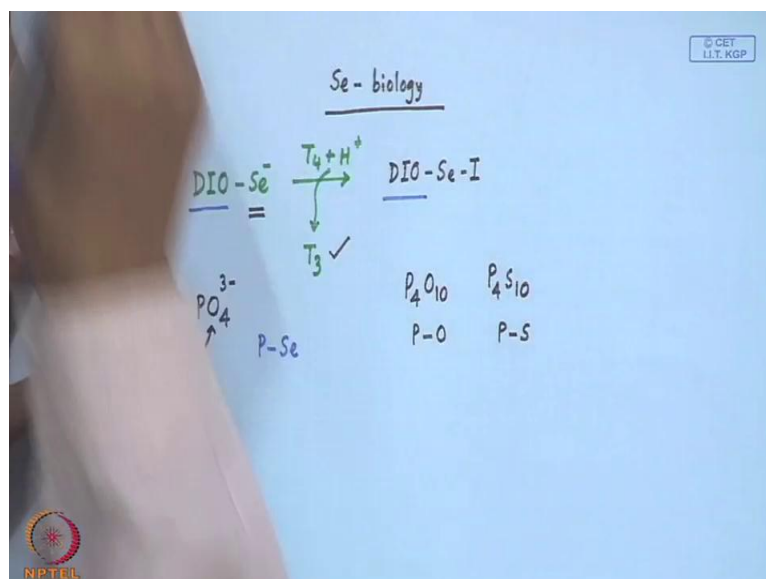
Selenium-containing proteins are produced from inorganic selenium via the intermediacy of selenophosphate ( $\text{PSeO}_3^{3-}$ ).

**Deiodinases:** As mentioned earlier, Se also plays a role in the functioning of the thyroid gland. It participates as a cofactor for the three thyroid hormone deiodinases.

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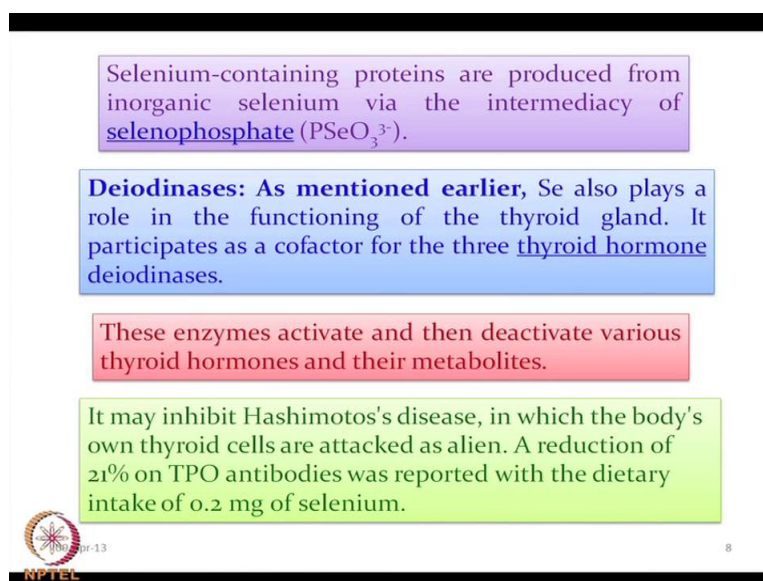
Selenium is happening in the formation of selenosisten and selenometonin molecule. So, as we have seen earlier mentioned in our pervious class also that in deordinases selenium is present for the removal of iodine.

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In this DIO molecule, in this particular DIO molecule selenium is present which is taking of this iodine.

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Selenium-containing proteins are produced from inorganic selenium via the intermediacy of selenophosphate ( $\text{PSeO}_3^{3-}$ ).

**Deiodinases:** As mentioned earlier, Se also plays a role in the functioning of the thyroid gland. It participates as a cofactor for the three thyroid hormone deiodinases.

These enzymes activate and then deactivate various thyroid hormones and their metabolites.

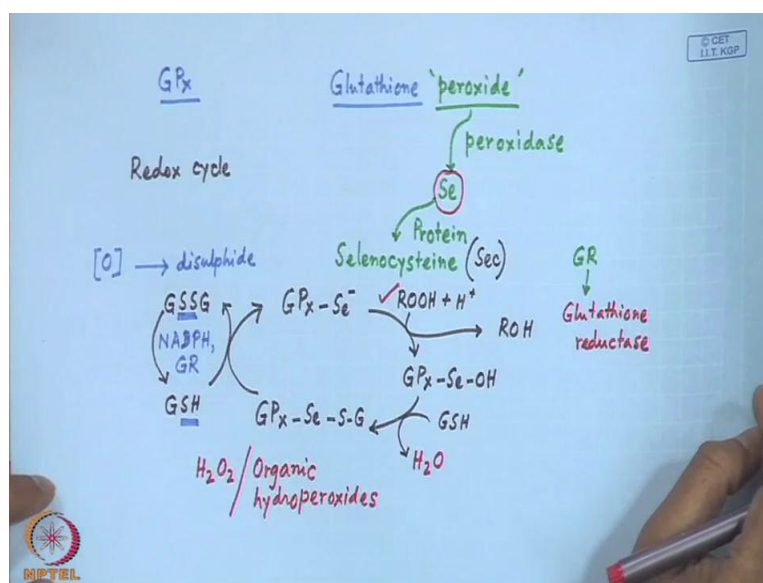
It may inhibit Hashimoto's disease, in which the body's own thyroid cells are attacked as alien. A reduction of 21% on TPO antibodies was reported with the dietary intake of 0.2 mg of selenium.

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So, it basically it is playing the corresponding functional role in the thyroid gland otherwise, we will not be able to produce the right amount of T<sub>3</sub> molecules from the T<sub>4</sub>. It participates as a cofactor for the 3 thyroid hormone deiodinases. So, there are 3 types of deiodinases which are responsible for the production of the right amount of T<sub>3</sub> from the T<sub>4</sub> molecules. These enzymes activate then deactivate the various thyroid hormone and they are metabolites. So, with these enzymes basically first we go for the iodination reaction and for the deiodination reaction we will use the corresponding deiodinases. And sometime it may inhibit the hashimoto's disease in the body's own thyroid are attacked as alien.

That if we have the thyroid cell and we all know that the thyroid cells are utilized for the production of the corresponding amount of throsine molecule, the hormone molecule. But, in some cases this particular one that means this particular one that means this particular thyroid cell can be taken as a alien that means it is unknown to them, unknown to the system. So, the reduction of the 21 percent of TPO and antibodies, which are the antibodies of the corresponding peroxide is reported an in that condition is also is not a good condition which is a disease condition. We should have some dieted intakes that means, through our food material in the form of food or in some other condition as solved also, we can take at least 0.2 milli gram of selenium in our system. So, this particular selenium presence of this selenium which is very important for this non biological part as well as the biological part.

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So, the first and foremost corresponding selenium enzyme which has been identified is the corresponding glutathione peroxidase, which is operating on the glutathione molecule which is a very important antioxidant molecule. So, if we have the first enzyme which is glutathione peroxidase, it can show the corresponding peroxidase activity. So, this particular peroxidase activity will see that the deiodinase activity is dependent on the corresponding presence of the selenium. So, peroxidase activity is also used the corresponding involvement of the corresponding selenium group.

So, this GPx glutathione peroxidase is so, glutathione peroxidase is operating on peroxide. So, its corresponding activity is the peroxidase activity which is also bearing the selenium atom. So, when we have the selenium atom, this is incorporated within the protein chain which is basically incorporated within the protein chain and in the form of selenocysteine residue. So, if we have the corresponding selenocysteine residue, this is within the protein, how it is going to incorporate the protein chain as selenocysteine.

So, like cysteine which we abbreviate as CYS, we abbreviate this as which is selenium and cysteine. So, we have the selenocysteine residue in the protein chain like that of our selenocysteine residues. So, those selenocysteine residues are responsible for the corresponding catalytic redox cycle. So, basically redox reaction means the oxidation and the reduction can take place. So, we can have the corresponding catalytic redox cycle involving glutathione and the glutathione reductase.



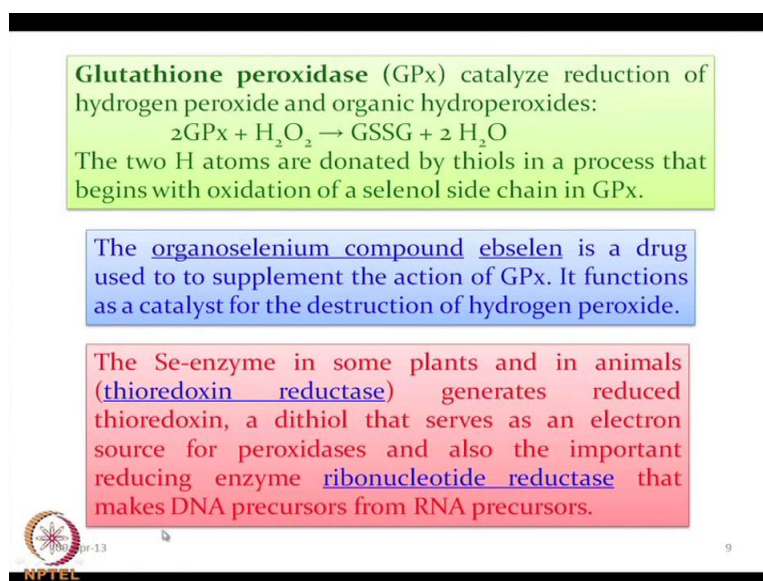
So, it is basically oxidized in this particular form. So, when this sulfur bearing compound corresponding glutathione is present is basically in the reduced form it is giving the G S H and in the oxidized form it is giving the G S S G form and when these are basically coupled with that of our glutathione peroxidase bearing selenium group which is acting on the organic alkyl peroxide in presence of proton forming the corresponding RO H group and our G P x is forming a Se OH that means, the selenol is forming.

So, these selenol is forming over there and the corresponding selenic acid is also there and this basically going for the corresponding G P x than the selenium group bearing thing that means the S minus. So, when it basically goes for the corresponding reaction with this G S H so, if we have the G S H is there which is coming from this side and this G S H so, G S H is go and attack to this particular selenium bearing glutathione peroxidase. So, it is forming the S and G group. So, what we see that in this cases that means the corresponding formation of the sulphite sulphite bound.

That means, the disulphide unit and we all know how does these disulphide unit are forming these disulphide unit are basically forming through oxidation of this thiol group. So, if we have S H, S H unit which can be oxidized to S S unit. The redox equivalent can be stored inside the molecule, in the same way that glutathione peroxide is basically acting that means, the inside the molecule itself can go for the corresponding transfer for these sort of S S formation with the use of N A D P H and G R which is glutathione reductase.

So, this peroxidase activity of this is dependent on the involvement of G R also, G R is our glutathione reductase and we get all these things. So, this particular formation of this selenic acid and the corresponding hydrogen peroxide is getting destroyed through the production of water molecule and through the consumption of these hydrogen peroxides and anionic form is again regenerated through this particular cycle. So, is basically working on the corresponding glutathione molecule and is basically consuming the corresponding hydrogen peroxide or the different organic hydro peroxide or organic this one this organic hydroperoxides. This hydroperoxides is basically consume this particular reaction because is a first of this type of enzyme which bears the selenium atom and first discovered word. So, that is why the glutathione peroxidase molecules are so important to know.

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**Glutathione peroxidase (GPx)** catalyze reduction of hydrogen peroxide and organic hydroperoxides:

$$2\text{GPx} + \text{H}_2\text{O}_2 \rightarrow \text{GSSG} + 2 \text{H}_2\text{O}$$

The two H atoms are donated by thiols in a process that begins with oxidation of a selenol side chain in GPx.

The organoselenium compound ebselen is a drug used to to supplement the action of GPx. It functions as a catalyst for the destruction of hydrogen peroxide.

The Se-enzyme in some plants and in animals (thioredoxin reductase) generates reduced thioredoxin, a dithiol that serves as an electron source for peroxidases and also the important reducing enzyme ribonucleotide reductase that makes DNA precursors from RNA precursors.

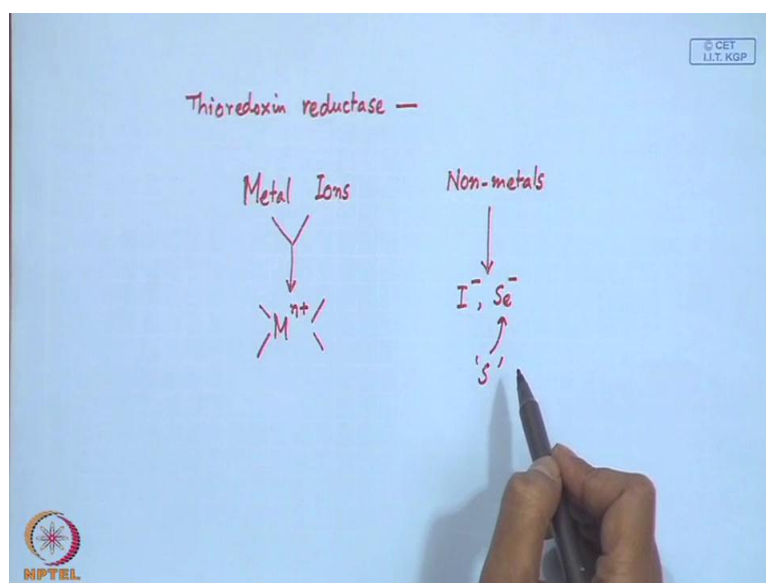


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And the second one which you have already seen the corresponding dehydrogenase is molecules and the third one which is also known which is the corresponding thioredoxin reductase molecule which is the thioredoxin reductase molecule. So, this particular molecule basically goes for this corresponding this is the glutathione peroxidase behavior what we are seen and that organoselenium compound ebselen is also utilized as drug for the corresponding action of this glutathione peroxidase. And the corresponding catalyst is utilized for the generation of this our destruction of this hydrogen peroxide. So, this thioredoxin reductase which is basically another the third type of selenium enzyme which generates the reduced thioredoxin from the dithiol again we get the dithiol and disulfide thing and this particular molecule is very much important for reducing the ribonucleotide reductase which we all know that is basically a selenoenzyme.

But, how we reduce the ribonucleotide reductase is now known is a selenium dependent process here where the ribonucleotide reductase are reduced for the generation of the corresponding RNA molecules, the DNA precursors from the RNA precursors. So, from the ribonucleotide reductase is going for the deoxy ribonucleotide and the deoxy ribonucleotides are incorporated to the corresponding DNA molecules.

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So, all these three types of molecules, what we are seen throughout this particular course that we have started our journey from the involvement of the different metal centers, the metal ions, metal ions in their... When we have the metal ions, we have the corresponding chance for getting this metal ions in the different oxidation states whether it is a  $M^{n+}$  in plus 2 or plus 3, and it is the typical environment.

But when we are talking in the last few classes on non-metals, it is the corresponding non-metal centre like that of our iodine as iodide or selenium as  $Se^{-}$  through some terminal units. And that they are further interacting with some other groups which we cannot get from the corresponding donor atoms like the corresponding sulfur base system, what we can have as the donor groups for this metal bearing metallo enzymes or the corresponding molecules, what the metal is bound to this particular sulphur groups as the corresponding donor groups.

Thank you very much.