# PHARMACOGNOSY AND PHYTOCHEMISTRY

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**Week 6**

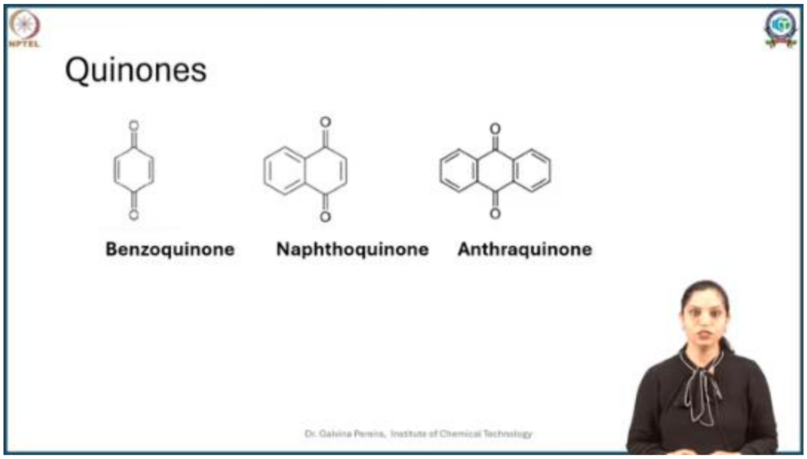
**Lecture27**

## Week 6: Lecture 27: Anthraquinone Glycosides

Thank you. Hello everyone, and welcome to the NPTEL course on pharmacognosy and phytochemistry. This week, we are delving into a set of compounds called glycosides. If you recall, glycosides are compounds wherein you have a sugar moiety, which is a glycone, attached to a genin, that is the aglycone moiety. Together, the addition of sugar makes the molecule more polar, whereas the aglycone is the moiety responsible for the pharmacological activity of the compounds.

Now, from this session onwards, we will see different examples of glycosides. In terms of their biosynthesis, depending upon the aglycones, they might have numerous biosynthetic pathways, such as polyketide biosynthesis for anthraquinone glycosides. They might have acetyl-CoA as a precursor if you have a sterol glycoside, that is via the isopentyl pyrophosphate pathway, or they might even have a shikimic acid pathway if they have a flavonoid glycoside. So, in the first set of sessions, we are going to delve into quinones.

Now, quinones, structurally, are moieties containing ketone. If this ketone, especially a dione, is attached to a benzene moiety, such compounds are called benzoquinones. If this ketone or dione is attached to a naphthalene moiety, it is called a naphthoquinone. And if it is attached to an anthracene moiety, it is called an anthraquinone. Similarly, you have numerous other compounds belonging to the quinone categories, but we will limit ourselves to these examples.




In this session, we will delve deeper into two anthraquinone-containing glycosides, and those are Senna as well as aloes. Now, what is the role of these anthraquinones in plants? Anthraquinones or quinone moieties are a very rich source of, you know, They perform redox reactions very effectively.

As a result, if you observe in our bodies, redox reactions are essential as part of the electron transport chain. Now, what happens here is quinones act as lipophilic carriers for this ETC chain. More specifically, you might have come across examples such as ubiquinones. They are key components of respiratory systems in plants. They help plants undergo numerous other metabolic pathways through their ability to perform redox reactions, and they are defensive.

In some cases, they are toxic as well. Now, if you consider anthraquinones, anthraquinones in nature are predominantly known for their laxative effects, and here are two examples we will study: Senna and Aloe. Senna and Aloe are both known as anthraquinone-containing drugs, and both have a strong purgative effect, traditionally as well as in modern medicine. Now, let's study Senna in depth. Senna is actually obtained from dried leaflets.

Now leaflets are nothing but compound leaves. So if you take a bigger, this is called as a simple leaf. You will see, but in some cases you might come across plants which have compound leaves. So in this case where you have this compound leaves, each component of this, so this particular component is called as leaflet. So Senna is actually a dried leaflet and it is collected from numerous species of Senna.

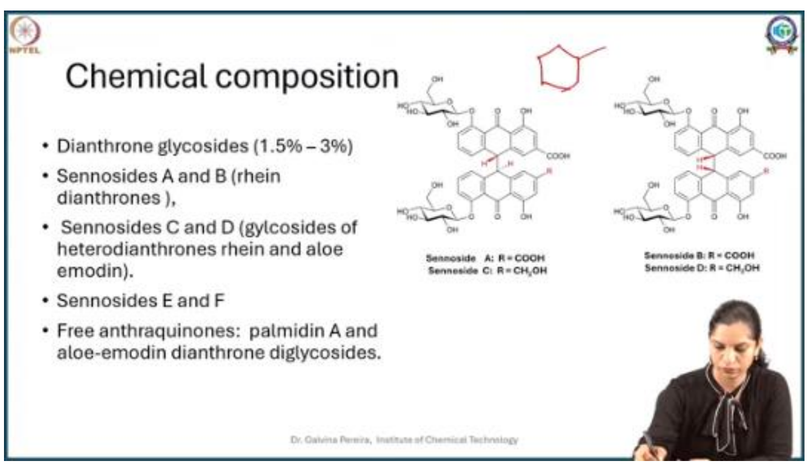
The predominant ones which are there in the market are the Alexandrian and the Indian Senna. The *Cassia Senna* or *Cassia Acutifolia*, the leaflets of which are sources of Alexandrian Senna. The *Cassia Angustifolia*, which is predominantly grown in South

Indian region, is also known as your Tinivelli Senna or Indian Senna. They belong to the family Leguminosae. In terms of their occurrence or geographical source, if you see your *Cassia acutifolia*, which is your Alexandrian Senna, it grows predominantly along the African regions of Egypt, along the River Nile in Sudan.

And In terms of your *Cassia angustifolia*, it is growing in Arabia, Somalia and India. If you see Alexandrian Senna, it is mostly taken from the wild sources whereas Indian Senna is mostly obtained from the cultivated varieties, chiefly in the Tiniveli region. If you see this plant, this plant is a tiny shrub which is sown mostly during the summer season and within one to two months time this plant is ready to harvest. So this plant is then the branches are taken, dried and the leaves are threshed.

Now, once the leaves are threshed, you get the dried leaves. Sometimes they are entire; sometimes they are broken. The entire ones come to the market for the preparation of senna. drugs or extraction of sennosides, whereas if you see the crude ones, which are broken or half, they are mostly used directly for the preparation of Gallinicus. Apart from that, another part of senna, which also contains the actives, is the senna pods.

So, senna pods are also available in the market for extracting the anthraquinone glycosides out of them. So, what are these anthraquinone glycosides which are present in them? So, anthraquinones, as you saw, are basically an anthracene moiety, and in this, you will see like this. So, in terms of—let me just put the aromaticity—you can just make it clearly aromatic.




And then, in terms of numbering, you can just put it like 1, 2, 3, 4, 5, 6, 7, 8, 9, 10. So, you have this kind of moiety, and this is called your anthraquinone moiety. In senna, this anthraquinone dimerizes. So, you can see here it's not 1, but 2 anthracene moieties: 1 and 2.

Two anthracene moieties, which kind of dimerize. Now, once they dimerize, you get what are called dianthrones. So, these dianthrone derivatives are chiefly the main components of senna, and they are present approximately in a range between 1.5 to 3 percent. Now, these anthraquinones contain hydroxy groups chiefly at the 1 and 8 positions.

So, often they are called 1,8-dihydroxy. So, these 1,8-dihydroxy anthraquinones are joined to each other. And in the case of senna, they are glycosides. That means they contain a sugar moiety attached. This sugar is chiefly glucose.

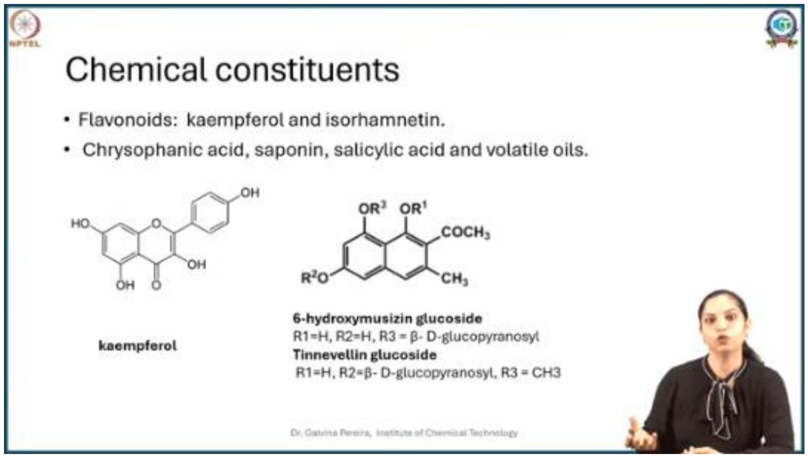
So, you can see here. The sugar is attached. Now, these anthraquinone moieties might be substituted. As you can see here, there is a carboxylic group. So, if there is a carboxylic group here as well as this R, as you see here.

This is also a carboxylic group represented by COOH. It is called a rheinanthrone. The reason is you will see that rhein is like this COOH. So to this anthraquinone, when I put a COH, I get my rhein. So rhein dianthrone glycoside is basically your sennoside.

Now, depending upon its configuration, specifically with respect to the hydrogen, if it is trans, it is called sennoside A, and if it is meso, it is called sennoside B. Similarly, instead of CH2OH, if this R is a CH2OH. So you will have one rhein and the second one. So if you replace this with CH2OH, it is called aloe-emodin. So if you see dianthrones, one is rhein, and one is aloe-emodin.

In that case, we call it a heterodianthrone. So if this is a heterodianthrone, we call it sennoside. C and sennoside D. So these sennosides C and D are the ones in a similar manner: C contains these hydrogens in a trans configuration, whereas D contains this configuration in a meso form. So you have sennosides A, B, C, D, as well as sennosides E and F, which have also been reported. Now, apart from that, it might have free anthraquinones which do not have sugars or

Such as aloe-emodin, rhein, you might even have some compounds like palmidin. Otherwise, you may also have monoanthrone glycosides, such as rhein glycoside and aloe-emodin glycoside, and so on. So, dianthrone as well as anthraquinone monoglycosides are the components present in senna. Apart from quinones, you will also find flavonoids, chiefly kaempferol and isorhamnetin, chrysophanic acid, saponin, salicylic acid, and some traces of volatile oil have also been reported. Apart from that, the leaves of senna are known to have mucilage in their epidermal cells, which swell when soaked in water and can be easily stained with ruthenium red.




Now, the differentiating point between Indian senna and Alexandrian senna is a compound called Tinnevellin glycoside. So, if you see this compound here, there are two derivatives. So, if you put your R1 and R2 specifically here as an H and here as a glucose, you get what is called hydroxymazicin. So, 6-hydroxymazicin is present in both Indian and Alexandrian senna.

But in this case, where you have your Tinnevellin, so R1 gets your H, and R2 here will have your glucose. And R3, instead of glucose, you will have your CH3. This is what you call Tinnevellin glucoside. It is exclusively present in Indian senna varieties. Apart from that, if you see in terms of appearance, Alexandrian senna leaflets are slightly ovate-lanceolate, whereas Indian

Indian Senna is just a kind of lanceolate. Alexandrian Senna is little grayish and has little marks on them because those Alexandrian ones are generally packed and pressed as bales. So they have those leaf markings also. So that can also help differentiate them. Apart from that, in the subsequent lectures, we'll be doing leaf constants.

So Alexandrian and Indian Senna can also be differentiated by their leaf constants. Now, chemical tests can evaluate the anthraquinone glycosides, chiefly the sennosides, by a chemical test called Bontrager's test. Now, what happens in this Bontrager's test is first you take the drug, as you can see it's a greenish powder of senna, and you need to hydrolyze it. The reason why we need to hydrolyze it is because we want to remove the sugar. The reactivity we want is the OH free.

So, in order to break this, hydrolysis has to be done, and this can be done by boiling the drug in the presence of dilute hydrochloric or sulfuric acid. So, any of these two would suffice; the point is just to get the sugar removed. Now, once the sugar is removed, you will see that the molecule becomes very lipophilic in nature. So, What happens here is this lipophilic molecule can then be extracted in chloroform.

So to this hydrolyzate, that is the solution containing hydrolyzed product, just add a little bit of organic solvent. Mostly chloroform is added, but you can add dichloromethane or any organic solvent which dissolves the cyanidins, that is the erglycol. Now take this compound or this extract and separate the chloroform layer. Now you can see here that the chloroform, because it is denser than water, has gone down. You can see it there as a separate layer.

Now, this chloroform layer, when it acquires a yellow color, this yellow color is due to the presence of cyanidins. So the chloroform layer acquiring a yellowish shade is a good indication that the free quinones are coming into your organic extract or organic layer. Take this organic layer and then treat it with your base. Now, this alkali can be ammonia, sodium hydroxide, or potassium hydroxide. When you treat it with a base, what happens is a salt formation occurs.

Generally, You can imagine something like this. This is already broken. So you will have your sodium, potassium, or ammonium salt being formed. And as a result, its solubility in chloroform decreases and its solubility in water increases.

anthraquinone which is now formed which is free of sugars despite that it will form a salt a pink color complex and will get into the ammoniacal or the alkaline layer. So this alkaline layer when it changes to a cherry pink coloration is a confirmation that your drug contains anthraquinone. So this is the most predominant test used to check the anthraquinone glycosides. Now the applications of Senna. Senna is known as laxative for the reason being it contains this dienthrone glycosides.

This dienthrone glycosides have ability to irritate the gastric mucosa. As a result you will see an increased peristaltic movement. Findings also find that it decreases the absorption of water via aquaporin pathway and this increased water in your intestines along with the increased peristaltic movement leads to its laxative effect. But it is also said that if you continue taking Senna for a longer period of time, it increases It is kind of a habit forming.

So once your intestine gets used to it, then you will have to take it continually to get the purgative effect. This is to be taken with prescription definitely and more of this is expressed or the effects of this are seen in the lower or the larger intestinal region. This is also you know suggested as a stimulant laxative during the pregnancy and lactation. Now we go on to the other drugs and this is something which you have seen. It's an aloe vera which is there in the image.

So from this aloe plant, you collect the juice from which is obtained. Now, this juice is generally obtained by making incisions. So cuts are made on the lower part. of the leaf, and this juice—whatever comes out when the cuts are made—is dried, and from that, you get what is called aloes. So aloes are basically, or aloe is, an unorganized drug which is obtained by making incisions on the base of leaves of different species of aloes. Now, there are many species of aloes in commerce; the most common or famous ones are *Aloe perryi*

*Aloe vera, Aloe barbadensis, Aloe ferox*—all of them are generally grouped together and placed in the family Liliaceae. So, aloe perryi is commonly known as Socotrine or Zanzibar aloe because of its region of occurrence. *Aloe vera*, also called aloe barbadensis, grows chiefly in Barbados or is also referred to as Curaçao aloe or aloe officinalis. *Aloe ferox* is It's actually a hybrid of this with other species of aloe, such as *Aloe africana* and *Aloe spicata.*

They are all known as Cape aloes. So, how do you prepare aloes? So when you cut the aloe leaves at the base—if you're preparing aloe mucilage at home, you would have seen this. So when you cut along the region of the outer epidermis, you will see some tiny yellow droplets forming. And if you hold this leaf upright, it will drain a nice yellow-colored latex.

This yellow-colored latex is what is used in the preparation of aloes. So depending upon the regions, the method of preparation does vary. But chiefly, the method involves cutting the aloe at its base and allowing the juice to drain. To facilitate this, what is done is they are generally kept in kerosene or metal cans. The reason being, they are spinous.

They are xerophytic and spinous, so you have to be very careful while handling them, and metal containers prevent that. So you wear gloves, keep them in metal containers, and let the juice drain. A V-shaped trough about a meter or longer is kept so that all the drained juice is collected. Now this can be collected in different things depending upon the geography. Some keep it in metal tins, some in plastic sheets, and some even in goat or animal skins.

Now once it is collected, it is boiled to get rid of the water. Now as it evaporates, the color changes, darkens, and eventually, you get what is called aloe stone. Now after concentration, it is allowed to dry, and on drying, you get this stiff, stony-like material being formed. Now this aloe stone is the one which is there in the market. So it comes under different names depending upon the plant from which it is prepared.

Now, what does this contain? The chief components of aloe are again anthraquinone glycosides, but slightly different here from Senna. The first thing is, in Senna, you had dianthrones. Here, it is a monoanthrone—that is, one anthraquinone moiety—and in Senna, you saw what are called O-glycosides. The point of linkage was an O. In this case, the point of linkage is a C. So, aloe is an example of a C-glycoside-containing drug.

So here, you have—depending upon the isomerism—barbeloin (that is, aloin A) and isobarbeloin (which is aloin B). Now, this is a pale yellow crystalline substance. Sometimes, it precipitates while you are concentrating. It is present in the higher amount. Apart from that, other minor compounds present are the resinous substances: alloisin, aloemodin, which are generally formed when you boil the drug—that is, due to hydrolytic decomposition.

The other things you see are, in the case of *curacao aloes*, you will find barbalo-resinotannol, and in some cases, it is even combined with cinnamic acid. Now, in socotrine, you will see no isobarbaloine. We saw the structure here: isobarbaloine. So, this is missing in Zanzibar as well as your socotrine aloes. So, k-pallo contains k-pallo resinotannol combined in the same way with para-coumaric acid.

Other constituents of this are, if you see, aloeic acid, aloesone, choline, chrysophanic acid, chrysamimic acid, homoalantoin, saponins, coniferol alcohol, free acids, and so on. Now, another important part of aloes is the clear, slimy mucilage, which you see in the parenchymatous region. So, that's made up of glucose, mannose, and uronic acid derivatives. Now, aloes can be evaluated in numerous ways.

One thing you can do is a borax test, which is a very distinctive test given by aloes. So, in this case, what is taken is your aloe stone. You crush it to find particles and boil it to dissolve. Even after boiling, you will see there are some components which are insoluble. So, in order to get rid of those components, it is filtered through kisilghar, and to that filtrate, Now, the filtrate definitely has your aloeins and glycosides. So, those are all coming in water. So, that clear filtrate you will take, and then you will add a little bit of borax. Now, heat it to dissolve, and you will find that your aloe, especially the aloeins, will react with borax. Now, this reaction gives you anthranols.

Now, this anthranols, if you take this little like 1 ml of this to a test tube containing water, about 10 ml and just observe it under UV, the longer wavelength, that is 365, you will see a typically greenish color fluorescence. This is given because of aloe moden anthranol. Another way to check aloe again the anthraquinone part of it is to treat it with bromine water or bromine solution. The more concentrated the better. Now what happens is when you put it the aloe moden and the other anthraquinone derivatives get brominated.

especially the alloys which are present in the higher concentration. So this bromine derivatives form a yellowish color product and this yellow precipitate is observed. Then there are nitric acid as well as nitrous acid test. In nitric acid you will see you take your solution add like you know just 5 ml of if you take 1% aloe solution and treat it with nitric acid. You will see a range in coloration, a vivid green for cape allos, a deep brownish red in case of curaco and a pale brownish yellow coloration in case of socotrine allos.

Now, instead of your borntrager’s test, here your allos give what is called as modified borntrager’s test. The reason remains the same. If you recollect your borntrager’s test, the first step was hydrolysis. hydrolysis what we use there was an acid hydrochloric acid or a dilute sulfuric acid so if you use those you will see that the carbon carbon bond is very difficult to break and as a result you will not get your anthraconone or a free anthranol.

So in that case, to get your free anthraquinone or an anthranol, instead of just treating it with dilute acids, we also add a Lewis acid called ferric chloride. So when you add ferric chloride, it facilitates the bond breaking here, resulting in the formation of or helping in the formation of anthraquinone. Now you have your free anthraquinone, and the same test can be repeated. So what was the test? You hydrolyze the compound glycoside to an anthraquinone.

The anthraquinone gets extracted in your chloroform, and this chloroform layer, when you treat it with an alkali, forms a pink or pink-red color complex. So same test, just a little addition of 5% ferric chloride to break the C-C linkage, is what is called the modified Bontrager's test. Now, apart from that, to distinguish between different sets of aloes, you have got what is called Plunk's isobarbaloin test or cupraloin test. So if you remember, isobarbaloin was absent in Socotrine and Zanzibar aloes, majorly present in Curacao and present in very trace quantities in Cape aloe.

So in order to check that, what you do is you take a dilute solution of aloes and add little drop by drop solution of saturated copper sulfate. Now initially, all the solutions will form a yellow coloration. Now to this, you go on adding again saturated sodium chloride solution and add or dilute it with excessive 90 percent alcohol. If you get a crimson or a wine color, you know, and which stays for about four to six hours, it's

Curacao aloes. If you get a coloration, but then eventually within some time it changes back to yellow, there's a chance that it's a Cape aloe. But if there is no color change and the color remains yellow itself, in that case, there's a good chance that you're dealing with Socotrine or Zanzibar alloys. Now, what are the uses of aloes? Like your senna, this also has a purgative effect due to its irritant action on your GI mucosa, as well as decreased absorption or decreased reabsorption of water in your gut. Apart from this, the mucilage, which is obtained from the leaves, has gained wider importance now.

It is used in mostly topical creams and preparations, such as, you know, cosmetics—numerous cosmetics. You will find aloe vera in your soaps. You will find it in your lotions and shampoos. You will find them in your anti-wrinkle or protective creams.

And there's a reason for it. One thing is, aloe gel—which is a mucilaginous substance—is very soothing and water-retaining. So it moisturizes well. And apart from that, it contains an enzyme called carboxypeptidase. Now, carboxypeptidase inactivates your bradykinin and produces an anti-inflammatory effect.

So the fresher the juice is, the greater the amount of enzymes and the better the activity is. So it plays a good role in healing burns and wounds. And the mucilage is also used nowadays as a hair conditioning agent. So here are a few references and image credits which I've used in the session. You can go through them for additional reading.

And thank you, everyone, for your patient listening. Thank you.