

PHARMACOGNOSY AND PHYTOCHEMISTRY

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Week 7

Lecture33

Week 7: Lecture 33: Flavonoids Containing drugs (Part 2:Soy bean, Milk thistle, Grape peel)

Thank you. Hello everyone, and welcome to the NPTEL session on pharmacognosy and phytochemistry. This week, we are learning about a set of protective yet vivid and colorful compounds, and those are flavonoids. In this session, we will be learning about a few more flavonoid-containing drugs. So, in this session, we'll be learning about soybean, milk thistle, grape peel, and their applications.

To start with, let's discuss soybean. Now, soybean is something in the Indian population. We have it in our meals. We have it in our flour, and we use it almost on a day-to-day basis in some households. So, soybean consists of the seeds which are obtained from the domesticated species of *Glycine max*.

Now, *Glycine max* is the cultivated and domesticated species which has been obtained from *Glycine soja*. *Glycine soja* is the original or what we call the wild species, and both of them belong to the family Fabaceae. They bear pods or leguminous pods, and inside these leguminous pods are located the seeds. So, soybean, if you see, is generally sown during the monsoon season wherein it grows, and in Indian conditions, you can take advantage of the monsoon. Towards the end of the rainy season, around September or October, you will see the crop is ready. It starts flowering and then bears pods. You can see the soybean pod in the image. As the pod ages, you will see that the green color fades to a little yellow and thereafter brown. So once this is done, the crop is harvested, allowed to dry, and threshed.

On threshing or waiting, you will get those soybean seeds. These soybean seeds have been used in food and also for numerous phytochemical compounds which have been isolated from them. Geographically, Brazil, the US, Argentina, and China are selected. They are the leading producers of soybean, but yes, India is also gaining, and we consume a lot of soybean. If you look at soy-based products, you will see that in Chinese and Japanese cuisine, there is soy sauce and tofu.

A number of soy products have been used in these countries, and soy has also been cultivated in these countries as well. So, soy beans are processed to extract oil and protein. So, let us see what chemical constituents it contains. When you talk about soybean, the chief component of soy is soy protein.

Soy bean

- Protein (50-60%), Hexameric protein Glycinin (300 -400kDa), Trimeric globulin type protein Beta-conglycinin
- Fixed oil (14-22%) linoleic acid (50-60%), oleic acid (20-30%), palmitic acid (6-10%), and linolenic acid (5-10%), stigmasterol and sitosterol
- Flavonoids: genistein, daidzein, and glycitein
- Soylécithin

genistein

estradiol

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In fact, for those who are vegans, It is said that they consume more soy milk or soy chunks. Soy chunks are the residue left after the oil is extracted from soybean. This is a rich source of protein, especially for the vegetarian population, and the protein content may go as high as 60%. Now, this protein chiefly contains two components.

Now, these two components, one of them is a hexameric protein called glycinin. With a huge molecular weight about 300 to 400 kilo diethyl and another globulin like trimeric protein which is your beta conglycinin. So glycinin and beta conglycinin are the main components but in addition to that you have other protein components as well. Now, some of these components also are responsible for giving allergies. You know, some people are allergic to soy products and that is why this protein component and determination of the elements is vital.

Now, the fixed oil which has been obtained from the expression of soybeans is. contains linoleic acid, oleic acid, palmitic acid, linoleic acid and in unsaponifiable matter it contains your plant sterols such as stigmasterol and sitosterol. But in the interest of this chapter we will take our focus on the lesser compounds which are present in this plant but yet are very potent and those are your soy isoflavones. So the soy isoflavone compounds present in your soybean are your genistin, daidzein and glycitein. So they remain in your soybean and as a result if you consume food rich in soy meal apart from protein you will also get this isoflavones.

Now why are these isoflavones important? Let's discuss their structures first. So if you remember isoflavones are the derivatives of flavonoids wherein we saw your ring B is attached to ring C but here instead of second place it is attached at the third position. So depending upon that you have your genistin. Genistin is a 4-hydroxy and in this case you will have 5-7.

Typically, flavonoids have a 5-7 dihydroxy pattern. The next flavonoid is daidzein. Daidzein lacks this hydroxy group. So, if you remove this hydroxy from genistin, you get daidzein. The third component is glycitein.

So, what happens is this hydroxy is missing in glycitein. But in addition, you can add a methoxy derivative. So, you have genistin, daidzein (which lacks a hydroxy group), and glycitein (which also lacks the hydroxy group but has a methoxy group in addition). Daidzein So, these three in their native form, and some in their glycosides, along with other flavonoids present in minuscule quantities, make up the flavonoid composition of this plant.

The focus here is that these isoflavones are known as phytoestrogens. Why? So, if you see estradiol—okay, the structure of estradiol—if I just take the backbone, which is vital for me. You can see it aligns, and I can kind of overlap here. You can see it aligns, and I can kind of overlap here.

The substitutions may not be the same, but I am just talking about the backbone. Now here, there is a 5-membered ring, but here somewhere we fit in a 6-membered ring. Now, it is said that owing to this coincidence or owing to the resemblance to the structure, the

isoflavones have a good ability to fit in the estrogen receptors. The work that they do is they act like an estrogen-mimicking agent and hence are called phytoestrogens. So flavonoids, especially those belonging to the isoflavone category, act as phytoestrogens.

And that's the reason soybean is vital. In fact, it is said that, you know, the reason why incidences of cancer are so much lower in Japan. One of the reasons was found to be that they, especially the Japanese population, having much of a soy-based diet was one of the responsible agents or one of the responsible factors. Causative things were attributed to fewer incidences of cancer in the Japanese population.

Apart from that, it also contains an emulsifying agent called soy lecithin. Soy lecithin is something that gives you a silky smoothness to your chocolates and acts as a very good emulsifying agent. Now, knowing this, where can we use soybean? Now, because it's an estrogen-mimicking agent, especially in menopausal women, it is known to protect, you know, during the menopausal stage, the mineralization of the bone decreases, the bone density decreases, and results in osteoporosis. So if you are consuming a diet that is rich in isoflavones, it is said that it will protect the mineralization of the bones and thereby protect you from osteoporosis.

These flavonoids also have a good anti-inflammatory activity. They act as anti-diabetic. They have a good ability to control your LDL cholesterol and help you, you know, especially in your CVS condition, cardiovascular disease condition, as well as gallstones. Because of their isoflavone or anti-inflammatory activity, numerous other effects are also attributed to soybean and soybean extracts.

This includes inhibition of angiogenesis, that is vasculature formation, especially on the cancerous cells. Now it also inhibits your tyrosine protein kinase, ribosomal S3 kinase and DNA topoisomerase especially the mammary 5 alpha reductase and hence it is known to prevent breast cancers in women. So having a diet which is rich in soy can kind of protect you from breast cancers. Now, in males, it is also beneficial and it is known to inhibit the male pattern baldness. Consuming soy products has also been proven beneficial, especially in postmenopausal or perimenopausal conditions such as, you know, like constipation, hot flashes so it controls that it kind of regulates it it acts as

estrogen mimetic and hence is proven beneficial for you so all in all considering diet which is rich in soy Soy chunks, soy sauce or even soy based products such as tofu and milk provides you source of all these compounds and is very beneficial for menopausal women. We now move on to the next drug and the next drug is milk thistle. Now milk thistle has been used in Ayurveda also, and is used in traditional medicines. In fact, it is one of the herb which has been reported to be used as early as 2000 years ago.

So what is this? So milk thistle consists of extracts which are generally obtained from the seeds of *Silybum marianum*. Now this is a member of the Asteraceae family. It bears numerous flowers. It is native to Europe, but because of its applications, you will find it cultivated in Asia, America, and Australia.

Like I said, it is even present in Indian traditional medicine. So it is used for hepatic disorders, and it contains compounds that will protect you from them. So what does it contain? It contains a compound or a set of compounds called silymarin. Now silymarin per se is not a compound.

Chemical Composition

- Silymarin is extracted from the ripe seeds.
- The primary active component is silymarin, a complex of flavonolignans including silybin (the most active), silychristin, isosilybin and silydianin.
- Tocopherols and fatty acids

Silybin A

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Silymarin is a combination of compounds. Together, they are known as or clubbed together as silymarin. So silymarin is a mixture of silibin, silicristin, isosilybin, and silydianin. So let's take silybin. So they are basically flavonolignans.

So, if you see this part where you put a hydroxyl group at the 3-4 position. So, this is a typical flavonoid nucleus. But in addition to that, you have something called a

phenylpropanoid being added to it. So, if you can, you can configure it again. This is the phenyl, and this is 1, 2, 3 propane.

So, you have a phenylpropane, and when you have 2 phenylpropanes, you can call them flavonolignan derivatives. Now, these flavonolignan derivatives, depending upon their isomerism, you can call this silibin A. Just change the isomerism—bring this bond ahead of the plane and send this behind the plane—you will get silibin B. Now, just change this: instead of this bond being behind the plane, if this comes ahead of the plane, it is called isosilybin.

Similarly, you have the other isomers coming in. You'll have silicristin and silydianin, which slightly differ in their ring arrangements. But overall, they possess the same central moiety. So, these compounds were initially difficult to separate. As a result, researchers grouped them together, and since they are structurally very similar, they were collectively called silymarin.

Silymarin is a mixture of silibin, isosilybin, silicristin and silydinin. Apart from it, your thistle also contains tocopherols and fatty acids. Now, because this has been extracted from seeds, they are rich in fixed oil and tocopherols, which also make up a good component of the extract. Now, where do you use this? From traditional medicine, you will see that it has a lot of hepatic benefits.

So milk thistle is used for liver disorders such as cirrhosis, hepatitis. So it chiefly targets your liver and gives you a very protective and healing effect on your liver. So many of the liver disorders are cured by this, including cirrhosis, hepatitis, hepatitis. Your toxin induced liver damage. In fact, it is even given for people having alcohol induced liver damage.

Now, this drug that is your silymarin, let's put it together. It acts by inhibiting the binding of proteins or binding of toxins or binding of any toxins. heptanes we call it to the liver cell receptors it decreases the oxidative stress now this is basically because of its detoxifying effect antioxidant effect at the same time we have in our body natural antioxidants and these are like your glutathione so it will enhance the level of glutathione thereby increasing or stimulating more antioxidant effects. It also increases protein

synthesis. And as a result, more and more, you know, good cells have been generated, good proteins have been generated.

And that's why your liver cells regenerate very fast. So, like I said, it has good healing as well as antioxidant effects. It is also used nowadays and prescribed to a limited extent in the treatment of fatty liver disease. So when you're looking for a liver-protective effect, this is a herb or a go-to herb in traditional medicine.

The next example of your flavonoid-containing drug is simple grape peel. Now, when you consume grapes, you must have seen that there are different variants of grapes, right from what you call green grapes to red, purple, or even black. Now, the darkest grapes are the Concord grapes, which have been shown in the image here. All of these have been obtained from *Vitis vinifera* and many other species of *Vitis*, probably through hybridization or cultivation, and belong to the family Vitaceae. They are all tendril-producing, aggressively growing plants, and they require good cultivation practices to ensure a good yield.

Now, in terms of production, China is the leading producer of grapes, followed by Italy, Spain, France, and then the US. Grape production is seasonal. It requires a temperate climate, but somehow, many grape species have adapted to tropical conditions as well. Now, grapes need careful cultivation, trimming, pruning, and removal of foliage.

So if there are too many leaves and they produce shade, the grape yield will be poor. So removal of foliage, removal of canopy—what they call it—or pruning, trimming, or sometimes even grafting is very vital, and at what stage it is done determines the quality of your grapes. Now, grapes contain, especially if you see the grape peel, one of the richest sources of polyphenolic compounds. They contain numerous polyphenols, and the most important of them are your anthocyanins. So, in your anthocyanins, you have malvidin.

Grape peel

- Grape peels are one richest sources of polyphenols due to the presence of anthocyanins- Malvidin-3-glucoside, Malvidin-3-*p*-coumaroyl glucoside and peonidin-3-glucoside
- flavonols, resveratrol, phenolic acids, and procyanidins
- It contains catechin, epicatechin and their gallate esters.
- hydroxycinnamic acids like caffeic acid, ferulic acid, and *p*-coumaric acid.

Malvidin-3-O-glucoside

Resveratrol

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So, you can see Malvidin here. Now, we discussed previously that anthocyanins carry a flavylum ion. So, this is it. In terms of hydroxy substitution, you have a 3, 5, and 7 hydroxy substitution, of which the 3 has glucose attached to it.

So it is a malvidin 3-glucoside. And we saw previously that initially, if you have a hydroxy group, it gives you more of your red or pink coloration. But as they get substituted more and more by methoxy, you get a purplish coloration. So malvidin is one of the compounds which will give you the purplish coloration, and peonidin comes somewhere near to that. So you have malvidin, you have peonidin.

Now, in some cases, what happens is the grapes get infested by fungus. And as a result, in order to defend against the fungus, they start producing compounds. You remember in your first session, I told you about compounds called phytoalexins. Phytoalexins are something like antibiotics. So, these compounds have been synthesized.

Instead of microbes, these kinds of compounds are synthesized by plants. So, they are not called antibiotics. They are called phytoalexins. So, they are synthesized by plants to ward off threats. So, chemically, if you see, they are phenols.

So, you might have seen antimicrobial compounds like Cresol, Resorcinol, and you know that because they carry these polyphenolic groups, they are toxic to bacteria. In the same way, resveratrol is a polyphenol, but it's attached to a stilbenoid kind of nucleus, and the stilbenoid nucleus is beneficial to us in numerous ways. So, Resveratrol is one of the

polyphenolic compounds which has been approved in therapy for cancer as a prophylactic as well as a supportive treatment.

Apart from that, it contains other flavonoids. It contains tannins such as catechin, epicatechin, as well as gallic esters. It contains cinnamic acid. Now, all of this, you know that the sugar content of grapes is very high, and as a result, the rate of infestation is very high in that. To prevent that, grapes produce lots of these phenolic compounds, and that is the reason grape peel is so rich in polyphenols.

So, it also contains defensive compounds like caffeic acid, ferulic acid, coumaric acid, and so on. Now, because it contains so many polyphenols, anthocyanins, flavanol derivatives, and tannin derivatives, it is very high when it comes to its antioxidant capacity. So, grape peel powder is a strong antioxidant. Now, because of the anthocyanin content, you will see that nowadays there is a need for natural colorants. People don't want synthetic colors to be added to their food.

So, if you're thinking of a color like blackcurrant or a purplish hue that you want, these grape anthocyanins are readily water-soluble. So, they are water-soluble pigments. In ice creams, we need not worry about the pH, and ice creams are often stored at colder temperatures. So, they have good stability. Grape peel powder can be found in frozen foods, yogurts, and cheeses.

In some cases, there are applications where your baked goods, such as cakes and pastas, also use it. But that's basically to improve their nutritional profile. When you take grape peel apart from the pigment and polyphenols, you will see that it is rich in fiber. It is the skin, so it will contain cellulose and a lot of other fibers. So adding grape peel to your pasta or cakes makes them fiber-rich.

And potentially, the polyphenols in it also act as antimicrobial agents. The anthocyanins deteriorate, but the other polyphenols do not. As a result, they have a good antibacterial effect, and potentially, the shelf life of this compound is improved. Now, because of its other antioxidant effects and the compounds present, it is known to enhance longevity in people through its antioxidant or what you call free radical scavenging effects.

It is known to manage or can be used in managing metabolic syndromes, improving vascular function, enhancing circulation, as well as reducing inflammation in the body. So these are a few examples of flavonoids in this session. Here are a few references if you wish to know more about these compounds. Thank you, everyone. Thank you.