

PHARMACOGNOSY AND PHYTOCHEMISTRY

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Week 3

Lecture 14

Week 3: Lecture 14: Carbohydrates based drugs: Sodium alginate, Carrageenan, Guar Gum

Hello everyone, and welcome to the NPTEL course in Pharmacognosy and Phytochemistry. We are learning about a few carbohydrate-containing drugs, and in this session, we will learn a few more examples. These examples are obtained from marine sources, which include sodium alginate and carrageenan, and guar gum, which is obtained from plant sources. To start with marine sources, let's discuss sodium alginate. Sodium alginate is a biopolymer obtained from seaweeds, especially brown algae.

This brown algae contains a slimy substance or a slimy carbohydrate, which is what we are looking for when discussing sodium alginate. It's a carbohydrate derivative extracted using alkaline extraction, basically with a dilute solution of sodium hydroxide or potassium hydroxide, from numerous species of brown algae, including *Macrocystis pyrifera*, *Laminaria hyperborea*, *Laminaria digitata*, *Ascophyllum nodosum*, and *Durabilia lessionia*. These brown algae are located or harvested abundantly from oceans, especially the Atlantic and the Pacific oceans. The good thing about these brown algae is that they grow naturally and abundantly, but in addition, there are numerous attempts being made to harvest, cultivate, and grow them so that they become more renewable.

Now, how do you obtain sodium alginate? As discussed, sodium alginate is a slimy polymer located inside the cells of those brown algae. So, you need to extract it. The first

step is to collect the brown algae from the oceans or seas. It's thoroughly washed because when obtained from sea sources, numerous tiny marine creatures adhere to it.

So we remove those with washings. So they are harvested, dried properly and then milled. The reason for milling is to expose or to break down the cells. Once the cells are broken down, the alginate which is located internally can be easily solubilized. Now this consists mainly of acid like alginic acid and you convert a sodium salt of alginic acid which is more water soluble.

So sodium alginate is extracted by exposing the alginic acid, which is located inside the cell with an alkali such as sodium hydroxide or sodium carbonate to convert it into a water soluble sodium alginate mass. Now this being soluble will be coming out and will dissolve in water. This solution is then further diluted. Why?

Because if you take sodium alginate it tends to form a little viscous solution and because of increased viscosity the particulates or the sand dust or tiny impurities will not settle down. So this is further diluted so that the impurities settle due to gravity, the viscosity decreases and then the supernatant is taken. Now this supernatant which is chiefly your sodium alginate can be treated in two ways. Let's see both the cases. In the first case, what you can do is you can treat it with calcium chloride.

Now sodium alginate is a water soluble polymer like I said the sodium salt but calcium alginate is water insoluble salt. So it will tend to precipitate or form a little more rigid gel as compared to sodium alginate and that is the reason this rigid gel forms a mass which can be separated by treating subsequently with hydrochloric acid. So you can treat it first with calcium chloride or any calcium salt to create calcium alginate and then subsequently generate or regenerate the alginic acid in presence of strong acids such as hydrochloric acid. Alternatively, you can directly use a strong acid such as sulfuric acid in which you will get a precipitate of alginic acid but this precipitate is still viscous, mucilaginous and then needs to be purified further.

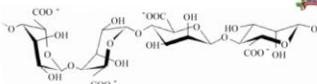
So this is further purified or neutralized because it's acid and some acid residues will still remain. So this is washed and alkalized with sodium carbonate. Now, again, when you do it with sodium carbonate, it's going to get converted into a sodium salt. But this time the

water is restricted and as a result, it doesn't form a gel, but it forms a kind of coarse acid. greasy or coarse viscous solution which can be dehydrated to obtain your sodium alginate.

Now if you see the chemical composition of sodium alginate, it varies from different species of brown algae. The content also varies. So if you see different species of brown algae, the content varies somewhere between 22% to 35% in most of the varieties. The Sodium salt of alginic acid, that is your sodium alginate is a very big polymer with a molecular weight of almost 35,000 to you can say, you know, about 15 lakh or so.



Chemical Composition



β -D-guluronic acid and α -L-mannuronic acid

- The alginic acid content on a dry solid basis varies from 22% to 35% in all the varieties of brown algae.
- Its sodium salt of alginic acid, a linear polymer of-guluronic acid and mannuronic acid; the chain length is long (mol. wt. from 35,000 to 1.5×10^6)
- The molecular chain has an irregular block layout with varying G-G, M-G, and M-M block proportions

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So, this has monomeric units of guluronic and mannuronic acid. Now, these guluronic and mannuronic acids are often associated as blocks. So, we can say two guluronic acid blocks, one mannuronic and one guluronic acid block, or two mannuronic acid blocks. Now, let's take an example of this.

In this case, what you see are two blocks of beta-D-guluronic acid. And here, what you see are two blocks of alpha-L-mannuronic acid. So, you can say this polymer is GGMM. Now here, if you see, what mostly happens is the moment you treat it with an alkali, you get a sodium salt of this. This is what you call sodium alginate.

Now, this happens because sodium is monovalent and here, your carboxylic acid carries a negative charge. But imagine, ions which have a valency of more than one, say, for example, calcium. In that case, what happens is because it's divalent, generally we get what is called the eggshell model. So, these polymers are associated like this.

So this is one block of sugar, this is another block of sugar and here you will have your COO tending to form some association with this. Now, this association is what creates or what makes your calcium alginate water-insoluble. So this is like an egg-in-a-box model. And you can see that's the reason your sodium alginate is more water-soluble. Whereas your calcium alginate tends to stiffen or precipitate, depending upon the pH as well as the concentration of calcium ions.

Now, if you see the uses, alginate forms a nice, clear solubilized jellies. So it is used in glazings. It is used to create soft, creamy paste. It's used as a thickening agent. It is used as a stabilizing agent, a polymer for emulsions.

It's a good suspending and thickening agent. But when it comes to its emulsifying properties, its emulsifying properties are not as good as compared to acacia and tragacanth. More often, being a carbohydrate, it acts as a very excellent binding and disintegrating agent. And that's the reason you'll find them being used in tablets and lozenges. It is in food because of its transparency.

It's used in jellies and ice creams. It is also used for sizing in textile industries. Now, slightly stiffer variants such as aluminium and calcium alginates, along with potassium alginate, have also been used in the pharmaceutical industry. Now, one application I want to emphasize here is when you have gastric ulcers. When you have ulcers in your stomach, as food is continuously digested, acids are secreted.

These acids enter those ulcers and further irritate them, causing significant discomfort to patients. In this case, capsules containing sodium alginate are administered along with calcium carbonate. Calcium carbonate initially neutralizes the acid. But, as I mentioned, with food, this process continues, and more acid is generated. This acid then reacts with sodium alginate and converts it into alginic acid.

Now, this alginic acid forms a nice, viscous, thick, jelly-like coating over your stomach ulcers or the inflamed area, protecting them from stomach acids thereafter. This is one interesting application where pH manipulation has pharmaceutical uses. Apart from this, sodium alginate has also been used in enzyme immobilization and as a medium in biopolymers and bioengineering. The next polymer is carrageenan.

Now, carrageenan is also referred to as Irish moss. It comes from a very beautiful fan-shaped red algal species, *Chondrus crispus*, also called carrageenan. And this belongs to the family Gigartinales. Now, this is also one algal species found on the Atlantic coast, the British Isles, or in Europe and America.

Now, these fan-like projections or tufted projections, this is something that grows very easily and rapidly. But this is stiff. You can say it's almost cartilaginous and may have slight undertones of green or dark purple. Now, once you take it out from the sea, you can expose it to the sun.

Once exposed to the sun, it will naturally bleach. A small amount of its pigment is taken care of. And as a result, you will get a yellow translucent appearance, and you obtain a dried algal sample in this form. So you get a translucent consistency. From that, you can obtain different types of carrageenan.

Now, different types of carrageenan are actually obtained from different species of red algae. The different types of carrageenan are kappa carrageenan. Now, kappa carrageenan - we will discuss the structure. It has a sulfate derivative. A monosulfate derivative.



Types of Carrageenan

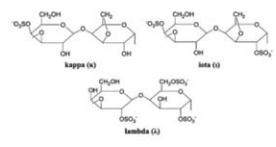
Carrageenan can be classified according to its structure and production process as :

By Structure

- **Kappa** – rigid and brittle gel, thermo-reversible, high gel strength, showing syneresis.
- **Iota** – elastic gel, thermo-reversible, no syneresis, thixotropic.
- **Lambda** – cold soluble, non-gelling, high viscosity.

By production process

- **Semi-refined** – opaque gel containing high cellulose and fiber levels, low degree of purity.
- **Refined** – clear, transparent gel, with a high degree of purity.



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And of all the carrageenans, kappa carrageenan is more rigid and stiff. So you can imagine a stiff jelly, like your microbial media agar-agar. So that kind of stiff jelly is given by kappa carrageenan. It's a thermo-reversible jelly. So you can heat it and kind of melt it down, and it has a high gel strength, but it shows syneresis.

So that means it will break and it will elute. We call it the whipping of gel. So that happens, whereas iota carrageenan—if you compare it to kappa—has two sulfate groups. And that's the reason it makes it a little softer. So in terms of kappa, which gives you a little rigid, brittle gel, this will give you an elastic, little soft, thermo-reversible gel.

But because it is soft, there is no whipping, there is no elution of liquid coming out. We refer to that as syneresis. And it's also thixotropic in nature. The last one contains about three sulfate groups. So these three sulfate groups make it the most soft gel rather than it doesn't gel at all. It's just a viscosity agent. It has no ability or strength to form gel and to retain shape. So it's a cold soluble polymer.

It's non-gelling and just imparts high viscosity. Now depending upon how much you purified it, you can also classify your carrageenan as semi-refined or refined. The semi-refined is a little opaque, containing more pigments and impurities. Some cellulose and fibers are also present and the purity is kind of compromised. If you see the refined one, which is mostly used in the pharmaceutical industry, it gives you very clear transparent gel and it has a good high purity and absolutely very lower concentrations of cellulose or other impurities.

Now, if you want to check the sources of these three different types of carrageenan, the kappa carrageenan—the most stiff jelly one—comes from *Kappaphycus alvarezii*, formerly known as *Eucheuma cottonii*. And it is also obtained from *Hypnea musciformis*. Now, if you see the middle one, the iota type, you get it from *Eucheuma denticulatum*, also known as *Eucheuma spinosum*. Now, this is going to give you a middle consistency—a little softer one—and the non-gelling but viscous ones are mostly obtained from *Gigartina* species.

Structurally, how do you prepare them? So, this algae, which grows on the rocks, you can just collect it. Again, they take long rakes and kind of pull it out from the waters. The seaweeds are harvested, and you need good cleaning because you can see how agglomerated it is—that needs to be cleaned of debris or any impurities. So, they are cleaned, bagged, sorted, and kind of rubbed once so that whatever adhering impurities are there are all taken care of. Subsequently, they are washed.

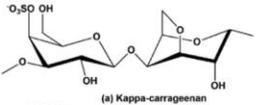
So, anything such as soil or sand adhering to it is also gone. And then, they are subjected to hot alkaline extraction. During this, the carrageenan, which is being extracted, is dissolved in water, and then this dissolved solution is further clarified by filtration. In some cases, you can even remove or concentrate the solution by using membrane filtration.

Now, this being a carbohydrate like your previous method, what you can do is to that aqueous solution if you add a water-miscible organic solvent like methanol or alcohols, you can precipitate it. You can even precipitate by using salt such as potassium chloride. So once that is done, you get a crude precipitate. This crude precipitate is then dehydrated and converted into fine powder by vacuum drying, subsequently grinding so that you get a good particle size. Now, structurally, if you see carefully, it is a polymer which is made up of three, six, and hydro-D-galactose. So this is your galactose. So you can see here you have your one galactose, you have your another galactose being here.

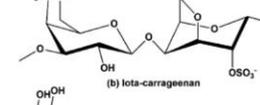



Constituents

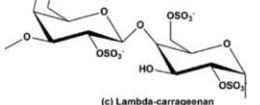
- The major constituent is galactans which is known as carrageenan.
- Carrageenan are classified on the basis of 3,6-anhydro-D-galactose and the position of ester sulphate groups.
- Three major types of carrageenan are characterized as Kappa, Iota and Lambda-carrageenans.
- Hydrolysis of the polysaccharides yield galactose, glucose, fructose, arabinose and calcium salt of acid esters of sulphuric acid.



(a) Kappa-carrageenan



(b) Iota-carrageenan



(c) Lambda-carrageenan

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So one is your alpha-galactose one. So you have your galactose being attached here. Now this is, say, one position 1, 2, 3, 4, 5. So you have your monosulfate derivative which is attached here, and kappa has one sulfate attached to galactose, and there is absolutely nothing which is attached to a 3,6-unhydrogalactose. But if you see iota carrageenan in it, there is one which is attached to your galactose

D-galactose, but if you see your n-hydro-D-galactose, that is especially your 3,6-n-hydrogalactose, you can see at your this is one, this is two, carbon number two, you will see one more sulfate derivative. Now coming to the last one, lambda, in this case, if you see here, this was your position one, two, three, four. Both of these galactose had sulfate at

their fourth position. When you are talking about lambda, the sulfate changes from their fourth to second position.

So, you have your sulfate being there at the second position on your galactose, and here this galactose is not anhydro-D-galactose. Here, you can see instead of that, you will have your one, two, sulfate at the second position, 3, 4, 5, and 6. So instead of forming an anhydro linkage, you have sulfate at the second as well as the sixth position. So this is a little difference between the three derivatives, that is your kappa, iota, and lambda.

But they are not pure. Apart from that, they contain little other sugars as adducts. So when you hydrolyze them, apart from your galactose, you get your glucose, fructose, and arabinose as well. Uses, So if you see this, it's used as an excellent emulsifying agent.

Carrageenans are good as stabilizing agents and solubilizing agents. I'll give you an example. If you've seen a gel-based toothpaste, you see a good viscosity to it. So that's basically your carrageenan being used to make a stiff jelly. So it's also there as or used as hydrogels.

Because of that consistency, it is used in tissue engineering. You get those films or transparent films, pellets or beads being prepared from it. You have your, like I said, toothpaste, creams, lotions and cosmetic products, which are very clear, your gels or sunscreen gels or some sprays or some viscous cosmetics, there they have been nicely applied. Apart from that, carrageenans have also been known for their antibacterial, anti-tumor and anti-hyperlipidemic effect.

In the food industry, it is also used in preparing milk products for imparting viscosity and gel-like consistency in ice creams just keeping a concentration of as low as 0.5 to 1%. Now we go to the third carbohydrate and this is not a marine base. This is a plant based and as you can see this is a simple gawar or guar. This is a

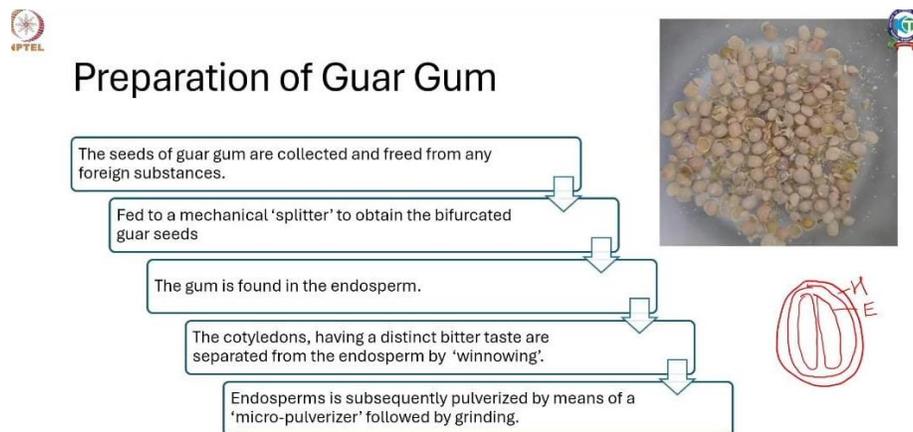
Indian vegetables we often consume and the seeds of it are used to prepare guar gum. It is also called jaguar gum and it is obtained from the seeds of guar that is your *Cyamopsis tetragonoloba*. Now this is a leguminous pod so it's a leguminosae family member and this is abundantly cultivated in India, Pakistan, US, Australia and Africa. In fact, if you go to

see, we are one of the global leaders when it comes to guar gum. And Rajasthan is one of the predominant states which gives you a major yield of guar gum, say up to almost 70% of the necessity required.

So, how do you prepare it? If you take these guar seeds and grind them, you will see that the husk easily comes away. So, initially, you take your guar seeds, nicely treat them or rub them with a cloth so that they are freed from any dust or particles.

So, they are kind of clean. Once they are clean, they are pressed into a mechanical splitter. You can see an image. So, it kind of splits. So, what you get is the outer hull separated, which is almost 20% of its weight.

And then, you get an inner endosperm layer. And within that endosperm layer are the cotyledons. Now, your gum is actually located in the endosperm. So, I'll just show you. So, if this is your guar seed, then you will have your endosperm layer.



So this is much like your seed coat or you can say your hull. This is much like your endosperm. And within this endosperm, you will find two nice soft cotyledons. So if you do or use a mechanical splitter you can get this inner part. Now what we require here is the endosperm because this contains the gum.

So the splitter seeds are removed. You can get rid of the outer hull just by winnowing or blowing initially and some separators such as cyclone kind of separators are used to get rid of it. Now in order to separate the endosperm further Processing is done. Further little grinding is done.

Now, cotyledons are comparatively softer as compared to the endosperm. So during the sifting stage, what happens is you can easily separate the cotyledons by winnowing once they are separated from the endosperm. So now you're left with heavy endosperms. These heavy endosperms, which are now the hull, are gone. The cotyledons are gone.

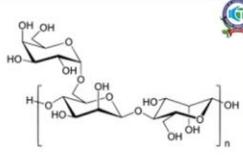
This endosperm is pulverized. The endosperm you can see here is a little grayish in color but on pulverization it becomes whitish. So it is pulverized and micropulverized converted into a fine powder and that fine powder is what is sold in the market as your guar gum. The inner cotyledons and other parts of it are still used in industry nowadays for preparing guar protein as well as in your animal fodder. Now what are the chemical constituents?

If you see the composition this is again a carbohydrate. It consists of guaran which is the main one and guaran is a linear chain which is made up of mannopyranose. Guarani actually consists of a linear polymer of 1,4-beta-D-mannopyranose along with an alpha-D-galactopyranose. Now the galactopyranose are often attached by 1,6 linkages. So you can see a 6



Chemical Constituents

- Guarani : a galactomannan, water-soluble part of guar gum contains mainly of a high molecular weight hydrocolloidal polysaccharide
- Guarani consists of linear chains of (1→4)-β-D-mannopyranosyl units with α-D-galactopyranosyl units attached by (1→6) linkages.
- However, the ratio of D-galactose to D-mannose is 1: 2.
- The gum also contains about 5-7% of proteins.



Guarani



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Whereas these linkages are 1 being attached to 4. So this is 1, 2, 3, 4 and this is 1, 2, 3, 4. four this is five and this is the six so that is how you number it so you'll get this linkages

the ratio of galactose is to mannose the mannose is always on the heavier side with mannose being two times the galactose this gum contains about five to seven percent proteins and that's the reason the resultant waste of the refining or producing industry goes as a animal fodder Now, in terms of uses, guar gum is used as a protective colloid because it's nice and mucilaginous as compared to other plant gums. It is much superior in the performance as an emulsifier.

It is used as a bulk laxative even for diabetic patients and it gives you a feeling of satiety or fullness once you consume it. So it kind of because of that fullness, it is also giving you what is called appetite depression properties. And it's also used in peptic ulcer therapy for the same reason because it forms a mucilaginous coating over a peptic ulcer. It is an excellent binding and disintegrating agent. Now, being a viscosity imparting agent, it's used in paper manufacturing, printing, polishing, foods and also in cosmetic industries where it acts as a stabilizer as well as viscosatives.

Now, Guar gum is abundantly available in India. One more interesting application is that it is used to treat water. So guar gum is taken and you can take your effluent water. This is treated with guar gum.

Guar gum eventually swells. It entangles all the impurities in it and eventually settles down. The supernatant, you will get it as a much clarified water. So that's there, now being mucilaginous in nature, it has the same functions as other carbohydrates, such as it acts as a prebiotic.

That's very good. The other part is for diabetic patients, it will cause a mucilaginous layer to be formed and till it is itself digested into carbohydrates that mucilaginous layer will hinder the absorption of carbohydrates and lipids now this has somewhere been also associated to the cholesterol levels so consuming guar gum has shown to decrease your serum cholesterol levels especially the LDL cholesterol By almost 15% or 10 to 15% or in some cases even 25% without affecting much the levels of HDL cholesterol. Now, like I said, because it inhibits, it is giving you hypoglycemic activity because it will not allow the other sugars to permeate.

And as a result, because it's not giving us sugars, it is also used as, you know, over the counter weight loss supplement. Apart from that, one more advantage is because it has decreased glycemic as well as decreased cholesterol, especially LDL cholesterol absorption. It is also reported to reduce blood pressure in patients. So, these are few references if you wish to read further on these drugs and thank you everyone for your patient listening.