PHARMACOGNOSY AND PHYTOCHEMISTRY

Dr. Galvina Pereira

Department of Pharmaceutical Sciences and Technology

Institute of Chemical Technology, Mumbai

Week 2

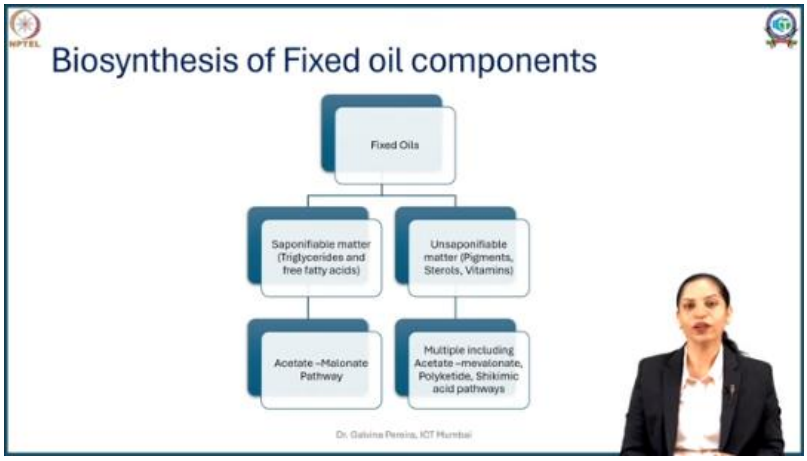
Lecture 8

Week 2: Lecture 8: Examples of lipid containing drugs castor oil, sesame oil & coconut oil

Hello everyone, and welcome to the NPTEL course on pharmacognosy and phytochemistry. In this unit, we are studying oleaginous or oil-containing drugs exclusively containing lipids such as fixed oils, fats, and waxes, as well as volatile oils. In the previous session, we studied the differences between fixed oils, fats, waxes, and volatile oils. Through this session, we are going to start with some examples of drugs containing especially fixed oils. Just to start with, how do fixed oils

come into nature? Fixed oils are actually reserve molecules, and they form stored energy for plant species as well as for us and animal species. So, fixed oils—you will see the predominant source of fixed oils is mostly the seeds. Bearing a few examples, many seed-containing drugs are used for the preparation of fixed oils. Most of your cooking oils—say, sesame oil, groundnut oil, sunflower oil—the majority of them are obtained from seed drugs where they function as a reserve storage for energy.

So, how are they biosynthesized? Fixed oil content can be broadly divided into two parts. The first part, which is the saponifiable matter—something that can be saponified. And the other part, which is a minor part, is called the unsaponifiable matter. The saponifiable matter is generally made up of triglycerides, that is, your fatty acids and



Say, for example, you might have different fatty acids which are attached to glycerol, as we discussed previously. So this one glycerol will form ester linkages with fatty acids. Now I'm just representing the fatty acids as they are. They might be similar. They might be different.

They might be saturated or they might be unsaturated. So all in all, these are what triglycerides look like. And this individual, you can just put it as a long-chain carbon-containing fatty acid. So your free fatty acids are We can call it here or your triglycerides.

They are obtained from a particular pathway called the acetate mevalonate pathway, wherein acetyl-CoA condenses, forms malonyl-CoA and undergoes a series of steps to form adducts. Now these adducts are generally in the form of two-carbon units, and that is why in nature you will see the most abundant fatty acids are in multiples of two. C12, C14, C16, C18, C20, and so on. The reason is their biosynthetic monomer is a C2, which later polymerizes to form a long-chain fatty acid through sequential cyclized steps.

When you go to unsaponifiable matter, it contains different molecules. So, for example, when you see cooking oil, it's not colorless. Now, fats—ideally, if you see triglycerides—by their nature, they are colorless. The color is attributed to pigments which are present in it. These pigments can be something like chlorophyll in the case of olive oil, or they can be carotenoids in the case of some other oils where carotenes are major.

So, if it is chlorophyll or carotenoid, the other unsaponifiable matter contains lipid-soluble ingredients. This includes the fat-soluble vitamins and carotenoids. The fat-soluble sterols

in animals include cholesterol; in plants, you have phytosterols. These include your sitosterol, stigmasterol, and other steroid derivatives. Now, they have multiple biosynthetic origins.

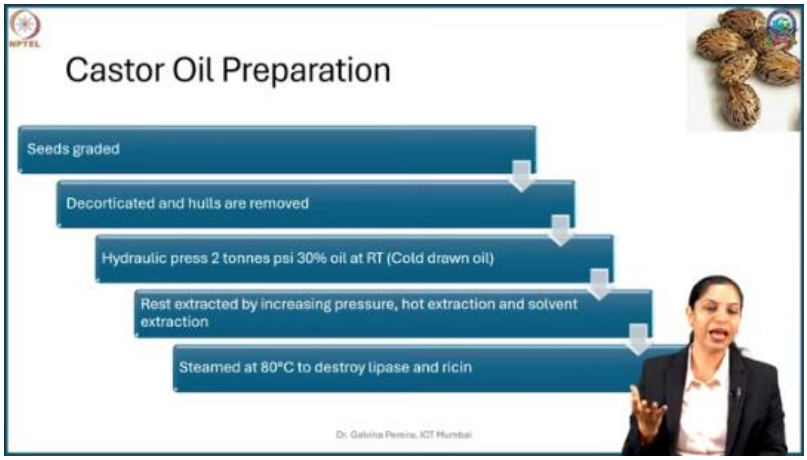
This might include something like your acetate mevalonate pathway, your shikimic acid pathway, or even a simple polyketide folding for your plant pigments as possible. So, the saponifiable matter generally comes from the acetate mevalonate pathway. The unsaponifiable matter comes from diverse pathways. Now, we will discuss a few examples of drugs containing fixed oils. In this session, we'll discuss castor oil, sesame oil, and coconut oil.

Let's start with the castor oil. Now, castor oil is something that is abundantly found in India. If you look, you will find regions in Maharashtra, Gujarat, or near Rajasthan where castor grows abundantly in the wild. It's also cultivated, particularly in Andhra Pradesh, Gujarat, Karnataka, and internationally in Brazil and Romania. Botanically, they are seeds.

What you do is extract the oil from the seeds of the plant Ricinus communis, which is a member of the Euphorbiaceae family. This Euphorbiaceae family member was initially wild but is now cultivated because of the oil it yields. Ricinus communis is a very fast-growing, suckering, perennial plant with glossy, palmate leaves that have about 5 to 12 deep lobes and are slightly serrated or coarsely toothed. They bear what is called a panicle inflorescence, and on top of it, you will find small spinous capsules. These spinous capsules, once mature, break open, releasing the seeds.

You can see some seeds here. They are nicely mottled or marble-finished seeds. If you look closely in this region, you will see a tiny outgrowth called a caruncle. Castor seeds can easily be identified by the presence of a caruncle. For cultivation purposes, when selecting quality seeds, it is best to obtain

Undamaged seeds. The reason for that is when you are thinking of preparing oil from castor seeds, if any damaged seed is procured in the process, the damaged seeds create an exposure to air, and this exposure to air creates rancidity. And that is something we don't want in a pharmaceutical-grade oil. So when you're thinking of castor oil preparation, the first thing you should do is grade the seeds.



Prefer the seeds in which the testa is intact and unbroken. The testa is very thin and papery, but that is required if you want a non-rancid oil. So good-quality, unbroken, undamaged seeds are taken. Now, once the seeds are taken, they are then crushed in a mechanical press, which is slightly glued. And when it is glued, the

testa or the seed coat kind of separates out. This seed coat, being a little papery, with a fan or a gust of air, is blown off, and what is left is the inner part, the endosperm. Now, this endosperm is pressed. Generally, this is done cold. We don't want harsh conditions.

So, cold drawn oil is done using a hydraulic press by applying a pressure about 1 to 2 tons per square inch PSI and at that level, you will see that 30% of the oil is drawn. Now this is something which is treated as virgin oil or pharmaceutical grade oil or a good quality oil because if you see it in terms of a free fatty acid content, which also corresponds to the rancidity, this is relatively less and it's considered to be the best one. The next or little lower grades for commercial or non-pharmaceutical applications can also be obtained if you further presses. Take it for example, you can have a hydraulic press pressure increase now to 3 tons that will remove additional more 10% oil or you can even heat it.

to get more oil. But what happens in the process that you might get more oil, but you will see more of this free fatty acids. So in the second, when you are using a high pressure, high temperature combination, you might end up with the oil which has about 5% free fatty acids. And that is not desired in pharmaceutical grade, but for commercial application, it's fairly good enough. So such oils are taken for commercial purpose.

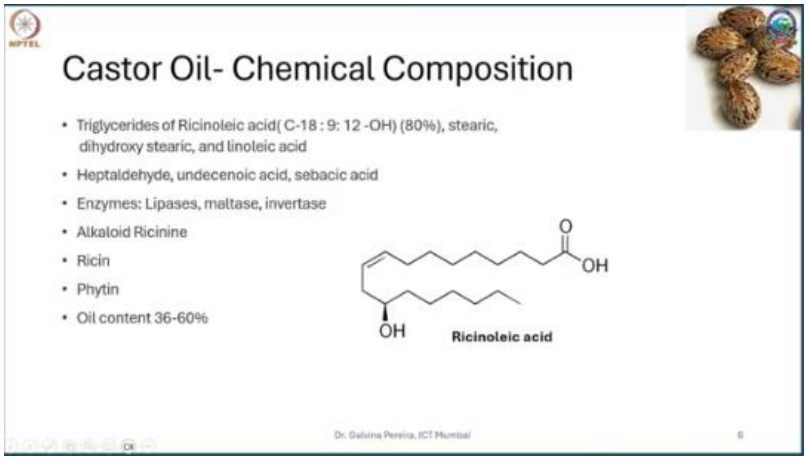
So that is in the last case where you still want to further extract what is done is the seed meal or the seed cake which is obtained by pressing is then put into solvent organic solvents such as hexane, petroleum, ether and now these solvents are evaporated to get the last part of oil. So on an average the seed contains about 50% oil and using various processes we could still get Almost 80% oil out of it. But the best 30% which initially comes out is generally sealed for pharmaceutical purpose. Now one more thing to remember about castor is it contains a compound called ricin.

And this ricin is a biohazard. That means it is poisonous if you consume it. And if you are thinking of using this oil for pharmaceutical grade, it cannot contain ricin. And ricin, being a lectin in nature, has a protein component and a carbohydrate component. So what is done is, once the oil is obtained, it is heated.

You can heat it at about 80 degrees Celsius, and the protein gets agglutinated or denatured. The ricin is rendered inactive. One more thing that is rendered inactive is the enzyme called lipase. Lipases are responsible for hydrolyzing the triglycerides, and these lipases are also intact in the seed. So if you keep the oil as such, they will keep hydrolyzing the triglycerides, releasing a lot of free fatty acids.

And, you know, free fatty acids cause rancidity. So steaming serves the purpose of agglutinating two proteins. One is lipase, which can cause the release of free fatty acids. And the next thing is, it neutralizes or agglutinates your ricin, which causes poisoning. Now, this oil which is left is kept safe.

Any solids which are deposited are then filtered, and then you can use the oil for your pharmaceutical grade. Now, castor oil, if you look at its composition, contains one compound called ricinoleic acid, which makes up about 80 to 85 percent of the oil. Now, ricinoleic acid, if you examine its structure, is a C18 carboxylic acid. That means it is a stearic acid derivative. Now, this stearic acid C18, if you divide it into halves at C9 and 10, it will have a double bond.



This very closely corresponds to your oleic acid. And then, at carbon number 12, it has a hydroxy group. Now, this hydroxy group gives it one very important property, which can be used to check the purity of castor oil. That means you can take this castor oil and try to dissolve it in alcohol. It is one of the very few oils that dissolves in alcohol.

Your other cooking oils won't dissolve in alcohol. So you can easily determine whether it's adulterated or not. In a similar manner, you will see that 5 ml of this castor oil can dissolve in about 10 ml of petroleum ether. So it has both lipophilic and polar solubility in alcohol. Apart from that, other components which are also obtained from castor are heptaldehyde.

Then you have a C11 compound that is undecanoic acid. Then, similar to your sebum, there is a C10 diacid, which is your sebaceous acid, which is also present in your skin creams nowadays, and definitely ricinoleic acid. Now, this castor meal has also been used for obtaining enzymes. You know, in biotechnology, you require enzymes, and castor seeds are an interesting source of that. So you can purify lipases, myotases, and even invertases from castor seeds.

It contains an alkaloid, a small content of ricinin, a toxic component ricin, 5 tins, and the total oil content, as I said, is almost 50% of the seeds. So it ranges between 36% to 60%. The castor oil is almost colorless to pale yellow, depending upon the grades, with a characteristic, you know, accreted color. taste and odor, and it's soluble right from alcohol to chloroform, ether, pet ether, but it's insoluble in paraffin or, what you can say, mineral oil. Going by the standards, it is an oil which is lighter than water, with a weight per ml of 0.9 percent, then refractive index 1.46 to 1.47 and saponification value of about 177 to 187,

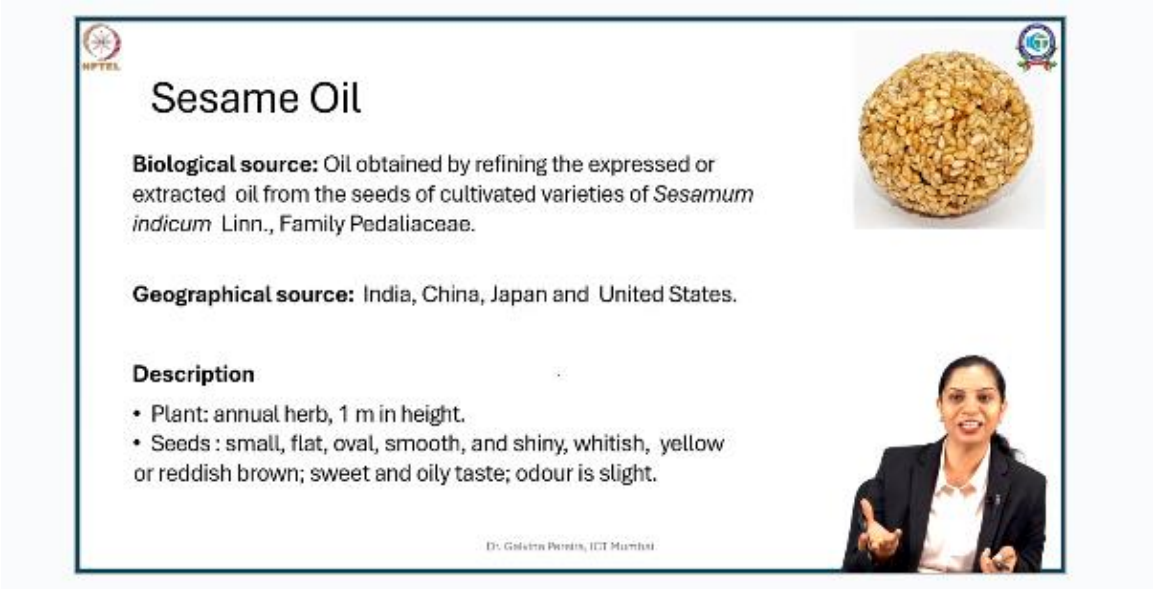
which is presumably good, and because of the hydroxy group, it has an acetyl value of about 143 and hydroxyl value of 150. Now, these are some things which are being used to determine the constants, I mean, determine the value or determine the assay of it. Castor oil has numerous applications.

It is given as a laxative. You will see a lot of elderly people taking eranda oil as a laxative ingredient. So it helps in constipation. The oil is used in the preparation of soaps, paints, enamels, varnishes, greases, and polishes. But because of its abundance in India, you can see, you know, very well, it's taken.

So you will find it in hydraulics and brake fluids with little modification, obviously. And these modifications can be, if you need to solidify the oil, you hydrogenate it. So in some cases, you use what is called hydrogenated castor oil, which has the consistency of vegetable ghee or dalda. Whereas in some cases, you make it more polar. You can make it more polar by introducing hydroxy groups.

So you have polyhydroxy castor oil, which is a polar derivative of castor oil, and that has also been used in the automobile industry. Now coming to fatty acids, if you see ricinoleic acid, it's used in contraceptive creams for its spermicidal activity. You can even break the acid into heptaldehyde. You can get undecanoic acid and sebacic acids, which are the fatty acids present in castor oil. And you can purify it for applications in chemistry as well as in cosmetics.

It's an interesting product if you want to create foams, particularly for trolley wheels. If you see those nylon leavens, urethanes, or even in rigid or semi-rigid foams, castor oil is used as a plasticizing agent. Now, it's also used as a lubricant for its good property that it doesn't freeze even at sub-zero temperatures. So, it's an excellent lubricant. Now, moving to your next oil, we have sesame oil.

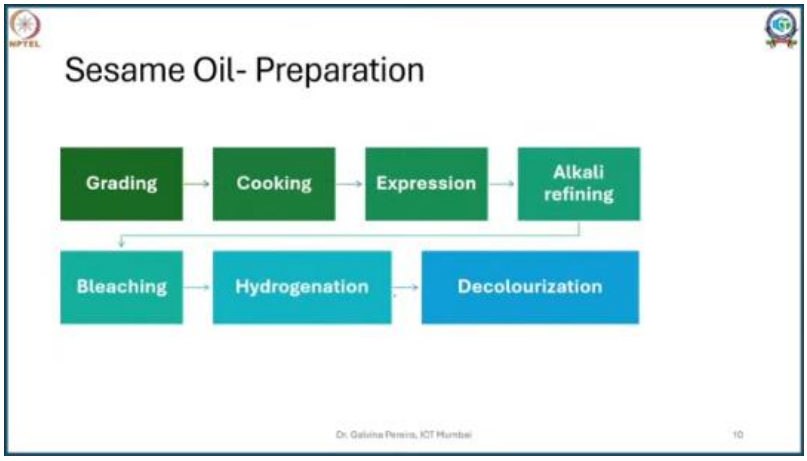


Now, everybody must be familiar with the image here. This is til ka laddu, and sesame oil is nothing but sesame. Now, the significance of til for us is that this is one of the oils which is prescribed in Ayurveda. So, if you see Ayurvedic tailors, most of the Ayurvedic oils use sesame oil as a base oil. It is so good and so stable.

And that is the reason they prescribe sesame oil. It's very inert or bland and doesn't contribute to any strong flavor or odor. And that's the reason most Ayurvedic preparations use sesame oil as a base oil. So, this is again a seed oil. Fixed oil is obtained by expression or from the cultivated varieties of sesame.

We have it. We've been using it in our culinary practices, and this belongs to the Pedaliaceae family. Now, it grows abundantly in India, China, Japan, and the U.S. Now, this is an annual plant; you will see it fruiting post-monsoon, bearing pods, and in these pods, you will see stacks of seeds or stacks of sesame seeds. On average, this plant grows to a height of about a meter, and if you take sesame seeds, they are nice.

They are smooth, flat, oval, and whitish. In some cases, they might be slightly yellowish to reddish-brown. And if you consume them, they have a slightly oily taste. The odor is fairly light or bland. How do you prepare them?

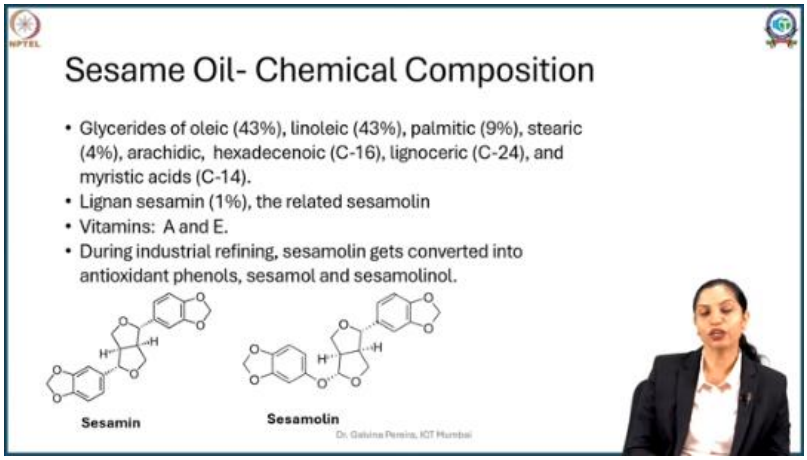


Again, sesame seeds—we want them intact. They are very tiny. So those pods bearing sesame seeds are threshed to separate the seeds. The sesame seeds are graded. We want the white ones.

If you take the brown ones, the quality of the oil goes down. So what we'll do is we'll extract the oil. Now you can press them as such with a mechanical press. But it is said that if you cook or steam these seeds, the oil content or the efficiency of extraction improves. Now, one limitation is if you overcook them, the seeds tend to become very soft and slimy, obstructing the extraction process.

So you need to be very wise, and they are carefully cooked with a minimal amount of steam. After that, they are expressed in a mechanical press. Now, this contains a lot of free fatty acids. So once the oil is expressed, it is allowed to separate properly. Once separated properly, it is treated with alkali to neutralize the free fatty acids. If any pigments are present, they are subjected to bleaching or sometimes passed through charcoal columns or cartridges to get a purified product.

They are partially hydrogenated and completely decolorized. So this gives you a good-quality, pristine, slightly pale yellow, nice, bland sesame oil. Now, sesame oil, if you see, contains triglycerides, chiefly of oleic, linoleic, palmitic, stearic, and arachidic acids. Now, if you see, oleic and linoleic are all C18; stearic and palmitic are C16. You can see arachidic, hexadecanoic, and lignoceric, which is very big—almost C24, that is 24 carbons—and myristic acid.



All of these triglycerides make it bland and stable. And you will see the majority of them fall in the saturated or monounsaturated range. So that's the reason Ayurveda considers this oil to be very stable. Now, in addition to that, this oil is found to contain an interesting set of compounds. We call them lignans.

Now, lignans are C6, C3 compounds. So, how do you put them? Let us take an example of a commonly occurring lignan. This is your sesamin. So, I'm just—it's a very symmetric, nice molecule. I put it down, and then, if you remember how we do it for phenylpropanoids, I'm just numbering it.

Okay, so 1, 2, 3, 4, 5, 6. So, you have your 6, and then 1, 2, 3. So, this is your C6, C3. Again, I can just put it like 1, 2, 3, 4. 4, 5, 6, C6, and again 1, 2, 3.

So, lignans are basically dimers of C6, C3, which are there in nature, and some of these lignans have estrogen-like activity and are also known as phytoestrogens. So, sometimes, when you consume excessive sesame seeds, they are attributed to estrogenic activity because they act like phytoestrogens. So, the common lignans which occur in your sesame oil are your sesamin and sesamolin, with a little difference—if you can see, it's an ether out here, whereas it is not there in this. Now, this might hydrolyze to give you an alcohol, and this alcohol we call sesamol.

So, sesamolin hydrolysis gives you sesamol, and you might also have sesamolinol. So, these are used for their lignan-like saving effect. Apart from that, it contains very trace, minute quantities of vitamin A and vitamin E, which are oil-soluble vitamins. You can

evaluate genuine sesame oil by checking the lignan and the lignan derivatives. Those are your sesamolin and sesamol.

What you need to do is just take the oil and take half the amount—if you are taking 2 ml of oil, take 1 ml of concentrated hydrochloric acid containing about 1% sucrose. If you get a pink color, that means it contains sesamol. This is what is called Baudouin's test. We also have the Villavecchia test. It is very similar, but instead of sucrose, we use furfural here.

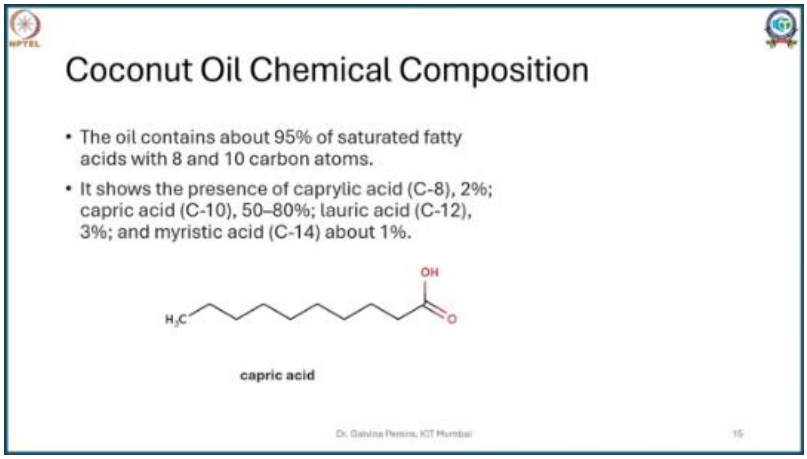
So, these tests are widely used. They check for the presence of sesamolin and free sesamol and can tell us whether your sample is genuine sesame oil or not. Applications, as I said, are traditionally used in Ayurveda because the oil is very inert; it's used as a demulcent, nutritive, and emollient. It's traditionally used for dysentery and urinary complications. Being an oil, it is used as a solvent for steroids, lipophilic antibiotics, lipophilic drugs, and certain steroidal hormones.

And it is also used in the manufacturing of margarine and some cosmetics, where it can form an oleaginous base. It is used as an emulsion for antacids and ointments. It is also, if you see the sesamolin component, that has insecticide properties and is often known to exhibit synergistic or what you call enhanced activity when given with pyrethrum. The last oil, or the last example we will go over, is from a very humble plant called coconut, and from that, you get what is called coconut oil. So, coconut oil—if you see a coconut, you see a whitish-colored inner endosperm layer.

We call it copra, and when you dry it, when it is sufficiently dehydrated, it's very rich in oil. Initially, it might just contain about 30% oil, but when you dehydrate it or when you get those dry copras, they contain almost as high as 70% oil. So, this coconut oil is the oil which is expressed from the endosperms of coconut, that is Cocos nucifera, which is a member of the Palmae family, and it grows on all tropical islands and tropical countries. You will find it cultivated chiefly in Asia and Africa for the same reason. The plant is very unique, so you can see the plant as a typical palm with a single trunk, appearing with very large leaves, as big as 10 to 20 feet, having numerous pinnately arranged or pinnately compound leaves—almost 200 of them sometimes—and they have a typical spiral

arrangement towards the apex of the trunk, where you find them mostly populated or crowded.

Now, what is done is the coconut is dried and expressed sometimes by heat, and then you allow it to settle. Once it is settled, you take the oil layer, and that is then treated, bleached if required, and used as coconut oil. The good part of coconut oil, why it is so important, is that it contains very small carbon-chain fatty acids. Like others we have seen so far—C16, C18, C24, and so on—when you see coconut, you can see here it is C8 caprylic acid, C10 capric acid, or C12 lauric acid. So, short-chain fatty acids—the advantage of short-chain fatty acids is they can easily be absorbed by us. And the next thing about this is they're all saturated fatty acids.



The reason your coconut oil solidifies in winter is that its short-chain fatty acids have a very ordered arrangement. As a result, they have a very nice, what is called, a melting point of 23 degrees Celsius for the whole oil put together. Now, coconut—if you see the oil or what you call it as butter—is nicely white or pearl white, unctuous, odorless, and it has a slight nutty or what you call it as coconut odor. Now, it is soluble in twice the volume of alcohol when heated. But in terms of its solubility, it is more soluble in organic solvents.

Now, this oil is unique because it has the highest saponification value. Saponification value is how much KOH is required for the fatty acids. So, because it has small fatty acids, it requires more KOH. Per gram, and that's why this is an oil which requires—or which has—a very high saponification number. And because it contains saturated fatty acids, it is one

of the oils with a very low iodine value, that is just 7 to 10. So, a unique oil with a very high saponification value and a very low iodine value.

Where do you apply it? Coconut oil is again used as a base in creams. It's an excellent hair oil. In India, we use it throughout as hair oil. We use it in cooking.

Now, if you see the pharmaceutical industry or the cosmetic industry, you have triglycerides prepared from caprylic and caproic acid. We call it caprylic capric triglyceride or CCTG, which is a clear, odorless liquid. It is synthetically prepared initially by purifying and then joining it to the glycerol molecule. But it has excellent emollient and conditioning properties, and it's abundantly used in the skincare industry. Now, another part is what is called fractionated coconut oil.

This is done by carefully melting, solidifying, melting, solidifying, and fractionating the coconut oil. Depending upon its boiling point or what is called its melting point or congealing point. And you get different fractions depending upon the solidification point. So, this fractionated coconut oil is also used as medium-chain triglycerides. And they also have good applications in the pharmaceutical industry.

Now, coconut oil, being something which is oleaginous and easily absorbable by the gut, is used in diseases associated with malabsorption of fat, such as cystic fibrosis, enteritis, or sometimes even steatorrhea, which is, you know, when fats are being excreted and not absorbed at all. In that case, you need to switch to a low molecular weight fatty acid substitute, and coconut oil is an excellent resource. So, for further reading, here are a few references, and thank you for your patient listening.